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Can gestational diabetes screening predict preeclampsia?

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Abstract

Objective: In this study, we planned to investigate the relationship between maternal characteristics, obstetric outcomes and test results by screening the pregnant women in our population who had 50-g oral glucose tolerance test (OGTT).

Methods: A total of 636 pregnant women, who had their gestational diabetes screening between January 2011 and July 2013 at a university hospital and whose medical records were reviewed retrospectively, were included in the study. Demographic, perinatal and newborn data of the pregnant women who included in the study were evaluated.

Results: According to the information we obtained from the gestational diabetes screening results of the pregnant women in our study, 464 pregnant women had normal results for 50-g OGTT (Group 1, control group), 71 pregnant women had positive results for 50-g OGTT but normal results for all values in 100-g oral glucose tolerance test (OGTT) (Group 2), 29 pregnant women had positive results for 50-g OGTT but positive for only one value in 100-g OGTT (Group 3) and 62 pregnant women had gestational diabetes (Group 4). There were differences among the groups in the parameters for age, parity, preeclampsia and polyhydramnios, but there was no significant difference in other parameters.

Conclusion: Even though there are differences in terms of ethnic origins, 50-g OGTT which is used as gestational diabetes screening test during pregnancy can predict preeclampsia. Our findings support the relationship between blood glucose level and preeclampsia, and contribute new information. However, more comprehensive prospective studies are required on this subject.

Keywords: Gestational diabetes, glucose intolerance, preeclampsia.

Özet: Gestasyonel diyabet taraması preeklampsiyi öngörebilir mi?

Amaç: Bu çalışmada kendi popülasyonumuzda 50 g oral glukoz tarama testi (OGTT) yaptıran gebeleri tarayıp test sonuçları ile maternal özelliklerin ve obstetrik sonuçların ilişkisini incelenmeyi planladık.

Yöntem: Çalışmaya, tıbbi kayıtları retrospektif olarak incelenen, Ocak 2011 – Temmuz 2013 yılları arasında gestasyonel diyabet taramasını bir üniversite hastanesinde yaptıran 636 gebe kadın dahil edildi. Çalışmaya katılan gebelerin demografik, perinatal ve yenidoğan özellikleri incelendi.

Bulgular: Çalışmamıza katılan gebelerin gestasyonel diyabet tarama sonuçlarından elde ettiğimiz bilgilere göre; 464 gebe 50 g OGTT normal (Grup 1, kontrol grup), 71 gebe 50 g OGTT pozitif ancak 100 g oral glukoz tolerans testi (OGTT) tüm değerler normal (Grup 2), 29 gebe 50 g OGTT pozitif ancak 100 g OGTT tek değer pozitif (Grup 3) ve 62 gebe gestasyonel diyabet (Grup 4) olarak gruplara ayrıldı. Gruplar arasında, yaş, parite, preeklampsi, polihidramniyos parametrelerinde fark saptandı, ancak diğer parametrelerde anlamlı fark saptanmadı.

Sonuç: Gebelikte gestasyonel diyabet tarama testi olarak kullanılan 50 g OGTT; her ne kadar etnik kökenler arasında farklılıklar olsa da, preeklampsi öngörüsünde bulunabilir. Kendi bulgularımız kan şekeri düzeyi ve preeklampsi arasındaki ilişkiyi destekler yöndedir ve yeni bilgilere katkıda bulunmuştur. Ancak konu ile ilgili daha geniş kapsamlı prospektif çalışmalara ihtiyaç vardır.

Anahtar sözcükler: Gestasyonel diyabet, glukoz intolerans, preeklampsi.

Introduction

Gestational diabetes (GD) is the glucose intolerance which starts during pregnancy or which is diagnosed during pregnancy for the first time.[1,2] While the incidence varies among the societies, it has been increasing day by day. The most important reason is the increase of obesity incidence and the decrease of threshold values in diagnostic tests.[3] Hyperglycemia developing

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during pregnancy has severe adverse effects. Preeclampsia, fetal macrosomia, polyhydramnios, birth trauma, perinatal mortality and neonatal metabolic complications are among these adverse effects. It is also known that the development of obesity and diabetes is more frequent during childhood of the babies delivered by women with gestational diabetes.[4]

