Abnormal One-Hour 50-Gram Glucose Challenge Test and Perinatal Outcomes

Anormal Bir Saatlik 50 Gram Glukoz Yükleme Testi ve Perinatal Sonuçlar

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ABSTRACT Objective: To investigate the association between abnormal one-hour 50-gram glucose challenge test and adverse perinatal outcome. **Material and Methods:** A retrospective study is performed in 212 patients screened for gestational diabetes between January 1999 and January 2005. Perinatal outcomes were compared between 123 patients with an abnormal glucose challenge test (blood glucose ≥140 gr with 50 gr glucose challenge test and normal with 100 gr oral glucose tolerance test) and 89 patients with normal 50 gr glucose challenge test. We used student t test, Mann-Whitney-U test, Chi square test for statistical evaluation. $p< 0.05$ is accepted as statistically significant. **Results:** There were no difference in demographic characteristics including age, gravidy, parity, and gestational week at the delivery between two groups. The patients with abnormal glucose challenge test results had maternal thyroid disease more frequently than control group ($p= 0.02$). Fetal macrosomia, antenatal death, shoulder dystocia, chorioamnionitis, preeclampsia, eclampsia, Cesarean delivery, postpartum endometritis, neonatal hypoglycemia, hypocalcemia, hyperbiluribinemia, and neonatal intensive care admission were comparable between two groups. **Conclusion:** Our data suggest that having an abnormal one-hour glucose challenge test is not an independent risk factor for an adverse perinatal outcome.

Key Words: Glucose tolerance test; prenatal care

ÖZET Amaç: Anormal bir saatlik 50 gram glukoz yükleme testi ile advers perinatal gelişmeler arasındaki ilişkiyi belirlemek. **Gereç ve Yöntemler:** Ocak 1999-Ocak 2005 arasında gestasyonel diyabet yönünden incelenen 212 hastayı kapsayan retrospektif bir çalışma yürütüldü. Glukoz yükleme testi sonucu anormal bulunan (50 gr glukoz yükleme testinde ≥ 140 gr ve 100 gr oral glukoz yükleme sonucu normal bulunan) 123 hasta ile 50 gr glukoz yükleme testi sonucu normal bulunan 89 hastadaki perinatal gelişmeler karşılaştırıldı. İstatistik değerlendirmelerde student t testi, Mann-Whitney-U testi ve Ki-kare testlerini kullandık. $p< 0.05$ olan p değerleri istatistiksel olarak anlamlı kabul edildi. **Bulgular:** İki grup arasında yaş, gebelik, doğum sayıları ve doğumun gerçekleştiği gebelik haftası yönünden fark yoktu. Anormal glukoz yükleme testi sonucu olan hastalarda maternal tiroid hastalığı kontrol grubuna göre daha sıktı ($p= 0.02$). Fetal makrozomi, antenatal ölüm, omuz distosisi, koryoamniyonit, preeklampsi, eklampsi, sezaryenle doğum, postpartum endometrit, neonatal hipoglisemi, hipokalsemi, hiperbilirubinemi ve neonatal yoğun bakım ünitesinde kalma süresi her iki grubunda birbirine benzerdi. **Sonuç:** Sonuçlarımıza göre anormal bir saatlik glukoz yükleme testi advers, perinatal gelişmeler yönünden bağımsız bir risk faktörü oluşturmamaktadır.

Anahtar Kelimeler: Glukoz tolerans testi; prenatal bakım

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Gestational diabetes is defined as carbohydrate intolerance of various degrees that initially begins or noticed during the current pregnancy.[1]

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Gestational diabetes is associated with fetal macrosomia, increased caesarean delivery incidence, preeclampsia, neonatal hypoglycemia and perinatal deaths.[2] It is considered that gestational diabetes diagnosis and treatment may reduce such risks even though it has yet to be completely proven.

Generally accepted diagnosis scheme for gestational diabetes and screening in many countries including our country is to perform 50-gram glucose challenge test (GCT) between 24-28 weeks of pregnancy, and to conduct a 3-hour 100 gram oral glucose tolerance test (OGTT) on patients that are GCT-positive as follow-up. The patients that have two or more abnormal values in the oral glucose tolerance test are diagnosed with gestational diabetes.

