

# Gestational Diabetes Mellitus and Iron Deficiency Anemia

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## ABSTRACT

**OBJECTIVE:** To determine whether gestational diabetes mellitus is influenced by the presence of iron deficiency anemia in early pregnancy.

**STUDY DESIGN:** This retrospective cohort study included 131 gestational diabetes mellitus and 300 non-gestational diabetes mellitus pregnant women that were screened and diagnosed between the 24-28 week of gestation. Gestational diabetes mellitus was diagnosed by two-step testing regimen. Anemia in pregnancy was defined as hemoglobin below 11 g/dL in the first trimester.

**RESULTS:** We found out that the mean hemoglobin value and mean corpuscular volume were significantly higher in the gestational diabetes mellitus group ( $12.2 \pm 1.26$  vs.  $11.72 \pm 1.17$ ;  $p < 0.001$  and  $89.29 \pm 7.55$  vs.  $84.64 \pm 6.93$ ;  $p < 0.001$ ). After the analysis of covariance for maternal age, body mass index, parity, birth weight there were significant differences in hemoglobin values and mean corpuscular volume values between two groups (respectively  $p = 0.002$ ,  $p < 0.001$ ). In the gestational diabetes mellitus group  $> 4000$  g newborns were significantly higher (19.8% vs. 6.7%) ( $p < 0.001$ ).

**CONCLUSION:** We demonstrated that gestational diabetes mellitus was associated with high levels of hemoglobin that was measured in first trimester.

**Keywords:** Gestational diabetes mellitus, Iron deficiency anemia, Mean corpuscular volume  
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## Introduction

Anemia, as determined by low hemoglobin (Hb) level, is common among women in reproductive years. It is quite common in pregnancies and affects approximately half of all pregnancies worldwide especially in underdeveloped countries. The World Health Organization (WHO) classifies anemia in pregnancy as hemoglobin below 11 g/dL.<sup>1</sup> Approximately 75% of anemias that occur during pregnancy are secondary to iron deficiency<sup>2,3</sup> which usually arises from increased requirements and inadequate intake. Early in pregnancy there are clear differences in mean corpuscular volume (MCV) in women with and without iron deficiency anemia (IDA). The women with IDA has an MCV value that is significantly lower (6.5 femtoliters-fl) than other women.

From the data of WHO, the incidence of IDA is 8% in developed countries, whereas 36% in developing countries.<sup>4,5</sup> In Turkey, according to the gestational period, prevalence of anemia is 22% in the first trimester, 27.5% in the second trimester and 22.4% in the third trimester.<sup>6</sup>

It is still not certain whether anemia results in an increased risk for poor pregnancy outcome. During the past few years, the relation between anemia early in pregnancy and an increased risk of preterm delivery have been suggested. Yip found that there is an association between moderate anemia and poor perinatal outcome.<sup>7</sup> Likewise, the relation of adverse pregnancy outcomes with high hemoglobin and increased iron stores have been documented. Stephansson et al.<sup>8</sup> found an increased risk of stillbirth and growth-restricted infants in women with hemoglobin concentrations greater than 14.6 g/dL. However Demmouche et al.<sup>9</sup> found no difference in birth weight between anemic and non-anemic pregnant women.

Gestational diabetes mellitus (GDM) affects approximately 7% of all pregnancies. There is not much information about the relationship between anemia with diabetes or GDM. There are limited studies including GDM and hemoglobin levels.<sup>10-12</sup> Lao et al.<sup>13</sup> showed that women with mild gestational glucose intolerance according to the WHO category of impaired glucose tolerance had significantly increased Hb concentration.<sup>14</sup>

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To determine whether the prevalence of GDM is indeed influenced by the presence of iron deficiency anemia, we performed this retrospective case-control study in women having singleton pregnancies and delivered in our hospital.

## Material and Method

The study was approved by the study review group of Etlik Zubeyde Hanım Women's Health Research and Educational Hospital. It was conducted retrospectively and included 131 GDM and 300 non-GDM women that were screened and diagnosed between the 24-28 week of gestation. Women with a history of type 1 and type 2 diabetes mellitus, with other causes of anemia such as thalassemia trait and those who had late booking or delivery elsewhere were excluded from this study.

In our hospital maternal Hb concentration, MCV, and blood group are checked routinely at the first visit of all pregnant. Patients with Hb level <11 g/dL at the first prenatal visit during pregnancy are considered to have anemia, and empirical treatment is usually suggested. In our country the incidence of b-thalassemia trait is 2%.<sup>15</sup> So hemoglobinopathies are routinely screened before the marriage by the suggestion of government. In 2012, 78% of all the marriages had been screened for thalassemia. Pregnant women with thalassemia trait women were consulted with the hematology clinics and were excluded from the study.

