Eastern Journal of Medicine

ORIGINAL ARTICLE

East J Med 30(1): 127-132, 2025
DOI: 10.5505/ejm.2025.66592

Maternal Pre-Labor Hematocrit Level: Does It Affect Fetal Outcomes ?: A Case-Control Study

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ABSTRACT

Iron deficiency anaemia is a widespread nutritional anaemic diseases worldwide. Recent studies have shown that anemia during pregnancy can have a negative impact on perinatal and maternal outcomes, although the correlations vary depending on the severity of the anemia. Therefore, we will evaluate the fetal outcomes of the pregnant women, whom we divided into three groups according to the hematocrit (HTC) value based on fetal ultrasound findings, birthweight (BW) and Apgar scores.

The study included nulliparous women with singleton pregnancies whose entire follow-up and treatment were carried out in a tertiary referral hospital and whose pregnancy was completed in the same hospital. The study participants were assigned to one of three groups depending on their HTC value. The patients with an HTC value below 30% were in group I; the patients with an HTC value between 30% - 36% were in group II; the patients with an HTC value of more than 36% were in group III. We examined demographic parameters, Apgar scores, BW and admission to neonatal intensive care unit.

578 pregnant women were included in the study and all participants were nulliparous. There were no significant differences between the three groups in terms of demographic data. There were significant differences in biparietal diameter, abdominal circumference and BW.

Women have different nutritional needs throughout their lives - especially before and during pregnancy, when sensitivity to nutrients is at its highest -. Ensuring a nutritious diet and adequate care and education for women is crucial for the mothers and newborns.

Keywords: anemia; pregnancy; hematocrit; newborn

Introduction

Iron is a vital element that is needed throughout life. Its deficiency, which manifests as iron deficiency anemia, is a widespread nutritional anemia in the world, with the World Health Organization (WHO) concluding that nutritional deficiency anemia affects more than a half billion people, or about 29.9% of the women aged 15-49 (especially in adolescent pregnancies) years, and that at least 36.5% of pregnant women are anemic. (1-3) In addition, nutritional deficiency anemia may develop due to vitamin deficiencies such as vitamin B12 and folic acid deficiency. (2,4,5)

Initially, iron deficiency anemia may be so mild that no symptoms occur. However, as the iron deficiency in the body increases and the anemia worsens, serious signs and symptoms may occur (WHO). In anemia, the hemoglobin (HB) content in the blood is thought to be below normal, followed by a decrease in the ability of red blood cells to carry oxygen to the tissues. (5) As a result, anemia may cause symptoms such as tiredness, chest pain, or short of breath. (5) HB is usually determined with an automatic cell counter in an anticoagulated blood tube filled to a

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Received: 18.10.2024, **Accepted:** 07.12.2024

certain level with well-mixed EDTA. In the test, all forms of HB are converted into the colored protein cyanohemoglobin and then measured with a colorimeter. Inadequate anticoagulation or an incomplete sample may lead to inaccurate readings. (6) If the degree of anemia needs to be determined quickly, the hematocrit (HTC) is a simple and practical test. (6) So we decided to group the patients according to the HTC values.

Anemia can be graded into four categories basis on HTC: normal (HTC > 36%); mild (HTC 30% - 36%); moderate (HTC 30% - 24%) and severe (HTC < 24%). (5,7,8) Although recent studies have shown that anemia in pregnant women has negative effects on maternal and perinatal outcomes, these relationships vary depending on the severity of the anemia. (9) Therefore, we will evaluate the fetal outcomes of the pregnant women, whom we divided into three groups according to the HTC value - one of the diagnostic criteria for anemia - based on fetal ultrasound findings, birthweight (BW) and Apgar scores.

Material and Method

The retrospective case-control study was conducted in the Perinatology and Obstetrics Departments of Etlik Zübeyde Hanım Women's Health Training and Research Hospital between 01 January 2015 and 31 January 2020. The study was conducted in accordance with the principles of the Declaration of Helsinki and approval was obtained from the local ethics committee (May 14, 2020; No.: 2020/07).