Since gestational diabetes screening tests are not perfect, some studies have discussed the possibility of risks in terms of poor perinatal outcome in patients with negative of borderline test results. In a study, it was claimed that pregnant women with abnormal glucose challenge test results were detected to have more chronic hypertension, sickle cell carrier state and higher levels of second trimester hCG. The same study also specified that abnormal GCT was an independent risk factor for adverse perinatal outcomes.[3]

Various degrees of disorders in the glucose metabolism may emerge as a result of abnormal maternal medical conditions. Whether the patients that were not diagnosed with diabetes in gestational diabetes tests, but have borderline diagnostic test results are under risk for adverse perinatal outcomes is a point of discussion. The aim of this study is to determine whether an abnormal GCT is an independent risk factor for poor perinatal outcomes.

MATERIAL AND METHODS

A total of 212 patients among 1886 pregnant women who had been screened for gestational diabetes in Akdeniz University Faculty of Medicine, Department of Gynecology and Obstetrics between January 1999 and January 2005 and had complied with the study criteria, were retrospectively assessed. All women had underwent a one-hour 50 gram glucose challenge test (GCT) at 24-28 weeks of their pregnancy.

In our hospital, GCT is carried out between 08:00 and 10:00 am regardless of the previous fasting status. Fifty grams of glucose is diluted in 250 ml of water and patients drink it. In our study, patients with blood glucose values lower than 140 mg/dl according to one-hour GCT were defined as the control group. The pregnant women who had venous blood glucose ≥ 140 mg/dl one hour after drinking glucose solution were regarded to have positive GCT results. The ones with positive GCT results went through a three-hour 100 g standard oral glucose tolerance test (OGTT). This test was performed following a 8-14 hour fasting period preceded by a 3-day-diet containing 300 g of carbohydrates. One hundred grams of glucose is diluted in 250 ml of water. The patient drunk the solution after a venous blood sample was taken, and plasma blood samples were taken at 1st, 2nd and 3rd hours consecutively.

In our study, the NDDG (National Diabetes Data Group 1979) criteria were taken as basis in terms of glucose values. According to these criteria, upper limit for the fasting blood glucose value was 105 mg/dl; it was 190 mg/dl for the 1st hour, 165 mg/dl for the 2nd, and 145 mg/dl for the 3rd hour. The patients with two or more abnormal OGTT values were defined to have gestational diabetes. The pregnant women with one abnormal value were defined to have impaired glucose tolerance test. The patients who had all of their values at normal limits as a result of the three-hour oral glucose tolerance test were defined as abnormal GCT and study group. The pregnant women with impaired glucose tolerance and gestational diabetes as well as those whose delivery and neonatal care did not take place at our hospital or did not present for routine follow-up visits or had discontinued their follow-up were excluded from the study. Additionally, those with multiple pregnancies and those who gave birth to infants with congenital or chromosomal abnormalities were also excluded from the study. The reason for the exclusion of these patients was the evidence about poor perinatal outcomes related to such pregnancies. One hundred twenty three pati-

ents with abnormal GCT results and 89 patients with normal GCT results (control group) were followed up for fetal macrosomia, antenatal death, shoulder dystocia, chorioamnionitis, preeclampsia, Caeserian rate, neonatal intensive care admission, postpartum endometritis and neonatal outcomes. For fetal macrosomia, the weight at birth was taken as 4000 g and above. Antenatal death was defined as intrapartum death or intrauterine death after 20 gestational weeks. The shoulder dystocia was based on the delivery records noted by the physician. Chorioamnionitis is the inflammation of fetal membranes and it was defined as the existence of at least two of the following findings: fever, fetal tachycardia and uterine sensitivity. Fetal tachycardia was defined as baseline heart rate 170 beats or above per minute. For preeclampsia, the systolic blood pressure should be measured as 140 mmHg and above or diastolic blood pressure as 90 mmHg and above. In addition to this finding, the definition included the detection of 300 mg or more proteinuria in 24 hours or protein a rate of 2+ in the urine during qualitative examination. Postpartum endometritis was accepted to cover the cases in which post-delivery fever and uterine sensitivity co-existed. Both groups were also compared according to maternal characteristics including maternal age, gravida, parity, gestational week at delivery, prenatal and postnatal weights, preterm birth, preterm and premature rupture of membranes, histories of previous birth (preterm birth or preterm and premature rupture of membranes), abnormal triple screening test results, thyroid disease and chronic hypertension. The patients who had abnormal thyroid function test results (any of TSH, free T3 and free T4 values) during pregnancy and who used thyroid hormones or antithyroid medications or had history of goiter in their past medical history were defined as patients with maternal thyroid disease.