We used two-step testing regimen which involves a 50-g "challenge" pre-test followed by the 100-g OGTT only if the initial result is abnormal. 50 g GCT was performed at any time of the day. If the results were between 140-199 mg/dL, 100-g OGTT was performed. The positive test was considered according to National Diabetes Data Group (NDDG). According to NDDG threshold glucose levels of 100g OGTT are 105 mg/dL (5.8 mmol/L) for fasting ,190 mg/dL (10.5 bmmol/L)

for the first,165 mg/dL (9.1 mmol/L) for the second and 145 mg/dL (8. mmol/L) for the third hour.Two or more values above the threshold were diagnosed as GDM.<sup>16</sup> Body mass index (BMI) was calculated as weight (kg)/ height 2 (m<sup>2</sup>).

We divided the patients into two groups: group 1 was the study group diagnosed as GDM, and group 2 was the control group without GDM. The two groups were compared for maternal demographics, Hb, MCV and pregnancy outcomes, which included the incidence of large for gestational age (LGA) infants and small for gestational age (SGA) infants (birth weight ≤10<sup>th</sup> percentile).

For statistical analysis, categorical variables were compared with the  $\chi^2$  test. Continuous variables that are normally distributed were expressed as mean  $\pm$  SD and tested by the independent samples t test. Statistical calculation was performed using a commercial computer package (Statistical Package for Social Sciences for Windows version 21.0; SPSS, Chicago, IL).

## Results

In the study group, there were 131 women. Hb value was >11 g/dL in 80.9% patients, 9-11 g/dL in 19.1% patients. In the control group Hb values were >11 gr/dL in 65.3% patients, 9-11 gr/dL in 34%, and only <9 g/dL in 0.7% patients. In the study group the mean maternal age, gestational week and BMI were significantly different than the control group ( $p<0.001$ ). The demographic data of the two groups were shown on Table 1. Also multiparity was seen significantly higher than the control group ( $p<0.05$ ) (Table 2). In the study group, <2500 g newborns (12.2% vs 2.3) and >4000 g newborns (19.8% vs.6.7%) were significantly higher than control group ( $p<0.001$ ) (Table 3).

Table 1: Demographic datas, Hb and MCV values of two groups statistics

	Group	n	Mean	Std. Deviation	p value
Maternal Age (years)	Study	131	30.42	5.066	0.056
	Control	300	29.87	5.569	
Gestational week	Study	131	37.679	1.9311	<0.001
	Control	300	38.684	1.1739	
Birth weight (gr)	Study	131	3312.9771	752.45311	0.992
	Control	300	3312.2667	429.66370	
BMI (kg/ m <sup>2</sup> )	Study	131	30.1561	5.05244	0.99
	Control	300	30.8532	4.04474	
Hb (g/dL)	Study	131	12.1548	1.26183	0.001
	Control	300	11.7243	1.16893	
MCV (fl)	Study	131	89.2855	7.55387	<0.001
	Control	300	84.6443	6.93392	

BMI: Body mass index, Hb: Hemoglobin, MCV: Mean corpuscular volume

Table 2: The parity of two groups

	Study group (N=131)	Control group (n=300)	p value
Primiparity	35 (26.7%)	111 (37%)	0.038
Multiparity	96 (73.3%)	189 (63%)	

Table 3: The mean birth weight between two groups

Weight (g)	Study group (n%)	Control group (n%)	p value
<2500	16(12.2)	7 (2.3)	<0.001
2500-4000	89 (67.9)	273 (91)	
>4000	26 (19.8)	20 (6.7)	

We found out that the mean Hb value was significantly higher in the GDM group ( $12.2 \pm 1.26$  vs.  $11.72 \pm 1.17$ ) ( $p < 0.001$ ). Also the MCV, was significantly higher in the GDM group ( $89.29 \pm 7.55$  vs.  $84.64 \pm 6.93$ ) ( $p < 0.001$ ) (Table 1). After the analysis of covariance for maternal age, BMI, parity, birth weight there was a significant difference in Hb values between two groups ( $p = 0.002$ ). Likewise we found a significant difference in MCV values between groups after the analysis of covariance for maternal age, BMI, parity, birth weight ( $p < 0.001$ ).

## Discussion

The data we focused on women with GDM and IDA demonstrated that GDM is associated with high levels of Hb, measured in the first trimester. Measurement of Hb concentration has become a standard laboratory test in pregnancy. In the first trimester maternal Hb concentration reflects maternal nutritional status. The best time to detect the risk associated with maternal anemia is the early pregnancy before the plasma volume is fully expanded.<sup>17</sup> In our study, Hb concentration that was measured in the first trimester was significantly higher in GDM group. Our anemic women had significantly lower MCV. Because MCV is a robust index of maternal iron status in women without hemoglobinopathies, our findings confirmed that the underlying etiology of the anemia was iron deficiency and not merely hemodilution.

