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The effects of first-trimester hemoglobin on adverse pregnancy outcomes

İlk trimester hemoglobin değerinin olumsuz gebelik sonuçları üzerine etkileri

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Abstract

Aim: Previous studies have demonstrated that variable hemoglobin levels are associated with adverse pregnancy outcomes such as postpartum hemorrhage, pregnancy-induced hypertension, intrauterine growth restriction, gestational diabetes mellitus and perinatal mortality. Here, we aimed to investigate the effects of hemoglobin (Hb) levels measured in the first trimester of pregnancy on pregnancy outcomes and identify the predictive value of Hb on adverse pregnancy outcomes.

Methods: This single-center, retrospective study included a total of 8,916 pregnant women who were diagnosed, followed, and delivered their babies in our Obstetrics and Gynecology clinic. The patients were divided into three groups according to their Hb levels as anemic (Hb <11 g/dL, n=1,846), normal (Hb <12.5 g/dL, n=4,898), and elevated (Hb ≥12.5 g/dL, n=2,172). Demographic and clinical features of the patients were obtained from hospital records. Adverse pregnancy outcomes were also noted.

Results: The mean age of the patients was 27.50 (4.45) years and BMI value was 25.03 (3.39) kg/m^2. The mean Hb level was 11.83 (0.88) g/dL and the mean hematocrit value was 36.004 (2.75%). Irrespective of Hb levels, among all patients, rate of pregnancy loss was 6.5%, rate of impaired glucose tolerance, 4.9%, gestational diabetes mellitus, 5.1%, pregnancy-induced hypertension, 7.4%, preterm birth 3.8%. The rate of newborns in need of neonatal intensive care unit was 3.5%, while 3.8% were born with low APGAR scores. Placenta previa was observed in 2.4% of patients, and placental abruption was seen in 1.3%. About 39.3% had a cesarean-section (C/S) delivery, 5.9% gave birth to low birth-weight neonates, and premature rupture of membranes was observed in 9.7% patients. There were no significant differences with respect to adverse pregnancy outcomes between the three groups (P>0.05 for all).

Conclusion: Our study results showed no significant differences between the three groups categorized by Hb concentrations measured in the first trimester in terms of adverse pregnancy outcomes.

Keywords: Anemia, First trimester, Hemoglobin, Pregnancy outcomes

Öz

Amaç: Literatürde yapılan çalışmalarda farklı hemoglobin (Hb) düzeylerinin postpartum hemoraji, gebelik ile indüklenen hipertansiyon, intrauterin gelişme geriliği, gestasyonel diabetes mellitus ve perinatal mortalite gibi olumsuz gebelik sonuçları ile ilişkisi gösterilmiştir. Bu çalışmanın amacı gebeliğin ilk üç ayında ölçülen hemoglobin (Hb) düzeylerinin gebelik sonuçları üzerindeki etkilerini araştırmak ve Hb'nin olumsuz gebelik sonuçları üzerindeki prediktif değerini belirlemektir.

Yöntemler: Bu tek merkezli, retrospektif çalışma, kadın hastalıkları ve jinekoloji kliniğimizde teşhis, takip ve doğumları yapılan toplam 8.916 gebeyi kapsamaktadır. Hastalar Hb düzeylerine göre anemik (Hb<11 g/dL, n=1.846), normal (Hb 11-12,5 g/dL, n=4.898) ve yüksek (Hb ≥12,5 g/dL, n=2.172) olmak üzere üç gruba ayrıldı. Hastaların demografik ve klinik özellikleri hastane kayıtlarından elde edilerek olumsuz gebelik sonuçları kaydedildi.