The data were transferred to the computer-compatible SPSS (Statistical Package for Social Sciences) 13.0 statistical data software program. The abnormal GCT group and the control group were compared in terms of their demographic characteristics and perinatal results. The data complying with normal distribution were compared via student t test and the data that did not comply with normal distribution were compared via Mann Whitney-U test; nominal data were compared via Chi-Square tests. $p< 0.05$ was considered to be statistically significant.

According to post-hoc power analysis at $\alpha =0.05$ level, the study has 0.54 power to detect 10% difference of complications between normal and abnormal GCT groups.

RESULTS

Two hundred twenty out of 1886 pregnant women of whom 50 g glucose challenge test was conducted in Akdeniz University School of Medicine Hospital were detected to have abnormal GCT results. The abnormal GCT prevalence was calculated as 11.6%. One hundred twenty three among 220 pregnant women with abnormal GCT results, who had all their pregnancy follow-up visits and deliveries at our hospital and complied with the study criteria, were included in our study as the abnormal GCT group. As for the control group, 89 pregnant women with normal GCT results whose follow-up visits and deliveries had taken place in our hospital and whose files could be obtained were randomised to be included in our study.

Table 1 shows the comparison between the abnormal GCT group and the control group with respect to demographic characteristics.

According to the data obtained from hospital records and laboratory analyses, no renal and cardiac disease were encountered in the abnormal GCT group and in the control group. Thirteen of the 123 patients in the abnormal GCT group were found to have thyroid disease (10.6%). None of the patients in the control group had thyroid disease. Maternal thyroid disease was significantly higher in the abnormal GCT group ($p= 0.02$). Table 2 shows the distribution of pregnant women among groups with accompanying maternal medical conditions.

Table 3 shows the comparison between the groups in terms of fetal and maternal results. Fetal macrosomia was observed in 11 of 123 cases (8.9%) in the abnormal GCT group. As for the 89 patients in the control group, only 6 patients were obser-

TABLE 1: Demographic characteristics.

	50 g Abnormal GCT (n: 123)	50 g Normal GCT (n: 89)	P Value
Age	29.29 4.79	30.42 4.8	0.09
Gravida	1.90 1.0	2.02 1.3	0.46
Parity	0.63 0.79	0.72 0.94	0.49
Gestational Week	38.5 1.30	38.2 1.24	0.07

TABLE 2: Maternal medical conditions.

	50 g Abnormal GCT (n:123)	50 g Normal GCT (n:89)	P Value
Chronic hypertension	3 (2.4%)	2 (2.2%)	0.92
Being a carrier of sickle cell	1 (0.8%)	0	0.39
Thyroid disease	13 (10.6%)	0	0.02

TABLE 3: Fetal and maternal results.

	50 g Abnormal GCT (n:123)	50 g Normal GCT (n:89)	P value
Fetal Weight (g)	3363.90 438.52	3337.66 404.73	0.65
Macrosomia	11 (8.9%)	6 (6.7%)	0.56
Hypocalcemia	0	1 (1.1%)	0.23
Hyperbilirubinemia	2 (1.6%)	1 (1.1%)	0.76
Preeclampsia	3 (2.4%)	1 (1.1%)	0.48

ved to have macrosomia and the macrosomia rate was 6.7%. Although an assessment of both groups in terms of macrosomia resulted in an observation that the macrosomia rate was higher in the abnormal GCT group as compared to the control group, the difference between the two rates was not statistically significant (p= 0.56).

In our study, the delivery method was also specifically examined. Upon an assessment of the indications in the abnormal GCT group, it was detected that the repeat Caesarean section indication in the abnormal GCT group was 28.2% while this ratio was detected as 29.8% in the control group. No statistically significant differences were detected between the two groups with respect to repeat Caesarean sections and elective Caesarean sections. In both groups, the patients underwent Caesarean section with the indications of cephalopelvic disproportion, fetal distress, dysfunctional labor, preeclampsia and preterm activity. No statistically significant differences were detected between the two groups upon a comparison in terms of these indications.