Inclusion – Exclusion Criteria: Nulliparous women with term (37-40 gestational weeks) singleton pregnancies who were admitted to the maternity clinics at Etlik Zübeyde Hanım Women's Health Training and Research Hospital between 01 January 2015 and 31 January 2020 without risk factors for delivery were included.

Pregnant women with the following risk factors or conditions were excluded from the study: Hospitalization for preterm premature rupture of membranes (PPROM) or preterm labor; induction of labor due to fetal growth restriction, hypertensive gestational disorders, and gestational diabetes mellitus; multiparity; multiple pregnancies; chronic diseases (systemic lupus erythematosus, diabetes mellitus, thyroid dysfunction, etc.); age under 18 years and over 40 years; body mass index (BMI) under 25 kg/m2 and over 40 kg/m2; late and post-term pregnancies as well as fetal malformations or fetal anomalies.

Data: A total of 578 pregnant women were included in the study. Data, including demographic information (age, weight, height, BMI and delivery week), pre-labor complete blood count (CBC) tests, fetal ultrasound findings, Apgar scores, BW and admission to the neonatal intensive care unit (NICU) were obtained from participants' medical records or hospital records.

Study Design: The study included nulliparous women with singleton pregnancies whose entire follow-up and treatment were carried out in a tertiary referral hospital and whose pregnancy was completed in the same hospital. The study participants were assigned to one of three groups depending on their HTC value. The pregnant women with an HTC value below 30% were in group I; the patients with an HTC value between 30% - 36% were in group II; the patients with an HTC value of more than 36% were in group III.

We examined demographic parameters, Apgar scores, BW and NICU admission. We compared these parameters in all three groups.

Analysis of Biological Samples: All CBCs were performed using the species-specific software of the ADVIA 120 hematology analyzer (Siemens Healthcare Diagnostics, Deerfield, USA)

Statistical Analyses: The data of the study were analyzed using the SPSS program, version 28.0 (IBM Corp., Armonk, USA). (10) The variables were examined using visual (histogram, probability plots) and analytical methods (Kolmogrov-Simirnov or Shapiro-Wilk tests) to assess the normality of the distribution. For the non-normally distributed numerical data, descriptive analyses were performed using medians and interquartiles (Q1-Q3). The Kruskal-Wallis tests were used to compare these parameters. Descriptive analyzes were performed for categorical variables using frequency and percentage. Relationships between categorical variables were analyzed using the chi-square test or Fisher's exact test (when the assumptions of the chi-square test do not apply because of low expected cell counts) and significant data were compared in paired groups with pairwise comparisons. The significance values were adjusted by the Bonferroni correction for multiple testing. A statistically significant p-value is considered to be less than 0.05.

Results

A total of 756 pregnant women were considered for the implementation of the study. After applying the exclusion criteria described in the Material and method section, 178 pregnant women were excluded from the study. As shown in the flowchart, 578 participants were included in the study and all participants were nulliparous (Figure 1). The

Table 1: Comparison of Demographic Features and Clinical Characteristics Between The Groups

