Efficacy of 50-G Glucose Challenge Test in The Diagnosis of Gestational Diabetes Mellitus

50 G Glukoz Yükleme Testinin Gestasyonel Diyabet Tanısındaki Etkinliği

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─────────── **Abstract** ───────────

Aim: Our aim in this study was to investigate the efficacy of 50 g glucose challenge test (GCT) in the diagnosis of gestational diabetes mellitus (GDM) and to determine a cut-off value for screening.

Methods: 50-g GCT was performed in 444 pregnant women at 24-28 gestational weeks. The threshold was taken as 130 mg/dl in order not to miss GDM cases. A plasma glucose level of ≥130 mg/dl at the first hour was considered to be a positive result and 100-g oral glucose tolerance test (OGTT) was given to these women.

Results: The cut-off value for 50-g GCT was found to be 145 mg/dl. The sensitivity and specificity of the test for predicting GDM at the levels of ≥145 mg/dl were determined to be 96.30% and 80.34%, respectively. The sensitivity and specificity of the test at the level of 88 mg/dl determined for fasting blood glucose cut-off value were found to be 48.15% and 70.84%, respectively.

Conclusion: It was concluded that the efficacy in making diagnosis of GDM was increased at the first hour blood glucose levels of ≥145 mg/dl, especially in 50-g GCT, and fasting blood glucose level could not be a good screening test for GDM. *(The Medical Bulletin of Haseki 2014; 52: 181-6)*

Key Words: Gestational diabetes, oral glucose tolerance test, pregnancy

─────────── **Özet** ───────────

Amaç: Bu çalışmada amacımız, 50 g glukoz challenge test (GCT) ile açlık kan glukoz değerlerinin gestasyonel diyabet (GDM) tanısında etkinliğini araştırmak, tarama için bir cut-off değeri belirlemektir.

Yöntemler: Dörtyüz kırk dört gebeye 24-28 gestasyonel haftaları arasında 50 gr GCT uygulandı. Gestasyonel diyabet hastalarını atlamamak için eşik değer 130 mg/dl olarak alındı. Plazma glukoz düzeyinin birinci saatte 130 mg/dl ve üzerindeki sonuçlar pozitif olarak kabul edildi ve bu gebelere 100 gr oral glukoz tolerans testi (OGTT) uygulandı.

Bulgular: 50 g GCT için cut-off değeri 145 mg/dl olarak bulundu. 145 mg/dl ve üzerindeki değerlerde testin GDM'yi öngörmede duyarlılık %96,30; özgüllük %80,34 olarak belirlendi. Açlık kan glukoz cut-off değeri için belirlenen 88 mg/dl'da duyarlılığın % 48,15 özgüllüğün %70,84 olduğu bulundu.

Sonuç: Özellikle 50 g GCT'de birinci saat kan glukoz değeri 145mg/dl ve üzerindeki değerlerde gestasyonel diyabet tanısı koymada etkinliğin arttığı , açlık kan glukoz düzeyin GDM için iyi bir tarama testi olamayacağı sonucuna varıldı. *(Haseki Tıp Bülteni 2014; 52: 181-6)*

Anahtar Sözcükler: Gestasyonel diyabet, oral glukoz tolerans test, gebelik

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Introductıon

Gestational diabetes mellitus (GDM) is glucose intolerance with onset or first recognition during pregnancy. Placental lactogen, placental growth hormone, cortisol, estrogen, and progesterone are the leading factors effective in the occurrence of insulin resistance (1).

A wide range of tests have been used to screen for GDM. Fasting blood glucose (FBG) measurement and random blood glucose (SBG) test are among these screening tests (2). They are easy to use; but there are insufficient data about the sensitivity and specificity of these tests. The most common screening test is 50-g glucose challenge test (GCT). The International Association of Diabetes and Pregnancy Study Groups (IADPSG) recommends a 75-g oral glucose tolerance test (OGTT) at 24-28 weeks of gestation in all women not previously found to have overt diabetes or GDM (3).