Bulgular: Hastaların ortalama yaşı 27,50 (4,45) yıl ve vücut kitle indeksi değeri (VKİ) değeri 25,03 (3,39) kg/m^2 idi. Ortalama Hb düzeyi 11,83 (0,88) g/dL ve ortalama hematokrit değeri %36 (%2,75)'ti. Hemoglobin seviyelerinden bağımsız olarak tüm çalışma grubunda gebelik kaybı %6,5, bozulmuş glukoz toleransı %4,9, gestasyonel diabetes mellitus %5,1, gebelik ile indüklenen hipertansiyon %7,4, erken doğum %3,8, yenidoğan yoğun bakım ünitesine duyulan ihtiyaç %3,5, düşük APGAR skorları %3,8, plasenta previa %2,4, plasental ablasyon %1,3, sezaryen (C/S) doğum %39,3, düşük doğum ağırlığı %5,9 ve erken membran rüptürü %9,7 oranında saptandı. Hemoglobin seviyeleri ve olumsuz gebelik sonuçlarını oluşturan değişkenler açısından anlamlı bir fark yoktu (Tümü için P>0,05).

Sonuç: Çalışmamızda ilk trimesterde ölçülen Hb konsantrasyonlarına göre ayrılan gruplar arasında olumsuz gebelik sonuçları açısından anlamlı bir farklılık saptanmadı.

Anahtar kelimeler: Anemi, İlk trimester, Hemoglobin, Gebelik sonuçları

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Introduction

Alterations in the hematological parameters occur depending on the trimester of pregnancy. In healthy pregnancies, major hematological changes which activate adaptation mechanisms of the human body include expanded plasma volume and red blood cell count, physiological anemia, mild neutrophilia, and mildly prothrombotic state to accommodate the growing and developing fetoplacental unit [1].

Hemoglobin (Hb) is the standard measure to assess physical capacity and anemia of pregnant women in the first perinatal visit. Physiological anemia is characterized by reduced Hb levels with a peak at late second trimester, followed by an increase during the third trimester [2].

Anemia is typically caused by decreased oxygen-carrying capacity of the blood or red blood cells depending on the age, gender, and pregnancy [3]. Due to physiological alterations in pregnant women, the diagnosis of anemia differs among pregnant women and non-pregnant women of reproductive age [3]. According to the World Health Organization (WHO), anemia is defined as Hb levels of <11 g/dL (hematocrit <33%) in the first and third trimesters and as <10.5 g/dL (hematocrit <32%) in the second trimester [4]. Accordingly, the prevalence of anemia is about 24.8% among pregnant women worldwide, leading to a major maternal and fetal health concern [5].

Previous studies have demonstrated controversial findings regarding the effects of Hb on pregnancy outcomes. The discrepancy between the findings can be attributed to the use of different study designs and sample sizes and the measurement of Hb at different time points. Nonetheless, it has been well-established that maternal anemia dramatically affects the fetal health [6].

Anemic hypoxia plays a key role in the dilation of the placental blood vessels. Although iron deficiency is the leading cause of anemia, compromised immune system, malnutrition with vitamin B12 and folic acid deficiency, decreased physical and mental capacity, sedentary lifestyle, low socioeconomic status, hemoglobinopathies, age (<20 years or >35 years), adolescent pregnancy, alcohol and tobacco use, short intervals between pregnancies, and infections can also pose an increased risk for anemia [7]. In a recent systematic review, an increased incidence of low-birthweight (LBW) and preterm birth was reported among anemic patients with low Hb levels related to maternal iron deficiency [8]. In addition, maternal anemia was shown to increase perinatal morbidity and mortality due to preterm birth and intrauterine growth restriction (IUGR) [9].

Although previous studies have demonstrated that maternal anemia is associated with adverse pregnancy outcomes with an increased rate of postpartum hemorrhage (PPH) and cesarean-section (C/S) delivery, the effects of maternal anemia on pregnancy outcomes are still unclear. Recent studies have, however, shown elevated red blood cell counts and hypercoagulability due to increased plasma volume during pregnancy, leading to pregnancy-induced hypertension (PIH), IUGR, gestational diabetes mellitus (GDM), and perinatal mortality [5,10].