	Group I (n=87)	Group II (n=279)	Group III (n=212)	*P*
Maternal demographic and laboratory values				
Age (years)[a]	28 (19-36)	27 (21-39)	27 (19-39)	0,254
BMI (kg/m2)[a]	30 (25-40)	29 (25-40)	30 (25-40)	0,915
WGDP (kg)[a]	12 (5-25)	13 (5-26)	13 (5-26)	0,337
50 g OGCT (mg/dL)[a]	104 (69-136)	101 (53-139)	104 (50-149)	0,918
Delivery mode (CS)[b]	34 (38,1%)	108 (39,7%)	70 (33%)	0,380
Smoking status (yes)[b]	3 (3,4%)	6 (2,2%)	7 (3,3%)	0,677
High school/Uni (yes)[b]	45 (51,7%)	149 (53,4%)	100 (47,2%)	0,215
HB (g/dL)[a]	9,4 (8,6-13,4)	11,1 (9,2-13,7)	13,2 (9,2-14,4)	0,000
HTC (%)[a]	28 (26-29)	33 (30-36)	40 (37-43)	0,000
Fetal demographic values				
Delivery time (week)[a]	39 (37-40)	39 (37-40)	39 (37-40)	0,496
BPD (mm)[a]	92 (88-98)	93 (85-103)	93 (87-98)	0,028
AC (mm)[a]	327(290-365)	335 (303-365)	336 (297-375)	0,009
FL (mm)[a]	73 (68-81)	75 (66-81)	75 (68-81)	0,087
BW (g)[a]	3050 (2530-3770)	3250 (2590-4150)	3260 (2540-4320)	0,001
Apgar (5th min.)[a]	10 (6-10)	10 (7-10)	10 (4-10)	0,906
Female gender[b]	44 (50,6%)	147 (52,7%)	98 (46,2%)	0,363
NICU (yes)[b]	3 (3,4%)	8 (2,9%)	5 (2,4%)	0,864

Abbreviations: Apgar: Appearance, Pulse, Grimace, Activity, and Respiration; AC: abdominal circumference; BMI: body mass index; BPD: biparietal diameter; BW: birth weight; CS: caesarean section; FL: femur length; n: number; NICU: neonatal intensive care unit; OGCT: oral glucose challenge test; Uni: university; WGDP: weight gain during pregnancy.
[a] Non-parametric data was expressed with median and interquartiles (Q1 – Q3);
[b] Parametric data was expressed with numbers and percentage.

demographic data of the groups are shown in Table 1. There were 87 (15.1%) patients in group I, 279 (48.3%) in group II and 212 (36.6%) in group III. The mean age was 27.2±4.6 years and the mean BMI was 30.1±3.7 kg/m2. There were no significant differences between the groups in terms of demographic characteristics such as smoking and educational status.

Table 1 shows that the demographic data of the three groups showed no significant differences between them. In accordance with the study design, the median HB (9.4 g/dL [8.6-13.4]) and median HCT (28% [26-29]) were significantly lower in group I than in the other two groups (p=0.00 for both). When the obstetric characteristics of the groups were analyzed, there were no significant differences in the results of the oral 50-gram glucose challenge test at 24 to 28

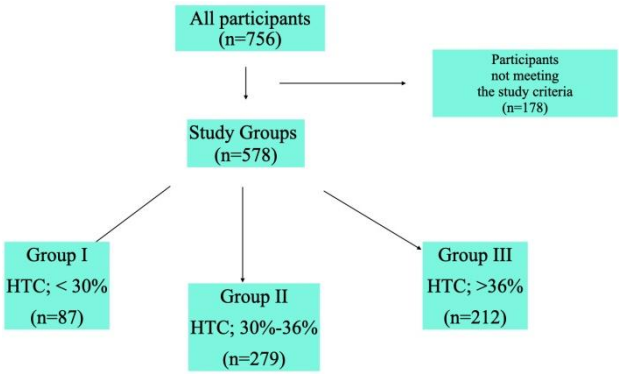

Fig. 1. The flowchart of the participants

weeks, time of delivery, mode of delivery, Apgar scores at 1 and 5 minutes, sex of the fetus, and admission to the NICU (Table 1).

Although there was no significant difference between the groups in terms of femur length (FL) (p=0.087), there were significant differences in biparietal diameter (BPD), abdominal circumference (AC) and BW (p=0.028, 0.009 and 0.001, respectively) (Table 1). The results of the pairwise comparisons of the groups for BPD, AC and BW are shown in Figure 2. BPD, AC and BW values were statistically significantly lower in Group I than in the other two groups. When the significant values were adjusted with the Bonferroni correction for more than one test, the adjusted p-value for BPD between Group I with Group II and Group II was 0.022 and 0.058, respectively, while the adjusted p-value between Group II and Group III was 1.0. For AC, the adjusted p-value between Group I with Group II and Group III was 0.020 and 0.007, respectively, while the adjusted p-value between Group II and Group III was 1.0. For BW, the adjusted p-value between Group I with Group II and Group III was 0.020 and 0.007, respectively, while the adjusted p-value between Group II and Group III was 1.0.