There are two different approaches in the screening of gestational diabetes. One- and two-step methods can be used in the screening. Two-step approach is based on applying 50-g oral glucose tolerance test (OGTT) first and then (if necessary) 100-g oral glucose tolerance test (OGTT). Some researchers have defined pregnant women with abnormal 50-g OGTT results but normal 100-g OGTT results as "glucose intolerance", "borderline diabetes" or "mild gestational hyperglycemia".[5,6] Some studies in the literature remarked that the maternal characteristics of pregnant women, whose 50-g OGTT results are higher but 100-g OGTT results are within normal limits, may be different than normal pregnant women, and that this may affect obstetric results negatively.[7,8]

In this study, we aimed to investigate the relationship between maternal characteristics, obstetric outcomes and test results by screening the pregnant women in our population who had 50-g oral glucose tolerance test (OGTT) in our population retrospectively.

Methods

A total of 626 pregnant women, who had their GD screening between January 2011 and July 2013 at a university hospital and whose medical records were reviewed retrospectively, were included in this study. Multiple pregnancies, chronic diseases (hypertension, renal and cardiac diseases) and congenital anomalies were excluded.

Pregnant women were screened in our clinic for GD between 24 and 28 weeks of gestation. OGTT was applied in the morning between 08:00 a.m. and 10:00 a.m. The patients were administered 50-g glucose diluted with 200 ml water. Routine pregnancy follow up was carried out for the patients whose 50-g OGTT 1st hour blood glucose level was below 140 mg/dL. The patients whose 50-g OGTT 1st hour blood glucose level was >200 mg/dL were directly considered as GD. 100 g 3-hour glucose tolerance test was applied after fasting for 8–14 hours to the pregnant women whose 50-g OGTT 1st hour blood glucose level were ≥140 mg/dL. During this test, first the venous blood sample was collected from the patients for the measurement of fasting blood glucose. After 100-g glucose diluted in 200 ml water was administered to the patients, venous blood samples were collected at 1st, 2nd and 3rd hours and the samples were analyzed at biochemistry laboratory. GD diagnosis was established according to Carpenter and Coustan criteria (fasting: >95, 1st hour: 180, 2nd hour: 155, 3rd hour: 140). Pregnant women were separated into 4 groups according to their OGTT results; these groups were defined in **Table 1**. Of the pregnant women included women, age, gravida, parity and gestational age information as demographic data; presence of preeclampsia (hypertension occurring together with proteinuria after 20 weeks of gestation), polyhydramnios (can be defined as the widest amniotic fluid sac being 8 cm or above or amniotic fluid index being over 95% for gestational age), oligohydramnios (can be defined as <5th percentile amniotic fluid index according to gestational age or ≤5 cm amniotic fluid index regardless of gestational age), cesarean rate, and cesarean rate due to fetal distress as perinatal outcomes; and APGAR scores of babies, weights, heights, hyperbilirubinemia (blood bilirubin being at pathologic levels according to gestational age, weight and gender),

Table 1. Demographic characteristics and comparison of gestational outcomes.

	Group 1 (n:464)	Group 2 (n:71)	Group 3 (n:29)	Group 4 (n:62)	p value
Age (mean)	29.4	31.1	32.4	34.6	<0.001
Parity (mean)	1.09	1.24	1.48	1.65	0.001
Polyhydramnios	17 (3.7%)	8 (11.3%)	2 (6.9%)	8 (12.9%)	0.003
Oligohydramnios	50 (10.8%)	3 (4.2%)	1 (3.5%)	4 (6.5%)	0.16
Preeclampsia	19 (4.1%)	5 (7%)	3 (10.3%)	13 (21%)	<0.001
Cesarean	243 (52.4%)	46 (64.8%)	15 (51.7%)	40 (64.5%)	0.09
C/S due to AFD	15 (3.2%)	2 (2.8%)	3 (10.3%)	3 (4.8%)	0.23

AFD: Acute fetal distress, **C/S:** Cesarean

Table 2. Comparison of perinatal outcomes.

