original article

The relationship between markedly elevated glucose challenge test results and the rate of gestational diabetes mellitus and gestational impaired glucose tolerance

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BACKGROUND AND OBJECTIVES: Even though the 50 g oral glucose challenge test (GCT) is the most commonly used screening modality for gestational diabetes mellitus (GDM), no consensus for the diagnostic approach is available to patients with a markedly elevated GCT result. We aimed to evaluate the diagnostic utility of markedly elevated GCT results and the impact of age using the oral glucose tolerance test (OGTT) as gold standard.

DESIGN AND SETTING: Retrospective study conducted in a women's hospital in Ankara, among patients who underwent GCT from January 2005 to December 2008.

PATIENTS AND METHODS: In this retrospective study, we included 626 pregnant women who underwent a 3-hour 100 g OGTT after a GCT result ≥180 mg/dL among 29 842 women. We calculated positive predictive values (PPV) of each GCT category to diagnose GDM and both GDM and gestational impaired glucose tolerance (GIGT).

RESULTS: A GCT result of ≥240 mg/dL provided 100% PPV for the diagnosis of GDM and a result of >230 mg/dL provided 100% PPV for the diagnosis of GDM + gestational impaired glucose tolerance (GIGT), according to both, National Diabetes Data Group (NDDG) and Carpenter and Coustan (CC) criteria. A result of ≥200 mg/dL provided 100% PPV for diagnosing GDM+GIGT in patients older than 35 years, according to the CC criteria.

CONCLUSIONS: The GCT result of 200 mg/dL is an ideal cutoff value for the diagnosis of GDM + GIGT in patients ≥35years, and OGTT can be omitted in these patients. In younger patients, the cutoff value should be chosen as 230 mg/dL.

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance of varying degrees of severity with onset or first recognition during pregnancy.[1] Approximately, 7% of all pregnancies (the prevalence ranges 1% to 14% depending on ethnicity) are complicated with GDM.[2] GDM is associated with increased fetal and maternal morbidity; therefore, a correct diagnosis is important,[3] but overdiagnosis increases medical costs and maternal anxiety.[4] There are controversies about diagnostic tests and criteria for GDM.[5,6] Since the oral glucose tolerance test (OGTT) is time consuming, expensive, and inconvenient, easier tests with the same diagnostic value have been studied.[7-11]

The 50 g oral glucose challenge test (GCT) is the most commonly used laboratory screening modality for GDM in many parts of the world.[5] It is easily tolerated among the majority of the pregnant women and can be performed at any time during the day because fasting is not required. Different screening thresholds have been utilized with varying sensitivities,[2] but there is no consensus on a diagnostic approach to patients with a markedly elevated GCT result.

In 1982, Carpenter and Coustan (CC) reported that patients with a GCT result of more than 182 mg/dL had a 95% chance of having GDM.[7] The 2003 Canadian Diabetes Association guidelines recommend-

ed diagnosing GDM if the glucose level 1 hour after the GCT is 190 mg/dL.[12] However, the American Congress of Obstetricians and Gynecologists (ACOG) guidelines for GDM advised GCT only for screening purposes and did not define any threshold.[3] Even though there is a lack of consensus in patients with markedly elevated screening results, there is a tendency to diagnose GDM, especially, with GCT results ≥200 mg/dL.[13] Our aim in this study was to evaluate the association between markedly elevated (≥180 mg/dL) GCT results and OGTT for the diagnosis of GDM and gestational impaired glucose tolerance (GIGT) according to both National Diabetes Data Group (NDDG) and CC criteria and whether this association differs in different age groups.

PATIENTS AND METHODS

This retrospective study was approved by the ethics committee of our hospital. We retrieved the records of patients who underwent a GCT between the years 2005 and 2008 from the hospital information system. We found 29 842 women who fulfilled the criteria. Among these women, 626 women with a GCT result ≥180 mg/dL underwent OGTT. These patients comprised the study group. We screened for GDM in all nondiabetic pregnancies using a 2-step standard protocol. At 24 to 28 weeks, all pregnant women without previously diagnosed diabetes were offered screening for GDM with a 1-h 50 g GCT during a routine prenatal visit, regardless of the time or the fasting. In this study, all the patients underwent both GCT and OGGT. The results of GCT and OGTT were not influenced by each other.