Discussion

Maternal nutritional anemia, the most widespread health problem, affects mainly low-income countries despite the high priority given to preventive maternal and child health care programs. According to the WHO in 2019, anemia affects approximately over a half billion reproductive aged women worldwide. Conversely, it affects 36.5% of pregnant women. (2) While the global prevalence of anemia in women of reproductive age has stagnated, the prevalence of maternal anemia has decreased slightly since 2000. (2) In addition, maternal anemia in developing countries varies between 53 and 90%, while in developed countries it is estimated at 8.3%. (11)

Maternal anemia not only affects the mother's health, but also has negative consequences for her well-being. (4,11,12) It also increases the risk of postpartum hemorrhage, puerperal infections and heart failure and can lead to increased maternal mortality. In addition, maternal anemia is associated with lower BW, premature birth and increased fetal mortality. (4,12,13)

The English-language research literature shows that preoperative anemia is widespread. (14,15) It is usually a consequence of the patient's operated disease. However, anemia detected preoperatively can lead to unfavorable postoperative outcomes, which are often independently associated with an increased risk of prolonged intensive care, prolonged hospital stay, postoperative complications, and poorer overall outcome. (14,15) As with preoperative patients, anemia often occurs in pregnant women at labor. (16) Kant et al. (16) investigated the prevalence of maternal anemia at the time of delivery. Approximately 78% of pregnant women are anemic at the time of delivery and the preterm birth rate is significantly high in these pregnant women. (16) In another study by Soumyashree et al, (17) maternal anemia prevalence at the time of delivery was 88.4% of pregnant women. In our study, anemia prevalence at the time of delivery was 63.3% of pregnant women. In a study conducted in Taiwan, the mean HB level of pregnant women admitted during labor was 12.2 g/dL, with the 10th and 5th percentiles of total HB levels being 10.8 g/dL and 9.9 g/dL, respectively. (18) In addition, they found that pregnant women with HB levels below 10.8 g/dL (10th percentile) had a 1.5- to 2-fold increased risk of unfavorable perinatal outcomes, including primary cesarean section, polyhydramnios, PPROM, preterm delivery, very low BW, and admission to the NICU, than pregnant women with HB levels ≥10.8 g/dL. (18) When we looked at our results, there was no statistical difference between the groups in terms of mode of delivery, delivery timing, sex of the fetus, Apgar scores at the first and fifth minute, and admission to the NICU. However, there was a statistically significant difference between BPD / AC measurements and BW. In contrast to the study by Chu et al. (18), the anemic mothers in our study had a lower BW than non-anemic mothers. We think that the smaller body size could be due to restricted oxygen circulation in the fetus' body and placenta. Ganju (19) and Thompson et al. (20) suggested that maternal anemia exposes the fetal placenta to an environment of oxidative stress. As a result, intrauterine fetal hypoxia due to anemia also leads to low BW due to placental angiogenesis caused by impaired oxygen and nutrient transfer.