	Group 1 (n:464)	Group 2 (n:71)	Group 3 (n:29)	Group 4 (n:62)	p value
Macrosomia	17 (3.7%)	5 (7%)	1 (3.4%)	6 (9.7%)	0.13
Delivery week (mean)	38.6	38.8	38.7	38.5	0.79
Birth weight (g) (mean)	3182	3308	3292	3286	0.15
Height of baby (cm) (mean)	51.4	50.8	50.9	51	0.99
5-minute Apgar (mean)	9	9	9	8.8	0.29
Intense care	55 (11.9%)	6 (8.5%)	6 (20.6%)	11 (17.7%)	0.2
Hyperbilirubinemia	55 (11.9%)	8 (11.3%)	6 (20.6%)	8 (12.9%)	0.44

and newborn intense care need as neonatal outcomes were recorded retrospectively and compared.

Statistical Analysis

We used ANOVA test and Spearman's correlation analysis for comparison among the groups. We made prediction evaluation with ROC curve. A p-value below 0.05 was considered as statistically significant.

Results

A total of 626 pregnant women applied OGTT were included in our study. The pregnant women were separated into 4 groups according to their results. 464 pregnant women had normal results for 50-g OGTT (Group 1, control group), 71 pregnant women had positive results for 50-g OGTT but normal results for all values in 100-g OGTT (Group 2) (Group 2), 29 pregnant women had positive results for 50-g OGTT but positive for only one value in 100-g OGTT (Group 3) and 62 pregnant women had GD (Group 4). Demographic characteristics and maternal results of the groups are provided in **Table 1**. As seen in **Table 1**, there was significant difference in the parameters of age, parity, preeclampsia and polyhydramnios of the groups. Mean maternal age was significantly high in GD group (p<0.001).

Among the groups, there was no significant difference in terms of birth weight, birth height, delivery week, macrosomia, oligohydramnios, cesarean rate due to fetal stress, cesarean rate, APGAR score, bilirubin levels, and intense care need (**Tables 1** and **2**).

In group 1, there was a weak but significant correlation between fasting (p=0.017, r=0.11) and 1st hour (p=0.009, r=0.12) blood glucose levels and birth weight. When 50-g OGTT test 1st hour blood glucose levels of the pregnant women in Groups 2 and 3 were analyzed, it was found that 1st hour blood glucose level of Group 3 was 164 while it was 156 in Group 2, and a significant difference was found between two groups (p=0.009).

Of 626 pregnant women who were evaluated, 583 women were normotensive and 43 women were preeclamptic. According to the 50-g OGTT results of women who were established preeclampsia diagnosis, mean fasting blood glucose and 1st hour blood glucose levels were higher than the values of normotensive pregnant women (**Table 3**). According to the 100-g OGTT results of women who were established preeclampsia diagnosis, mean fasting blood glucose and 1st hour blood glucose levels were also higher than the values of normotensive pregnant women. In the ROC curve of these pregnant women, 1st hour blood glucose value (AUC 0.7) had a higher prediction value for preeclampsia than fasting blood glucose value (AUC 0.58) (p=0.018). It was seen that ≥134 mg/dl threshold value of 1st hour blood glucose was able to predict preeclampsia cases with 62% sensitivity and 70% specificity (p=0.0001) (**Fig. 1**).

Discussion

A large number of studies have been reported since gestational diabetes has been defined; however, clinical significance of pregnant women who have abnormal results for 50-g OGTT but not considered as GD according to 100-g OGTT results is controversial.[9]

Table 3. Relationship between 50-g OGTT and preeclampsia.

	Preeclamptic group n=43	Normotensive group n=583	p value
FBG (mg/dl) (mean)	83.9	78.2	0.003
1st hour BG (mg/dl) (mean)	149.1	122.6	<0.001

BG: Blood glucose, **FBG:** Fasting blood glucose.

We retrospectively investigated the perinatal outcomes of our pregnant women population who were established with glucose intolerance during pregnancy.

In our study, we found no significant difference in the parameters except age, parity, polyhydramnios and preeclampsia when the group found to be normal for 50-g OGTT was compared with other groups. Mean age and delivery number of this group was found to be significantly low when compared with other groups. This shows that GD risk increases in advanced gestational age. There is a weak but significant relationship between fasting and 1st hour blood glucose levels and birth weight. In this case, considering racial differences, the threshold value can be accepted lower to prevent gestational complications in especially risky pregnancies.