Although GDM screening is absolutely recommended, there is no consensus on screening, diagnosis and follow-up of the disease among World Health Organization (WHO), American Diabetes Association (ADA) and American College of Obstetricians and Gynecologists (ACOG) (4-6). ADA advocates the use of laboratory screening tests for only pregnant women with risk factors (7). World Health Organization (WHO) recommends the screening test to be performed on pregnant women with high fasting glucose values or random glucose values, pregnant women in certain ethnic groups, pregnant women with a history of fat baby in their previous pregnancies or pregnant women older than 25 years of age (5). ACOG suggests that screening of all population might be more sensitive (6)

The diagnosis of GDM is made with abnormal 100-g OGTT values. The GDM diagnosis is made if at least two of fasting, 1-2-3. hours plasma glucose values (95,180, 155 and 140 mg/dl values) are equal or higher than the threshold value (8).

Our aim in this study was to investigate the efficacy of FBG values obtained with 50-g GCT in the diagnosis of GDM and to determine a cut-off value for screening.

Methods

The study was approved by the Ethics Committee of Selçuk University Selçuklu Medical School for this study. Routine FBG values of 444 pregnant women who attended Kulu State Hospital between January 2012 and September 2012 were recorded. Afterwards, 50-g GCT was performed in these pregnant women between 24 and 28 weeks of gestation. Fifty gram glucose dissolved in 200 mL of water was administered regardless of whether the patients were fasting. Plasma glucose concentrations were measured using the glucose oxidase method 1 hour after the venous blood samples were obtained. The threshold value was taken as 130 mg/dl in order not to miss GDM cases that can be seen with lower GCT results. A plasma glucose level of ≥130 mg/dl was considered to be a positive result and 100-g OGTT was given to these pregnant women. Before 100-g OGTT, the pregnant women were asked to diet for 3 days including at least 150 gram carbohydrate per day. The pregnant women were given no food starting at 12 a.m. before OGTT administration. After 10-12 hours fasting, plasma glucose levels were measured using the glucose oxidase method. Then 100 gram glucose dissolved in 400 mL of water was administered and the plasma glucose was measured at 1 hour, 2 hour and 3 hour intervals. The results of the 100-g OGTT were evaluated by using the Carpenter-Coustan modification of the O'Sullivan-Mahan criteria. A FBG level of 95 mg/dl, 1-hour blood glucose level of 180 mg/dl, 2-hours blood glucose level of 155mg/dl and 3-hours blood glucose level of 140 mg/dl were accepted to be limit values according to Carpenter-Coustan modification of the O'Sullivan-Mahan criteria. If any two or more of the test results were higher than the indicated limit values, the pregnant women were diagnosed to have GDM.

Statistical Evaluations

NCSS (Number Cruncher Statistical System) 2007&PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA) program was used for the statistical analysis. During the assessment of the study data, the student t-test was used for comparison of the normally distributed parameters (age, 50-g GCT, FBG) between the groups, in addition to descriptive statistical methods (mean, standard deviation, frequency, percentage). ROC curve analysis and diagnostic screening tests were used to determine the cut-off point for FBG and 50-g OGTT test values. The results were evaluated in 95% confidence interval and at a significance level of $p < 0.05$.

Results

The study was performed on 444 pregnant women who attended Kulu State Hospital between January 2012 and September 2012. Twenty-seven of the cases had GDM and 417 of them did not have GDM. The age of the subjects with GDM were determined to be statistically significantly greater than that of those without GDM (p=0.004). GDM was mostly seen in the age group of 31-35 years (Table1).

While the average 1-hour blood glucose value on the GCT in pregnant women with GDM was 179.41±31.20 mg/dl, the average 1-hour blood glucose value in those without GDM was found to be 121.72±27.46 mg/dl. A statistically significant difference was observed between 50-g GCT measurements according to GDM status (p=0.001). 50-g OGTT levels in subjects with GDM were significantly higher (Table 2).