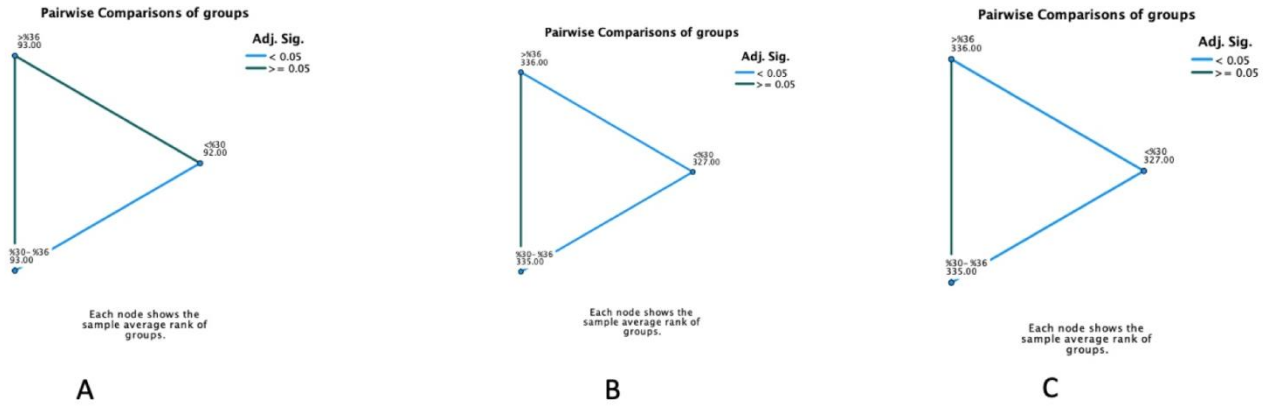

Fig. 2. The pairwise comparisons of the groups (A: pairwise comparison for BPD; B: pairwise comparison for AC; C: pairwise comparison for BW)

In present study, the educational status of mothers was not a significant difference between the groups (p=0.215). Our results are consistent with two studies conducted in Ethiopia. (21,22) However, Kassaw et al. (23) found a significant difference between the groups of anemic and non-anemic mothers. Mothers who were unable to attend school had low BW compared to mothers who attended high school. (23)

In conclusion, we also think that irregular intake of iron supplements and inadequate and unbalanced diet are independent risk factors for pre-labor anemia. Although no statistical significance was found in our study, we think that inadequate intake of iron supplements and an unbalanced diet may be related to an inadequate educational status of pregnant women. The prevalence of pre-labor anemia in women is a moderate public health problem. The extent of low BW was relatively high. In pregnancy, maternal anemia is the most important predictor of low BW. Women have different nutritional needs throughout their lives - especially before and during pregnancy, when sensitivity to nutrients is at its highest. Ensuring a nutritious diet and adequate care and education for women is crucial for the mothers and newborns.

Recommendations For Health Policies: Family physicians should advise families and individuals on iron levels and nutrition before, during and after pregnancy. They should help eliminate iron deficiency by monitoring and treating individuals with iron deficiency. In addition, one of the best ways to identify existing or potential problems due to iron deficiency during pregnancy is through pre-pregnancy counseling. (23) Public service announcements should be made to follow these recommendations and increase public awareness of this issue to improve maternal and fetal outcomes and public health.

The Strengths and Limitations: The limitations of the study, as it was designed as a retrospective study. Therefore, the data and information of some pregnant women could not be accessed. In addition, the lack of a power analysis is an inherent limitation of the study. Additional limitation of the study is the lack of data from studies on other types of anemia, iron levels, and descriptive analyzes of anemia (e.g., HB electrophoresis). These factors should be investigated in the investigation and treatment of anemia. The strength of the study is that it was conducted in a tertiary referral center where the same protocols are routinely used for patient follow-up and we empirically administer 30 mg of iron supplements to all pregnant women from 16th week of gestation.

Disclosure Statement

Ethics: The study was designed in accordance with the principles of the Declaration of Helsinki and ethical approval was obtained from the local ethics committee (May 14, 2020; No.: 2020/07). All pregnant women gave written informed consent.

Competing interests: None.

Funding Statement: None.

Authors' Contributions: The authors have confirmed that they contributed to the study as follows: study conception and design: FBF and SO; data collection: MK, YAR and AA; analysis and interpretation of results: AA, and EGD; drafting of the manuscript: FBF; supervision of the study: MLD and YU. All the authors have read the full manuscript and approved the results and final version.

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