DISCUSSION

Our study assessed whether abnormal GCT was an independent risk factor in terms of perinatal outcomes and it was found that abnormal GCT was not an independent risk factor for adverse perinatal outcomes.

In this study, concomitant, associated diseases were handled; it was observed that the maternal thyroid disease was seen at a higher rate in the abnormal glucose challenge group as compared to the control group, and the difference between the groups was found statistically significant (p= 0.02). The study published by Olivieri et al. in 2000 demonstrated that the average free thyroxine concentrations were significantly smaller in healthy pregnant women with impaired glucose tolerance test results.[4] In contrast to that, the study by Agarwal et al. published in 2006 examined the thyroid function abnormalities and anti-thyroid antibody prevalence in women with a high risk of gestational diabetes.[5] Eighty patients who developed gestational diabetes according to WHO criteria were compared to 221 patients who did not develop the disease in terms of the thyroid function tests, and no statistically significant difference was detected between the two groups. In our study, the maternal thyroid disease was defined to cover patients who had abnormal test results for any of TSH, free T3 or free T4 values, the ones receiving thyroid hormones or anti-thyroid medications or having a history of goitre. Naturally, such a definition does not characterize only a group with an active thyroid disease, but it also encompasses a larger group in such a way to include all the patients that mentioned in their history that they went through or experienced a thyroid disease. As a matter of fact, six of 13 patients who had abnormal glucose challenge test results had normal values for all the thyroid function tests in their current pregnancy, however, they reported presence of a thyroid dise-

ase in the past. No clinical hyperthyroidism or hypothyroidism was detected in any of the remaining seven patients via laboratory tests. Very mild levels of abnormalities were detected in these seven patients in terms of TSH. These minimal changes may be due to the sui generis physiological status of the pregnancy or the laboratory. As a result, it would not be correct to establish a precise association between the abnormal glucose challenge test result and impaired thyroid metabolism in this retrospective study that we carried out. We are convinced that such a suspicious association should be verified via prospective studies with more patients.

In our study, no fetal results were encountered in the records such as shoulder dystocia, newborn intensive support, respiratory distress syndrome or tachypnea. In our study, preeclampsia was observed in the control group at a rate of 1.1% and in the abnormal GCT group at a rate of 2.4%. It was reported that the preeclampsia incidence complicated 2-3% of all pregnancies in the literature although it is known to vary depending on age, ethnicity and parity. Two percent of women that have preeclampsia develop eclampsia. None of the patients in our study were complicated by eclampsia. In a way similar to eclampsia, other rarely seen maternal results such as chorioamnionitis and postpartum endometritis were not encountered in the medical records of any patients included in the study.

We encountered publications indicating that gestational diabetes was associated with increased operative delivery risk and high Caesarean section rates. In our study, there was no evidence that the operative delivery risk and Caesarean section risk were increased in pregnant women with abnormal glucose challenge test.

Our study demonstrated no difference between the patients with abnormal glucose challenge test and the patients in the control group. Our study was a study that had similar characteristics with the studies conducted by Stamilio et al. and also Dudhnba et al. with regards statistical assessment and materials as well as method. It is seen that the people with abnormal glucose challenge test results in the studies of Stamilio et al. and Duduhnbai et al. had different demographic characteristics when compared to the control group.[4,6] Both studies found that the age, parity and body mass indexes were found to be significantly higher in the abnormal glucose challenge test group as compared to the control group, and found that the gestational age at birth was significantly smaller. Considering that our aim was to assess only the effect of abnormal glucose challenge test on the perinatal results, we believe it is an advantage for our study that the variables such as age, parity and gestational age at birth, which could affect the results by themselves, did not vary between the two groups. The study by Stamilio et al. detected a higher rate of chronic hypertension and sickle cell anemia carrying status in the abnormal glucose challenge group in terms of concomitant, associated diseases. It is not known how these findings can be interpreted clinically or what their clinical importance is.