Pregnancy is a condition that favors oxidative stress. Iron overload and the associated oxidative stress contribute to the pathogenesis and increase risk of type 2 diabetes and other disorders.<sup>18</sup> Excess iron can affect insulin synthesis and secretion. The insulin increases the oxidation of lipids that causes the decreasing of glucose utilization in muscles and increasing gluconeogenesis in liver.<sup>19</sup> Because an increase in oxidative stress is part of normal pregnancy, routine iron supplementation in women without iron depletion might also contribute to oxidative stress. Scholl et al. confirmed the presence of increased oxidative stress in association with increased iron

stores during pregnancy.<sup>11</sup> Furthermore, increased iron stores in the general population have been associated with increased incidence of diabetes.<sup>20</sup>

Chen et al.<sup>21</sup> detect an association between maternal serum ferritin and GDM. They found a 2-fold increase in risk of GDM for women in the highest quartile of serum ferritin in the first trimester and nearly a 3-fold increase in the third trimester. This positive relation suggests that iron stores may play a role in the development of GDM. Lao et al.<sup>22</sup> found that nonanemic gravidas who developed GDM had high levels of serum ferritin, iron and transferrin saturation compared with controls.

Afkhami-Ardekani et al.<sup>10</sup> reported that iron status in women with GDM was significantly higher than non-GDM group. Lao et al.<sup>12</sup> found that the incidence of GDM in women with IDA was significantly lower than in nonanemic women. The nutritional improvement and correction of anemia could be contributing factors to the increasing prevalence of diabetes and GDM. Further studies on the role of nutritional factors in the development of diabetes and GDM are warranted, especially in developing countries. Although there are previous studies focusing on supplementary iron intakes during pregnancy and GDM risk have produced inconsistent findings, Bowers et al showed no significant association between iron supplementation and GDM.<sup>23</sup> Also Chan et al.<sup>24</sup> found no increase at the risk of GDM with the iron supplementation from early pregnancy.

The LGA and SGA infants were higher in our study group. It is known that GDM is considered as an independent risk factor for newborn macrosomia.<sup>25</sup> However Lao et al.<sup>14</sup> found that the anemic group had significantly increased incidence of LGA infants.

In conclusion, however we demonstrated that GDM was associated with high levels of Hb that was measured in the first trimester the number of patients was the limitation of this study. We suggest that pregnant women without iron deficiency should not use iron replacement therapy. For a certain knowledge about the correlation between IDA and GDM, further studies with high population are needed.

## Gestasyonel Diabetes Mellitus ve Demir Eksikliği Anemisi

### ÖZET

**AMAÇ:** Erken gebelik döneminde var olan demir eksikliği anemisinin gestasyonel diabetes mellitus gelişimine etkisini araştırmak.

**GEREÇ VE YÖNTEM:** Bu retrospektif kohort çalışmaya 24-28. gebelik haftaları arasında gestasyonel diabetes mellitus tanısı almış 131 gebe (çalışma grubu) ve gestasyonel diyabet için tarama testi negatif olan 300 gebe (kontrol grubu) dahil edilmiş-

tir. Her iki gruptaki gebelerin ilk trimester hemoglobin ve ortalama korpuskular hacim değerleri anemi yönünden değerlendirilmiştir.

**BULGULAR:** Çalışmamızda ortalama hemoglobin değerleri ve ortalama korpuskular hacim gestasyonel diyabetli hasta grubunda anlamlı olarak daha fazla idi (sırasıyla  $12,2 \pm 1,26$  vs.  $11,72 \pm 1,17$ ;  $p < 0,001$ ,  $89,29 \pm 7,55$  vs.  $84,64 \pm 6,93$ ;  $p < 0,001$ ). Maternal yaş, parite, doğum ağırlığına göre yapılan kovaryans analizine göre her iki grup arasında hemoglobin ve ortalama korpuskular hacim değerleri açısından anlamlı fark mevcuttu (sırasıyla  $p = 0,002$ ,  $p < 0,001$ ). Gestasyonel diyabetli hasta grubunda  $>4000$  g yenidoğanlar anlamlı olarak daha fazlaydı ( $19,8\%$  vs.  $6,7\%$ ) ( $p < 0,001$ ).

**SONUÇ:** Gestasyonel diabetes mellitus gelişimi ilk trimesterde ölçülen yüksek hemoglobin değerleri ile ilgilidir.

**Anahtar Kelimeler:** Gestasyonel diabetes mellitus, Demir eksikliği anemisi, Ortalama korpuskular hacim

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