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Is There A Risk For Developing Impaired Glucose Tolerance In The Pregnancy With Routine Iron Supplementation?

Gebelikte Rutin Demir Takviyesinin Bozulmuş Glukoz Toleransı Gelişme Riskine Bir Etkisi Var Mıdır?

Ümit Yasemin SERT[1], Hatice KANSU ÇELİK[1], Burcu KISA[1], Yaprak ENGİN-ÜSTÜN[1]

[1]University of Health Sciences Dr. Zekai Tahir Burak Women's Health Care, Education and Research Hospital, Ankara, TURKEY

ABSTRACT

Aim: Gestational diabetes mellitus (GDM) is one of the most important metabolic disorder associated with adverse pregnancy outcome and maternal-fetal mortality and morbidity. Impaired glucose tolerance (IGT) is also a predictor for poor pregnancy outcome. The aim of the study is to demonstrate the correlation between iron, iron binding capacity (IBC), hemoglobin (Hb) and ferritin levels and IGT.

Material And Methods: This retrospective study was performed among 100 patients (IGT group:50, Normal OGTT group:50) who were admitted to University of Health Sciences Dr. Zekai Tahir Burak Woman's Health, Education and Research Hospital, attended to the first antenatal visit at 6-11 weeks of gestation, and were applied with two step OGTT between 24-28 weeks of gestation. First trimester serum Hb, ferritin, iron, IBC and OGTT results have been evaluated and compared between two groups.

Results: The serum levels of iron, IBC and ferritin have found no significantly different between two groups ($P<0.05$) while Hb levels are significantly high in IGT group (13.38±1.02 mg/dl vs. 12.72±1.03 mg/dl; $P=0.015$)

Conclusion: Hb levels are found to be significantly higher in IGT group therefore; routine iron supplementation for pregnant women should be individualized regarding the first trimester Hb levels.

Keywords: Gestational diabetes, impaired glucose tolerance, ferritin, hemoglobin.

ÖZ

Amaç: Gestasyonel diabetes mellitus (GDM), kötü gebelik sonuçları ve maternal ve fetal mortalite ile ilişkili ciddi bir metabolik bozukluktur. Bozulmuş glikoz toleransı (BGT) de kötü gebelik sonuçlarını öngören önemli bir parametredir. Çalışmamızın amacı demir, demir bağlama kapasitesi (DBK), hb ve ferritin seviyeleri ile BGT arasındaki ilişkiyi ortaya koymaktır.

Gereç ve Yöntemler: Bu retrospektif çalışma Dr Zekai Tahir Burak Kadın Sağlığı Eğitim ve Araştırma Hastanesi'ne başvuran, ilk antenatal takiplerine 6-11 haftalar arasında gelen ve 24-28 haftalar arasında 2 basamaklı OGTT uygulanan toplam 100 hasta ile yapılmıştır (BGT:50 hasta, Normal OGTT:50 hasta). İlk trimester hemoglobin (hb), ferritin, demir, demir bağlama kapasitesi (DBK) ve OGTT sonuçları iki grup arasında karşılaştırılmıştır.

Bulgular: Demir, DBK ve ferritin seviyeleri iki grup arasında istatistiksel olarak farklı bulunmamıştır ($P<0.05$). Hb seviyesi ise BGT grubunda anlamlı olarak yüksek saptanmıştır (13.38±1.02 mg/dl vs. 12.72±1.03 mg/dl; $P=0.015$)

Sonuç: Hb seviyeleri BGT grubunda anlamlı oranda yüksek saptanmıştır. Bu sebeple gebelikte rutin demir takviyesi ilk trimester hb seviyeleri de göz önünde bulundurularak bireyselleştirilmelidir.

Anahtar Kelimeler: Gestasyonel diyabet, bozulmuş glukoz toleransı, ferritin, hemoglobin

INTRODUCTION

Gestational diabetes (GDM) is genarally defined as glucose intolerance of different levels of severity which first detected in the pregnancy (1). According to the datas of American Diabetes Association(ADA), it is determined and complicated 7% of all the pregnancies in the world (1). The prevelance of GDM depends on several charcteristics of the population such as diet, lifestyle, individual pregnancy factors, ethnicity, obesity, familly history and genetics (2).

Pregnancies complicated with GDM have increased risk of maternal and fetal complications as the risk of cesarean operation and operative vaginal delivery, macrosomia, shoulder dystocia, neonatal hypoglycemia and hyperbilirubinemia, increased risk of developing type 2 DM in the future for both mother and fetus and severe pregnancy complications such as preeclampsia, polyhydramnios, and stillbirth (3-5).