In the present study, we aimed to investigate the effects of Hb levels measured in the first trimester of pregnancy on pregnancy outcomes and to identify the predictive value of Hb on adverse pregnancy outcomes.

Materials and methods

Study population and study design

This single-center, cross-sectional, retrospective study was conducted at a tertiary hospital between January 2018 and June 2019. A total of 8,916 pregnant women who were diagnosed, followed, and delivered their babies in our Obstetrics and Gynecology clinic were retrospectively reviewed. According to the WHO criteria, the patients were divided into three groups based on their Hb levels as anemic (Hb <11 g/dL, n=1,846), normal (Hb 11-12.5 g/dL, n=4,898), and elevated (Hb ≥12.5 g/dL, n=2,172). The anemic patients were considered to have mild anemia (10 to 10.9 g/dL) according to the WHO criteria, as the lowest Hb level was 10 g/dL in our study. None of the patients had moderate (7 to 9.9 g/dL) or severe (<7 g/dL) anemia. Exclusion criteria were as follows: Having irregular screening visits during pregnancy, missing birth data, missing Hb levels in the first trimester, age <16 years or >35 years, multiple pregnancies, congenital abnormalities, hepatic and renal impairment, diabetes mellitus, PPH, a history of preterm birth, recurrent pregnancy loss, previous placental abnormalities, complicated pregnancy, a body mass index (BMI) of ≥30 kg/m^2, hypothyroidism or hyperthyroidism, and alcohol or tobacco use. A written informed consent was obtained from each participant. The study protocol was approved by the University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Ethics Committee (2011-KAEK -25-2020/06-07). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Data collection

Demographic and clinical characteristics of the patients were obtained from hospital records. In addition, pregnancy complications, type of delivery, birth weight, Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) scores, the need for neonatal intensive care unit (NICU) were noted. Complete blood count analysis was performed using the Coulter LH780 analyzer (Beckman Coulter Inc., CA, USA). Adverse pregnancy outcomes included pregnancy loss, GDM, PIH, preterm birth, need for NICU, placenta previa or placental abruption, C/S delivery, premature rupture of membranes (PROM), and low APGAR scores (<7). Pregnancy loss was defined as any natural miscarriage occurring before 20 weeks of gestation. LBW was defined as a birth weight of less than 2,500 g, while preterm birth was defined as a live birth occurring at <37 completed weeks of gestation. PROM was defined as spontaneous rupture of fetal membranes prior to the onset of labor. The NICU stay was needed in case of jaundice, respiratory distress, preterm birth, neonatal sepsis requiring cardiorespiratory support [11].

Impaired glucose tolerance (IGT) was defined as an elevated fasting plasma glucose concentration (100 to 126 mg/dL). The diagnosis of GDM was made based on a 75-g oral glucose tolerance test (OGTT) results (a fasting blood glucose of >92 mg/dL, ≥180 mg/dL at one hour, and ≥153 mg/dL at two hours). The patients with elevated glucose levels (≥140 mg/dL)

in 50-g OGTT underwent 100-g OGTT and those with two or more elevated glucose results were diagnosed as having GDM (a fasting blood glucose level of ≥95 mg/dL, ≥180 mg/dL at one hour, ≥155 mg/dL at two hours, and ≥140 mg/dL at three hours). The patients with a fasting blood glucose level of ≥200 mg/dL at two hours were also diagnosed with GDM [12]. The diagnosis of PIH was made based on a systolic blood pressure of ≥140 mmHg and/or a diastolic blood pressure of ≥90 mmHg after 20 weeks of gestation [13]. Placenta previa was defined as the abnormal implantation of the placenta into the lower uterine segment, covering the cervical opening partially or completely [14]. Placental abruption was defined as the separation of a normally implanted placenta before delivery of the fetus [14].