Based upon this significance, it was considered to calculate a cut-off point for 50-g GCT. ROC analysis and diagnostic screening tests were used to determine the cut-off point for 50-g GCT (Table 3).

The sensitivity, specificity, positive prediction value, negative prediction value and accuracy in the prediction of GDM in cases with a 50-g OGTT value of ≥145 mg/dl were determined to be 96.30%, 80.34%, 24.07%, 99.70% and 81.31%, respectively. The relative risk at this point is 80.89% (Table 3). Area under the ROC curve obtained and standard error were determined to be 0.718 and 0.058, respectively (Table 4, Figure 1).

The average FBG values in pregnant women with GDM without GDM was found to be 89.22±13.14 mg/dl and 83.04±11.85 mg/dl, respectively. A statistically significant difference was found between FBG measurements according to GDM status (p=0.009). FBG levels in cases with GDM were significantly higher (Table 2).

Based upon this significance, it was considered to calculate the cut-off point for FBG. ROC analysis and diagnostic screening tests were used to determine the cut-off point for FBG. The cut-off value found for FBG level was 88 mg/dl. The sensitivity, specificity, positive prediction value, negative prediction value and accuracy in the prediction of GDM in cases with ≥88 mg/dl were determined to be 48.15%, 70.84%, 9.70%, 95.45% and 69.46%, respectively (Table 5). Area under the curve in ROC curve obtained and standard error were determined to be 0.585 and 0.061, respectively (Table 4, Figure 1).

Table 1. Age evaluation according to GDM Status

	GDM (+) (n=27) Mean±SD	GDM (-) (n=417) Mean±SD	p
Age (year)	29.73±5.51	26.31±5.78	0.004**
	n (%)	n (%)	
≤20 years	1 (%3.7)	66 (%15.8)	
21-25 years	5 (%18.5)	141 (%33.9)	
26-30 years	8 (%29.7)	112 (%26.9)	
31-35 years	10 (%37.0)	65 (%15.6)	
≥36 years	3 (%11.1)	33 (%7.8)	
Student t-test was use GDM: Gestational Diabetes Mellitus			

Table 2. 50 g GCT and FBG evaluation according to GDM Status

	GDM (+) (n=27)	GDM (-) (n=417)	P
	Mean±SD	Mean±SD	
50-g GGT (mg/dl)	179.41±31.20	121.72±27.46	0.001**
FBG (mg/dl)	89.22±13.14	83.04±11.85	0.009**
Student t- test **p < 0,01 GCT:Glucose Challenge Test SD: Standart deviation			

Table 3. The results of diagnostic screening tests at various points for 50-g GCT

50-g GCT (mg/dl)	Sensitivity (%)	Specificity (%)	Positive prediction value (%)	Negative prediction value (%)
≥135	100.00	67.39	16.56	100.00
≥140	100.00	75.30	20.77	100.00
≥145	**96.30**	**80.34**	**24.07**	**99.70**
≥150	81.48	82.97	23.66	98.58
≥155	77.78	86.81	27.63	98.37

Discussion

Gestational diabetes mellitus is defined as glucose intolerance with onset or first recognition during pregnancy. GDM is among the leading causes increasing the morbidity in the mother and the fetus during pregnancy as well as perinatal mortality. Therefore, screening tests for diabetes are performed in all pregnant women. Although there continues to be a lack of consensus on the glucose tolerance tests used for screening, one-hour 50-g glucose test is used as the most common screening test worldwide.