There is a large group of patients who have abnormal results for 50-g OGTT and normal results or positive single value for 100-g OGTT. Their strategies and perinatal outcomes in the future are not clearly known. In the study of Stamilio et al., it was shown that perinatal complications are higher in pregnant women with borderline GD;[5] therefore, it was concluded that such patients would benefit more careful follow-up and diabetic diet. In our study, polyhydramnios (11.3%) was observed more in this group than the group with normal results for 50-g OGTT (3.7%). In a study performed in Turkey, advanced maternal age, increased parity and macrosomia were higher in pregnant women with borderline GD.[9] Rey et al. found the risks of fetal macrosomia and newborn hyperbilirubinemia higher while Okun et al. found the rate of fetal macrosomia higher in pregnant women who had abnormal results for 50-g OGTT and positive single value for 100-g OGTT.[10,11] In our study, we found advanced maternal age and increased parity higher in pregnant women with borderline GD; however, there was no relationship between elevated blood glucose level and macrosomia. In this regard, the results obtained were similar to those found in the study of Verma et al.[12] Some researchers used "National Diabetes Data Group" screening algorithm and WHO protocol, and found increase in the perinatal outcomes including cesarean, fetal macrosomia and preeclampsia in pregnant women who had positive single value for 100-g OGTT.[13,14] Contrarily, Ramtoola et al. used WHO protocol and found no significant difference in perinatal outcomes.[15] In our study, we found no significant difference in this group in terms of cesarean rate, APGAR score and intense care risk.

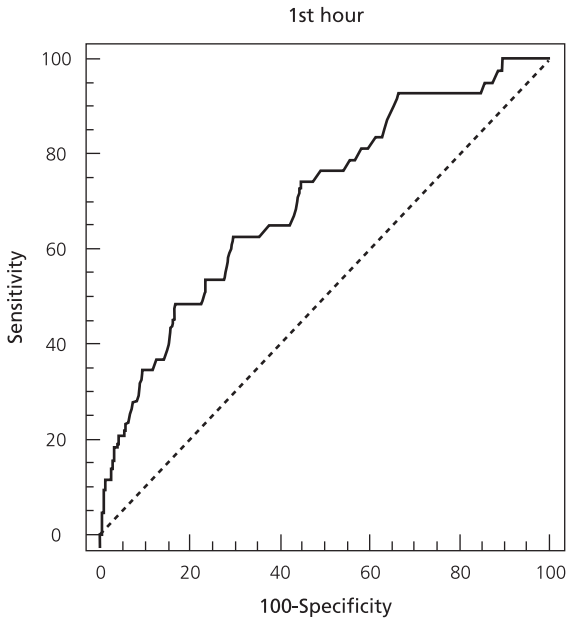

Fig. 1. ROC curve evaluating the activity of 1st hour blood glucose value in predicting of preeclampsia (AUC: 0.7; p=0.018).

Insulin resistance is one of the risk factors of preeclampsia and it may lead to vascular endothelial dysfunction. Ergin et al. reported that the pregnant women with GD having abnormal single value in OGTT were under more risk for gestational hypertension compared to women with normal OGTT values.[16] Also, Yalçın and Zorlu showed the ethnic significance by presenting the elevating rate of GD incidence in Turkish pregnant women through a lower threshold value for glucose screening test.[17] Also, many researchers carried out studies revealing the relationship between insulin resistance and preeclampsia development.[18,19] In our study, we found preeclampsia risk significantly higher in GD group compared to women in the group with normal results for 50-g OGTT. In the literature, the relationship between gestational glucose intolerance and maternal hypertensive diseases were reported in previous studies.[14,20–22] Also, gestational glucose intolerance and maternal hypertensive disorders were presented together with the racial differences in the studies.[23,24] However, there has been no study showing the relationship between OGTT and blood glucose threshold value. In our study, we found fasting and 1st hour blood glucose levels in 50-g and 100-g OGTTs higher significantly in preeclamptic

cases compared to normotensive pregnant women in line with the literature and determined a threshold value.

Conclusion

Even though there are differences in terms of ethnic origins, 50-g OGTT which is used as GD screening test during pregnancy can predict preeclampsia. Our findings support the relationship between blood glucose level and preeclampsia, and contribute new information. Although there was a significant relationship between 1st hour 50-g OGTT results and birth weights we found in our study, more comprehensive prospective studies are required on this subject.

Conflicts of Interest: No conflicts declared.

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