Statistical analysis

Statistical analysis was performed using the SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean (standard deviation (SD)), median (min-max), or number and frequency. The Kolmogorov-Smirnov test was used to assess the normality of data. One-way analysis of variance (ANOVA) was performed to analyze significant differences between the groups and the Bonferroni test was used to test significance. The Pearson chi-square test was applied to evaluate the relationship between categorical variables. Binary multiple logistic regression analysis was carried out to identify the effects of age, BMI, and Hb and hematocrit levels on adverse pregnancy outcomes. A *p* value of <0.05 was considered statistically significant.

Results

Of a total of 8,916 pregnant women included in the study, 20.7% (n=1,846) were anemic, 54.9% (n=4,898) had normal Hb levels, and 24.4% (n=2,172) had elevated Hb levels. Irrespective of Hb levels, pregnancy loss was observed in 6.5%, IGT in 4.9%, GDM in 5.1%, PIH in 7.4%, preterm birth in 3.8%, need for NICU in 3.5%, low APGAR scores in 3.8%, placenta previa in 2.4%, placental abruption in 1.3%, C/S delivery in 39.3%, delivery with LBW in 5.9%, and PROM in 9.7% patients. The patient groups according to the Hb levels and adverse pregnancy outcomes are shown in Table 1.

The mean age of the patients was 27.50 (4.45) years. The mean BMI value was 25.032 (3.39) kg/m^2. The mean Hb level was 11.827 (0.882) g/dL and the mean hematocrit value was 36.004 (2.75%) Descriptive data of the patients are summarized in Table 2.

Age and BMI values were evaluated among the three groups according to the Hb levels (Table 3). There was a significant difference only in the mean BMI value among the groups (*P*=0.001). Multivariate analysis was performed to examine the reason for significance. Accordingly, the mean BMI value was significantly lower in the anemic group than those with normal and elevated Hb levels (*P*=0.001 and *P*=0.001, respectively).

Categorical variables were compared between three groups. There was no statistically significant difference between three Hb groups in terms of pregnancy loss (*P*=0.165), impaired glucose tolerance (*P*=0.769), gestational diabetes mellitus (*P*=0.916), pregnancy induced hypertension (*P*=0.841), preterm delivery (*P*=0.257), NICU admission (*P*=0.482), low APGAR scores (*P*=0.118), placenta previa (*P*=0.708), placental abruption (*P*=0.311), cesarean-section (C/S) delivery (*P*=0.474), low birth weight (*P*=0.588) and PROM (*P*=0.956) (Table 4).

Table 1: Patient groups according to hemoglobin levels and adverse pregnancy outcomes

Variable		n	%
Hb (g/dL)	Mild anemic	1,846	20.7
	Normal	4,898	54.9
	Elevated	2,172	24.4
Pregnancy loss	No	8,334	93.5
	Yes	582	6.5
IGT	No	7,924	95.1
	Yes	411	4.9
GDM	No	7,910	94.9
	Yes	425	5.1
PIH	No	7,722	92.6
	Yes	613	7.4
Preterm birth	No	8,021	96.2
	Yes	314	3.8
NICU	No	8,040	96.5
	Yes	295	3.5
APGAR <7	No	8,012	96.2
	Yes	315	3.8
Placenta previa	No	6,093	97.6
	Yes	150	2.4
Placental abruption	No	6,159	98.7
	Yes	84	1.3
C/S delivery	No	3,787	60.7
	Yes	2,456	39.3
LBW	No	5,875	94.1
	Yes	368	5.9
PROM	No	5,637	90.3
	Yes	606	9.7

Data are given in number and percentage, unless otherwise stated. Hb: hemoglobin, IGT: impaired glucose tolerance, GMD: gestational diabetes mellitus, PIH: pregnancy-induced hypertension, NICU: neonatal intensive care unit, APGAR: Appearance, Pulse, Grimace, Activity, and Respiration; C/S: cesarean-section, LBW: low birth weight, PROM: premature rupture of membranes.