Hyperglycemia develops in 1%-6% of pregnancies to meet the criteria for a diagnosis of GDM (9). This value shows variability between 1-14% according to the various countries and different populations (10). The prevalence of GDM became the subject of various researches. In a study by Chang AL et al. performed on 2966 patients, the prevalence of GDM was determined to be 6.2%. The authors determined that the mean age in patients with GDM was statistically greater in those without GDM (11). In a study by Wahi P et al., the rate of the GDM group in the pregnant population was found to be 6.94% (12). In a retrospective study by Rajab KE et al. performed on 49.552 pregnant women, the prevalence of GDM was found to be 10.1% (13). In a study by Sagün et al. performed on 426 pregnant women, the prevalence of GDM was found to be 5.2% (14). Also in our study, in harmony with the literature, GDM was determined in 27 (6.1%) of 442 pregnant women.

It is known that maternal age is a risk factor for GDM. The American Diabetes Association (ADA) determined 25 years of age as a cut-off point for GDM and showed the age of ≥25 years among the risk factors for GDM (7). The relationship between GDM and maternal age has been investigated in various studies. In a study performed by Dudhbhai M et al., the authors showed that the age of patients with impaired 100-g OGTT and GDM were higher compared to those with normal OGTT (15).

In a study by Turgut et al. performed in 2011, the authors determined that the percentage of GDM was increased markedly with advancing age. They found the highest rate to be 33% at 44 years of age (16). In a study by Ozyurt et al. performed on 370 pregnant women, the prevalence of GDM was found to be 9.2%. They also
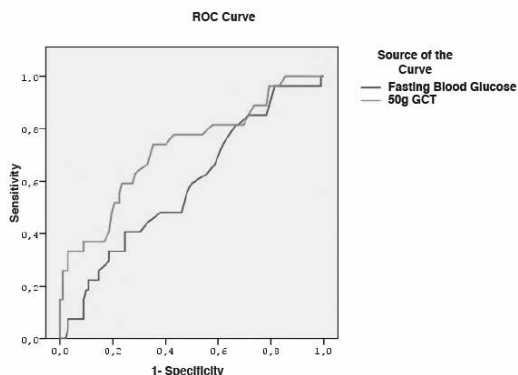

Figure 1. ROC curve obtained for FBG and 50-g OGTT

Table 4. The results of diagnostic screening tests at various points for FBG

FBG (mg/dl)	Sensitivity (%)	Specificity (%)	Positive prediction value (%)	Positive prediction value (%)
86	48.15	64.10	8.02	95.00
87	48.15	66.75	8.61	95.19
88	**48.15**	**70.84**	**9.70**	**95.45**
89	44.44	73.98	10.00	95.34
90	44.44	76.14	10.81	95.47

Table 5. Area Under the Curve 50g GCT and FBG

	Area Under the Curve				
	Area	Std. Error(a)	p	95% Confidence Interval	
				Upper	Lower
50-g GGT	0.718	0.058	0.001	0.605	0.831
FBG	0.585	0.061	0.176	0.466	0.704

found that the number of pregnant women diagnosed with GDM increased with advancing age (17).

In our study, it was also determined that the number pregnant women diagnosed as having GDM increased with advancing age. The mean age of the pregnant women with GDM and those without GDM was found to be 29.73±5.51 years and 26.31±5.78 years, respectively. The difference was statistically significant (p=0.004). In the research of GDM prevalence in various age groups, it was observed that GDM was more common especially in pregnant women aged 31-35 years (30.8%) compared to those in the other age groups.

Today, various studies have been performed to determine a cut-off value for 50-g GCT used for GDM screening. Based upon the fact that especially ethnic characteristics might affect the results of the test, many investigators in the world have offered a threshold value for 50-g GCT (18,19). One of the biggest difficulties in determining a threshold value for GCT in identifying women who will need to continue to OGTT or in establishing a direct diagnosis of GDM is racial differences. Many investigators have worked to find a threshold value for their own societies. Thus, values such as 130, 135, 140 mg/dl were suggested for necessity of OGTT (8,20,21). Nahum and Huffaker recommended race-specific screening test thresholds as screening test results differed significantly by race (22). In a study by Gandevani et al. performed on 1804 pregnant women, the authors determined 135 mg/dl to be the cut-off value for GCT which showed a sensitivity and specificity of 95% and 80%, respectively (23). De Serday et al. determined in a study on 473 pregnant women that 137 mg/dl to be the most convenient cut-off value for 1-hour GCT. They found the optimal sensitivity for the 1-hour 50-g test screening at this value as 66.7% (24).