National Diabetes Data Group (NDDG) handled the pregnant women as two categories: normal glucose tolerance and GDM while WHO describes an intermediate group named IGT (6,7). A recent prospective cohort study of

Yazışma Adresi/ Correspondence Address:
Umit Yasemin SERT
University of Health Sciences Dr. Zekai Tahir Burak Women's Health Care, Education and Research Hospital, Talatpaşa Bulvarı, 06230, Ankara, TURKEY
Tel/Phone: +90 312 306 50 00
E-mail: ysmn.sert88@gmail.com

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3637 women has demonstrated an increase on adverse pregnancy outcomes including the patients with IGT (8). Altough there are conflicting datas on the effect of IGT on pregnancy outcome, there are distinct evidences for increasing risk of developing future DM (9). All the abnormal glucose metabolism defined in pregnancy should be thought as GDM according to the WHO recommendations (10).

Routine antenatal screening for GDM is usually performed at 24-28 weeks of gestation, although it is considerable to screen the high risk population in the first antenatal visit to catch up the missing undiagnosed diabetes mellitus. Even though there are several studies, guidelines and recommendations focusing on the diagnosis and management of glucose metabolism abnormalities, there is still lack of consensus on the management between the observers. Especially the part of diagnose of GDM and management of impaired glucose levels in the absence of GDM is still debated (11).

Anemia in the pregnancy is an important health problem associated with adverse pregnancy outcome and still preserves the reputation of being seen more than 20% of the population in the 80% of the countries. Although there is a tendency of physiologic anemia in the pregnancy, it should be distinguished from iron deficiency which may require appropriate treatment and related to severe health problems(12). The definition of the anemia is also controversial. It is defined as the Hb levels<110 g/l antenatally and <100g/l postnatally by World Health Organization(WHO) while the British Comitee for Standarts in Heamatology guidelines emphasizes trimester related cutoff values by keeping in mind the physiologic haemedulution (<11.0 mg/dl in the first trimester, <10.5 mg/dl in the second and third trimesters and <10.0 mg/dl in the postpartum period) (13).

Untreated anemia in the pregnancy has an important effect on mother's daily wellbeing by causing unwanted symptoms such as fatigue, headaches, palpitations, dizziness and decreased energy(14). It is also found to be associated with preterm birth, placental abruption, postpartum hemorrhage, infection, eclampsia, obstructed labor and maternal death(15, 16). The studies have demonstrated a strong correlation between anemia and neonatal complications. Premature birth, low birth weight, decreased school success and IQ levels are the major findings in the neonates of anemic mothers (17).

Iron status and the iron intake during the pregnancy is considered to be associated gestational diabetes mellitus development in several studies (18,19). This study has been conducted to determine correlation between Hemoglobin (Hb)levels, iron status, iron binding capacity (IBC), ferritin levels and impaired glucose tolerance (IGT) and GDM.

MATERIAL AND METHODS

This retrospective study based on patients' records which was held in the Department of Obstetrics and Gynecology of Zekai Tahir Burak Woman's Health, Training and Research Hospital in Ankara, Turkey between January-April 2010. The institutional review board approved the study. Exclusion criteria included a diagnosis of chronic disease before conception (diabetes, hypertension, thyroid dysfunction, uncontrolled endocrine illness, or abnormal renal function), fasting plasma glucose levels exceeding 126 mg/dL or a 2 h postprandial or OGTT value exceeding 200 mg/dL at gestational week 24–28, history of a positive glucose tolerance test in the first trimester.

The patients who attended to the first antenatal visit at 6-11 weeks of gestation, had all the antenatal visits regularly and were applied with two step oral glucose tolerance test (OGTT) between 24-28 weeks were included the study. A positive 50 g GCT was defined as a glucose level of at least 140 mg/dL 1 h after glucose challenge. Women who had a positive 50 g GCT were advised to follow a normal diet 3 days before the 100 g oral glucose tolerance test (OGTT). GDM was diagnosed if there were two or more abnormal values on a 100 g OGTT performed according to the criteria identified by Carpenter and Coustan (FPG: 95 mg/dL, 1st h: 180 mg/dL, 2nd h: 155 mg/dL, 3rd h: 140 mg/dL) [20]. IGT is defined as increase of single value of 100 gr OGTT. Controls were defined as pregnant women with a negative 50 g GCT (1st h < 140 mg/dL)(10). Demographic characteristics including age, parity, and first trimester serum Hb, ferritin, iron, IBC and OGTT results were noted.

Study group (IGT group) compared to control group (normal OGTT) in terms of Hb, ferritin, iron and IBC.

SPSS (Statistical Package for the Social Sciences) version 21.0 was used fort he statistical calculations. The data were presented with the number of patients and percentage and defined by mean ± standart deviation and median (minimum-maximum). Numbers and percentages were used as descriptive statistical methods in evaluating the data. The relationship between the group variables was analyzed by chi-square analysis, and the t-test was performed to determine whether the two groups' variable differed according to the continuous variable. The findings were assessed at the 5% significance level in the 95% confidence interval.