In the conclusion of the study conducted by Stamilio et al. it was stated that average birth weights, rate of Caesarean sections and shoulder dystocia rates were higher in the abnormal glucose challenge group as compared to the control group, and it was claimed that abnormal glucose challenge test was an independent risk factor for negative perinatal results including macrosomia, antenatal mortality, shoulder dystocia, endometritis and Caesarean section. In the mentioned study the abnormal GCT cohort more frequently had adverse perinatal outcome (odds ratio [OR] 5.96, 95% confidence interval [CI] 1.47, 24.16). As a result, an abnormal glucose challenge test was defined as an independent risk factor for negative perinatal results. According to the results obtained from the same analyses, variables such as body mass index, nulliparity and gestational age at birth were also noticeable as variables which may have an impact on the perinatal results. A similar study carried out by Duduhnbai et al. found that abnormal GCT did not enhance negative perinatal results as compared to the control group, that is, the group with normal GCT.

In the study conducted by Stamilio et al., the Coustan-Carpenter criteria were used for the diagnosis of gestational diabetes whereas in our study, we used the criteria of the National Diabetes Data group as the basis for abnormal glucose tolerance test values. If the Carpenter-Cousten criteria had been taken, a higher number of patients would had been diagnosed as gestational diabetes and the number of abnormal GCT patients would be smaller.[7] Naturally, it would be excepted that there would be more overlapping for all the maternal and fetal results between the abnormal GCT group and the control group.

To touch upon the limitations on our study, first of all, our study is a retrospective study and all our information is based on the data in the hospital records. We should also point out that our study is not powerful enough to compare the conditions with a prevalence less than 6% such as preeclampsia, chorioamnionitis and postpartum endometritis. It was observed that the weights of patients before and after pregnancy were regularly recorded, however that the heights of patients were rarely recorded. Therefore, it was not possible to assess the direct association of the body mass index as a parameter, which has a very important role in the pathophysiology of diabetes and gestational diabetes, with the perinatal results in our study and its relations with abnormal GCT.

Rey et al. reported that positive glucose challenge test and a single high level in OGTT raised the risks for fetal macrosomia, neonatal hypoglycemia and neonatal hyperbilirubinemia.[8] Okun et al. demonstrated that the macrosomia incidence was increased for patients with abnormal glucose challenge test results and normal OGTT values.[9] In another study, Verma et al. reported that there was no relation between the increased glucose levels measured via a glucose challenge test, glucose tolerance test, fasting blood glucose or postprandial test at 2 hours and macrosomia in people with abnormal GCT and negative OGTT.[10]

Similar to these studies, the National Diabetes Data group screening algorithm and WHO protocol has been questioned by some researchers for perinatal results including shoulder dystocia, Caesarean section, fetal macrosomia and preeclampsia for patients that have not been diagnosed with diabetes, however, for the ones with certain levels of glucose intolerance it has been specified that there was an increase in such risks.[11-14] In contrast with that, Ramtoola et al. reported that there was no increase in perinatal mortalities in patients not diagnosed with diabetes in the study they carried out using WHO diagnostic criteria.[15]

The results obtained in all those previous studies differ from each other extensively. One reason for this may be absence of a globally recognized common screening test and diagnosis scheme for gestational diabetes, and presence of too many uncontrollable variables aggravating the discrepancies of the results such as ethnic, regional and personal characteristics in those studies.

It has been demonstrated in many studies that fetal and maternal risks increase in association with gestational diabetes. However, the effect of glucose metabolism impairments that develop in pregnancy other than gestational diabetes, for example, abnormal glucose challenge test on perinatal outcomes is controversial as can be understood by the mentioned studies. The studies targeted at understanding whether any impairment in glucose metabolism indicated or caused an increased risk for poor perinatal outcomes, and pointed that pathophysiologic mechanisms are missing in literature. We are convinced based on the available data that glucose challenge test should be used only to detect gestational diabetes. We believe that double-step glucose screening test is the most appropriate method in screening gestational diabetes.

In conclusion, following up patients for abnormal glucose challenge test for diagnosis of gestational diabetes is an approach that is ineffective in terms of costs. It also unnecessarily increases patient stress since it is still disputable whether the gestational diabetes screening improves perinatal results.

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