In our study, while average of the result of 1-hour GCT in pregnant women with GDM was 179.41±31.20 mg/dl, it was found to be 121.72±27.46 mg/dl for those without GDM. The difference was statistically significant (p=0.001). Based upon this significance, we performed a study to determine a cut-off point for 50-g GCT. In conclusion, the cut-off value of first hour glucose that we used in screening for GDM was found to be 145 mg/dl. When we considered GCT threshold value to be 145 mg/dl, the sensitivity and specificity values, positive predictive and negative predictive values were found to be 96.30%, 80.34%, 24.07% and 99.70%, respectively. The sensitivity especially at this value was determined to be quite high. ROC curve analysis and diagnostic screening tests were used to calculate the cut-off point. Area under the curve occurred and standard error were found to be 0.718 and 0.058, respectively. Based on all these results, it was demonstrated that the result of 145mg/dl (cut-off value that we found in 50-g GCT) was a good threshold value and it should be proceeded to direct diagnostic test with the results in this value and higher than this value.

Various tests were used for GDM screening until today. Especially whether FBG level could be used for screening or not became a subject of research. In various studies, many investigators researching the importance of FBG in screening for GDM determined a cut-off value for screening. When Khan et al. considered the cut-off value as 82 mg/dl in their study performed to determine the cut-off value for FBG in screening for GDM, the authors found the sensitivity, specificity, positive predictive and negative predictive values of the test to be 66.66%, 81.25%, 70% and 78.78%, respectively. When they considered the cut-off value as 95 mg/dl, the authors found the sensitivity, specificity, positive predictive and negative predictive values of the test to be 64%, 85.71%, 80% and 72.72%, respectively (25). Pericchini et al. determined the cut-off value for FBG as 86 mg/dl and they found the sensitivity and specificity of the test to be 81% and 76%, respectively. The authors found that this cut-off value might be applied easier than 140 mg/dl which was the limit value of 50-g GCT in screening for GDM (26). In a study performed by Agarwal MM et al., when the cut-off value for FBG was considered to be 80 mg/dl, the sensitivity was 94.7% and false negative rate was 1.6%. When the authors considered the cut-off value for FBG as 95 mg/dl, they found the specificity and false positive rate to be 94% and 4.2%, respectively (27).

In our study, the average FBG values in pregnant women with GDM was found to be 89.22±13.14 mg/dl and the average FBG in those without GDM was found to be 83.04±11.85 mg/dl. This difference was statistically significant (p=0.009). Based upon this significance, it was considered to calculate a cut-off point for fasting blood glucose. The cut-off value for FBG level in GDM screening was found to be 88 mg/dl. The sensitivity, specificity, positive prediction value, negative prediction value and accuracy in the prediction of GDM in cases with a FBG level of ≥88 mg/dl were determined to be 48.15%, 70.84%, 9.70%, 95.45% and 69.46%, respectively. Area under the ROC curve obtained and standard error were determined to be 58.5% and 6.1%, respectively. The greater is the area under the ROC curve, is the better sensitivity and the lower specificity of the test. The value of the area and the sensitivity we found were observed to be low values.

In this study, GCT, which is commonly used in GDM screening, was determined to be a favorable screening test. According to our study, 145 mg/dl was found to be the cut-off value for 1-hour glucose in GCT. It was seen that the specificity of the test was quite high especially

at the values ≥145 mg/dl. Additionally, it was concluded with this study that FBG could not be an efficient test in GDM screening since the sensitivity and specificity of the values determined for FBG were low.

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