Table 2: Descriptive characteristics of patients

	Mean	Median	SD	Min	Max	IQR
Age, year	27.50	28.00	4.458	18	35	7
BMI, kg/m^2	25.032	25.100	3.394	18.5	34.7	5.3
Hb (g/dL)	11.827	11.800	0.882	10.0	13.8	1.3

SD: standard deviation, min: minimum, max: maximum, IQR: interquartile range, BMI: body mass index, Hb: hemoglobin

Table 3: Quantitative measurements according to hemoglobin concentrations

	Mild decrease (Hb <11 g/dL)		Normal (Hb 11-12.5 g/dL)		Elevated Hb (Hb ≥12.5 g/dL)		*P*-value [a]
	Mean	SD	Mean	SD	Mean	SD	
Age, year	27.49	4.480	27.50	4.466	27.50	4.424	0.997
BMI, kg/m^2	24.606	3.529	25.106	3.310	25.225	3.434	0.001

[a] One-way analysis of variance (ANOVA), SD: standard deviation, BMI: body mass index

Table 4: Categorical variables according to hemoglobin concentrations

		Mild decrease (Hb <11 g/dL)		Normal (Hb 11-12.5 g/dL)		Elevated Hb (Hb ≥12.5 g/dL)		*P*-value[a]
		n	%	n	%	n	%	
Pregnancy loss	No	1,729	93.7	4,558	93.1	2,047	94.2	0.165
	Yes	117	6.3	340	6.9	125	5.8	
IGT	No	1,638	94.7	4,339	95.2	1,947	95.1	0.769
	Yes	91	5.3	220	4.8	100	4.9	
GDM	No	1,642	95.0	4,329	95.0	1,939	94.7	0.916
	Yes	87	5.0	230	5.0	108	5.3	
PIH	No	1,597	92.4	4,224	92.7	1,901	92.9	0.841
	Yes	132	7.6	335	7.3	146	7.1	
Preterm birth	No	1,656	95.8	4,384	96.2	1,981	96.8	0.257
	Yes	73	4.2	175	3.8	66	3.2	
NICU	No	1,663	96.2	4,391	96.3	1,986	97.0	0.482
	Yes	66	3.8	168	3.7	61	3.0	
APGAR <7	No	1,651	95.6	4,379	96.2	1,982	96.9	0.118
	Yes	76	4.4	175	3.8	64	3.1	
Placenta previa	No	1,254	97.9	3,322	97.5	1,517	97.6	0.708
	Yes	27	2.1	86	2.5	37	2.4	
Placental abruption	No	1,260	98.4	3,369	98.9	1,530	98.5	0.311
	Yes	21	1.6	39	1.1	24	1.5	
C/S delivery	No	791	61.7	2,071	60.8	925	59.5	0.474
	Yes	490	38.3	1,337	39.2	629	40.5	
LBW	No	1,200	93.7	3,217	94.4	1,458	93.8	0.558
	Yes	81	6.3	191	5.6	96	6.2	
PROM	No	1,154	90.1	3,080	90.4	1,403	90.3	0.956
	Yes	127	9.9	328	9.6	151	9.7	

[a] Pearson chi-square test. Data are given in number and percentage, unless otherwise stated. Hb, hemoglobin; IGT, impaired glucose tolerance; GMD, gestational diabetes mellitus; PIH, pregnancy-induced hypertension; NICU, neonatal intensive care unit; APGAR, Appearance, Pulse, Grimace, Activity, and Respiration; C/S, cesarean-section; LBW, low birth weight; PROM: premature rupture of membranes.