RESULTS

The demographic characteristics and laboratory outcomes of the groups are shown in Table 1.

Table 1: Demographic characteristics and labotory outcomes of the groups

	IGT group	**Normal OGTT group**	**P**
Variables	n=50	n=50	
Age (years) / Mean±SD	29.75±5.91	27.59±5.95	0.169
Parity / Median (Min-Max)	1(0-3)	1(0-2)	0.350
Gestational week / Median (Min-Max)	7(6-11)	7(6-11)	0.233
Iron (μg/dL) / Median±SD	92.07±34.67	83.69±34.86	0.357
Iron Binding Capacity (μg/dL) / Median±SD	228±57	246±53	0.232
Ferritin (μg/L) / Mean±SD	34.84±29.72	31.79±20.83	0.752
Hemoglobin (mg/dl) Mean±SD	13.38±1.02	12.72±1.03	**0.015**

There were no statistically significant differences between groups in terms of age, parity, gestational week, levels of iron, ferritin, and IBC ($P > 0.05$).

The Hb levels of IGT group were found to be significantly higher than normal OGTT group (13.38±1.02 mg/dl vs. 12.72±1.03 mg/dl; P=0.015).

DISCUSSION

In the present study, we evaluated the correlation between iron, IBC, Hb and ferritin levels and IGT. We found that serum Hb levels are significantly high in

pregnant women with IGT.

Iron is an essential part of metabolic functions including oxygenation, glucose homeostasis and cellular functions (20). Iron deficiency is an important health problem among the pregnant women and the recommends of the WHO emphasize the supplementation of iron (daily 30-60 mg) to be able to prevent iron deficiency anemia in the pregnancy which can lead inadequate fetal iron status. Increasing need of iron to supply physiological expansion of blood volume, requirements of the fetus, and placenta are the major considerations for replacement (21).

GDM is associated several risks for both mother and fetus in the pregnancy and postpartum period. Although there are conflicting datas for the endogenous and exogenous (supplemental) use of iron, there are strong evidences for the relation of GDM and increasing iron levels (22). Daily supplementation of iron especially with vitamin C combination induces the free oxygen radical production, lipit membrane detriment and carsinogenesis. Iron directly plays role in GDM by effecting the insulin secretion, inducing the lipit oxidation, decreasing the muscular glucose uptake and enhancing the gluconeogenesis (23, 24).

In a meta-analysis of the studies published in 2018 have shown the clear positive correlation between serum iron levels and GDM(25). Animal studies have also supported the postulates of impaired glucose tolerance by iron supplementation while the glucose tolerance was improved by iron restriction or chelation(26). Human studies have also demonstrated clinical improvement in insulin sensitivity by reducing the iron levels with blood donations, phlebotomy and iron chelators (27).

Lao et al. has found no significant difference between the patients with IGT and control group in terms of serum iron and IBC while the serum ferritin levels were significantly higher in IGT group (28). We demonstrated no significant difference of serum iron and IBC between groups correlatively without regarding the other risk factors such as body mass index (BMI), race and ethnicity.

Ferritin is a marker demonstrating the total iron stores and also be assigned as acute phase reactant (APR) in inflammatory processes. Although there are comprehensive studies for the connection of increasing levels of ferritin and presence of GDM and IGT, it can be postulated that the increasing level of ferritin is due to the inflammatory process in diabetic women. This correlation can be described with the positive correlation between diabetes and C-reactive protein (CRP) and hepcidin levels who are also inflammatory markers (29-32). Amiri et al. has found that 2.4 fold increasing risk for GDM with ferritin levels >80 ng/ml while low ferritin levels (less than <20 ng/ml) reduce the risk 82%(33). In our study the levels of ferritin varied between 31-34 ng/ml and no significant difference has been detected. The ferritin levels >80 ng/dl was found in four patients: three of the patiens with IGT, and one with normal OGTT. This result can be explained with the inadequate number of the patients evaluated in the study.

The increasing levels of Hb has been defined to be associated with IGT in our study (P=0.015). Hb concentration is effected by hemodilution especially after the first trimester of the pregnancy as we evaluated the first trimester Hb levels excluding the physiologic dilution. This study had some limitations. First, our study was retrospective design and number case of study was small. Second, increasing levels of Hb can be a result of iron overload, smoking status and high altitude which are not examined in our study. Kataria et al. has also demonstrated that increasing Hb levels is associated with GDM correlatively to our study (25).

In conclusion, regarding the results of our study and correlatively with similar researches, routine antenatal use of iron supplementation needs to be evaluated with comprehensive studies, since the strong evidences supported by studies have shown the correlation between iron and GDM development.

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