Discussion

Anemia is one of the most common medical disorders during pregnancy and its prevalence and severity vary depending on the populations studied. Although there are many studies investigating the relationship between anemia and maternal morbidity, mortality, and adverse pregnancy outcomes in the literature, controversial results have been reported [15-17]. The discrepancies among the studies primarily result from the gestational week in which Hb levels are measured and the severity of anemia. Due to increased plasma volume, Hb and hematocrit levels tend to decrease with increasing gestational week. Screening for anemia is recommended before 20 weeks of gestation due to the occurrence of physiological anemia in later weeks [15]. In the light of these data, we, therefore, investigated the effects of Hb levels measured in the first trimester of pregnancy on pregnancy outcomes and identified the predictive value of Hb on adverse pregnancy outcomes. According to the WHO criteria, we divided the patients into three groups according to their Hb levels as anemic (Hb <11 g/dL), normal (Hb <12.5 g/dL), and elevated (Hb ≥12.5 g/dL). Our study results showed that 20.7% of the patients had mild anemia, which is consistent with a previous study conducted in Europe [15,18]. However, we were unable to find a significant difference in the incidence of PIH, GDM, preterm birth, LBW, C/S delivery, PROM, and placental abruption among the three groups.

In a study conducted in Turkey, Vural et al. [10] examined the effect of anemia on preterm birth (<37 weeks), LBW (<2,500 g), and anemia (Hb <11 g/dL) in different stages of pregnancy and reviewed medical records of 39,587 Turkish pregnant women. They divided the participants into three groups as Hb <10 g/dL, Hb 10-11 g/dL, and Hb >11 g/dL. They found a significant increase in LBW and preterm birth rates in the Hb <10 g/dL group compared to the non-anemic group. In addition, C/S rates were significantly higher in the anemic group. In another study, Hamalainen et al. [19] evaluated adverse pregnancy outcomes in pregnant women with anemia during three trimesters and found that maternal anemia detected only in the first trimester was associated with LBW, using a cut-off value of 100 g/L for anemia. However, they were unable to find a significant correlation between anemia in the first trimester and small for gestational age and preterm birth. In their population-based study, Levy et al. [20] showed that maternal anemia (Hb <10 g/dL) measured in the first trimester was an independent risk factor for both preterm birth and LBW. However, they were unable to identify a significant correlation between maternal anemia and adverse perinatal outcomes. Similarly, Sehgal et al. [21] examined the effect of anemia on course and pregnancy outcomes in anemic (8-10.9 g/dL) and non-anemic (≥11 g/dL) primigravidas aged 20 to 30 years with a gestational age of 16 to 18 weeks and found no significant difference in the IUGR and LBW rates between the study groups. In addition, there was no increase in the LBW and preterm birth in the anemic group. No significant correlation between anemia and week and type of delivery was observed. Based on these findings, the authors concluded that mild to moderately anemic pregnant women had similar outcomes as a normal pregnancy, if anemia could be detected early in pregnancy and treated appropriately. Unlike the aforementioned studies, patients with moderate (7 to 9.9 g/dL) or severe (<7 g/dL) anemia were excluded from our study. The inclusion of only mild anemic women in the study yielded no significant correlation between mild anemia and preterm birth, PROM, LBW, and C/S rates.

Preeclampsia (PE) is another pregnancy complication which has been extensively studied for its possible association with Hb levels in the first trimester. Some authors have proposed that the link between PE and Hb concentrations lies beneath increased blood viscosity: Hyperviscosity decreases blood flow in the placental tissue, leading to impaired perfusion and reduced oxygenation. In addition, Hb has been thought to have a direct effect on nitric oxide (NO) regulation and endothelial functions. Free Hb binds to NO and depletes it, resulting in vasoconstriction [22]. In patients with PE, the increase in blood volume is not likely to be adequate compared to those with normal Hb levels and, thus, Hb concentrations tend to increase [23]. In the light of these data, several studies have been conducted considering that these alterations may occur even in early stage of pregnancy, i.e., the first trimester [16,22,23]. In a study, Wang et al. [22] reported that the risk for PE increased, when Hb levels exceeded ≥150 g/L. However, there was a significant correlation between elevated Hb levels and an increased risk for PE in women with a pre-pregnancy BMI of ≥24 kg/m^2, although it became non-significant after adjusting for confounders. Cakmak et al. [16] evaluated the relationship between Hb levels in the first trimester and adverse pregnancy outcomes in a Turkish population and found PIH to be more common in the women with a Hb level of ≥13 g/dL compared to the others. However, in this study, the effect of BMI on PE development could not be assessed due to missing BMI data of the participants. In another study, Aghamohammadi et al. [23] examined whether high maternal Hb levels in the first trimester was associated with PIH in Iranian nulliparous women aged 20 to 34 years with a BMI value of <26 kg/m^2 and found that high maternal Hb levels (≥13.2 g/dL) in the first trimester was a risk factor for PE. Consistent with this study, we included a similar study population and found no significant increase in the PE risk in the patients with elevated Hb levels, although the sample size was relatively high in our study.

Iron is an essential micronutrient which plays a role in several physiological processes. Previous studies have shown that excess iron increases oxidative stress and insulin resistance, resulting in GDM by exerting toxic effects to the β-cells [24-26]. Gao et al. [27] examined the relation of Hb concentrations in the first trimester and GDM and found significantly higher Hb levels in GDM patients compared to the control group. In addition, the number of patients who were overweight or obese according to the pre-pregnancy BMI values was significantly higher among those with elevated Hb levels, yielding a higher number of GDM patients. Logistic regression analysis also revealed that a Hb level of ≥13 g/dL was an independent risk factor for GDM. In another study including 21,577 singleton pregnancies, Wang et al. [22] investigated whether Hb levels in early pregnancy were associated with the risk of GDM, PE, and preterm birth. The women with GDM and PE had significantly elevated Hb levels in the first trimester of pregnancy compared to the control group. In addition, the Hb levels were significantly higher in the women

with a pre-pregnancy BMI of ≥24 kg/m^2; however, the correlation between GDM and pre-pregnancy BMI values among the women with a BMI of ≥24 kg/m^2 and <24 kg/m^2 became non-significant, after adjusting for confounders. Beibei et al. [24] assessed the relation of serum iron concentration, Hb level, and iron supplements before and during pregnancy with GDM risk and observed a U-shaped correlation between serum iron concentration and GDM risk, indicating that iron supplements before pregnancy increased the risk of GDM. However, although elevated Hb levels were associated with an increased GDM risk in the early pregnancy, this association became non-significant after pre-pregnancy BMI values and systolic and diastolic blood pressures were included in the analysis as adjustments. In addition, the authors found no significant correlation between iron supplementation in the first and second trimester and GDM risk. Consistent with these findings, we observed no significant difference in GDM risk among the women with mild anemia and normal and elevated Hb levels. Similarly, the women with mild anemia in the first trimester had lower BMI values, consistent with previous studies. Also, although the women with normal and elevated Hb levels had similar BMI values in our study, we found no significant increase in the GDM risk in the women with elevated Hb concentrations.

Strength and limitations

There are some limitations to this study. Due to the retrospective nature of the study, the data regarding iron supplementation are missing in the women with mild anemia detected in the first trimester. Although iron supplementation is recommended in our routine clinical practice for all pregnant women, the number of women receiving iron supplements is unclear. However, some of the previous studies demonstrated that anemia treatment in early pregnancy did not significantly affect the incidence of PPH, preterm birth, small for gestational age, LBW, and stillbirth [17,28]. In a study, treatment of mild anemia in early pregnancy reduced adverse maternal and perinatal outcomes [15]. Another limitation of the current study is that it included Hb levels measured only in the early trimester. However, several studies reported that the first-trimester Hb measurement was more valuable and clinically relevant than the second- and third-trimester measurements [29]. The main strength of the present study is the large sample size, which can theoretically detect statistically significant effects. Also, it is optimally representative of the Turkish young healthy pregnant women.

Conclusions

In conclusion, our study results showed no significant difference between the Hb concentrations in the first trimester and adverse pregnancy outcomes. However, the present study included low-risk women with mild anemia rather than women with complicated pregnancies and, therefore, further large-scale, prospective studies including different severities of anemia and data regarding iron supplementation are needed to draw a definite conclusion.

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