We reviewed the results according to both NDDG (8 patients) (plasma glucose thresholds: fasting 105 mg/dL, 1-h 190 mg/dL, 2-h 165 mg/dL, 3-h 145 mg/dL) and CC criteria (8 patients) (plasma glucose thresholds: fasting 95 mg/dL, 1-h 180 mg/dL, 2-h 155 mg/dL, 3-h 140 mg/dL). By both criteria, GDM is defined as at least two plasma glucose measurements at or higher than the reported cutoff values. GIGT is defined as a 1 plasma glucose measurement at or higher than the reported cutoff values during the diagnostic test.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) (SPSS Inc, Chicago, IL, USA) version 10. Receiver-operator characteristic (ROC) curves were generated and areas under the curve (AUC) were calculated for each data set of GDM, and both GDM and GIGT were diagnosed by NDDG and CC criteria. The significance of AUCs were controlled with Bonferroni Corrections (type I error rate=0.05/4=0.0125). For the purpose of analysis, screening test results were categorized by 10 mg/dL increments. We investigated positive predictive values (PPV) of each GCT category to diagnose GDM and GDM + GIGT, according to the NDDG and CC criteria. The cutoff points were computed if all the patients were diagnosed as GDM and GDM + GIGT (100% PPV) in a given 50 g GCT results. We further investigated cutoff points of GCT results in patients ≥35 years of age.

RESULTS

The mean (standard deviation) age of subjects were 31.4 (5.9); 11% (n=69) were less than 25 years old, 59.6% (n=373) were 25 to 34 years, and 29.4% (n=184) were equal to or more than 35 years old. Thirty-four percent subjects (n=213) had GDM, 53% (n=332) had GDM + GIGT by NDDG criteria, and 48.1% (n=301) had GDM, and 73.3% (n=396) had GDM + GIGT by CC criteria. The diagnosis of GDM was confirmed in only 25.4% of patients according to the NDDG criteria and 37.7% according to the CC criteria with GCT results between 180 and 189 mg/dL, and 39.5% of patients according to the NDDG criteria and 60.5% according to the CC criteria with GCT results between 200 and 209 mg/dL. A GCT result of ≥240 mg/dL provided 100% PPV for the diagnosis of GDM according to both criteria and was chosen as cutoff points (**Table 1**). For GDM and GIGT together, the diagnosis was confirmed in 40.7% of the patients according to the NDDG criteria, 50.8% according to the CC criteria with GCT results between 180 and 189 mg/dL, 65.4% according to the NDDG criteria, and 74.1% according to the CC criteria with GCT results between 200 and 209 mg/dL. A GCT result of ≥230 mg/dL provided 100% PPV for the diagnosis of GDM + GIGT according to both criteria (**Table 1**).

The AUC calculated by the ROC curve analysis of GCT results ≥180 mg/dL for diagnosing GDM and GDM + GIGT using NDDG and CC criteria are given in **Table 2**. The AUC for GDM using the NDDG and CC data were 0.653 and 0.658, which are statistically significant ($P<.0001$ and $P<.0001$, respectively). The AUC for GDM + GIGT using NDDG and CC criteria were 0.674 and 0.680, which are statistically significant ($P<.0001$ and $P<.0001$, respectively). ROC curves of each analysis are given in **Figure 1**.

In patients ≥35 years, a GCT result of ≥220 mg/dL provided 100% PPV for the diagnosis of GDM according to both criteria, and for the diagnosis of GDM + GIGT according to the NDDG criteria. A result of ≥200 mg/dL provided 100% PPV for diagnosing GDM + GIGT in patients older than 35 years according to the CC criteria and was chosen as the cutoff point (**Table 3**). The AUC calculated by the ROC

Table 1. Rate of GDM and GDM + GIGT diagnosed according to GCT results using NDDG criteria and Carpenter and Couston criteria in all ages.

National Diabetes Data Group									
	GDM					GDM + GIGT			
		+	-	Total			+	-	Total
GCT	≥240	6 (100%)	0	6	GCT	≥230	10 (100%)	0	10
	<240	207 (33.4%)	413 (66.6%)	620		<230	322 (52.4%)	294 (47.6%)	616
	Total	**213 (34%)**	**413 (66%)**	**626**		**Total**	**332 (53%)**	**294 (47%)**	**626**
Carpenter and Coustan criteria									
	GDM					GDM + GIGT			
		+	-	Total			+	-	Total
GCT	≥240	6 (100%)	0	6	GCT	≥230	10 (100%)	0	10
	<240	207 (33.4%)	413 (66.6%)	620		<230	322 (52.4%)	294 (47.6%)	616
	Total	**213 (34%)**	**413 (66%)**	**626**		**Total**	**332 (53%)**	**294 (47%)**	**626**

GDM: Gestational diabetes mellitus; GIGT: gestational impaired glucose intolerance; GCT: glucose challenge test.

curve analysis of GCT results ≥180 mg/dL for patients older than 35 years for diagnosing GDM and GDM + GIGT using NDDG and CC criteria are given in **Table 4**. The AUC for GDM using the NDDG and CC data were 0.599 and 0.597, which are statistically not significant because of Bonferroni corrections (P=.0293 and P=.0331, respectively). The AUC for GDM + GIGT using NDDG criteria was 0.629, which is statistically significant (P=.0070), and the AUC for GDM + GIGT using CC criteria was 0.630 (P=.0127), which is has borderline statistical significance after Bonferroni correction. ROC curves of each analysis are provided in **Figure 2**.

Table 2. Receiver-operator characteristic curve analysis of GCT results ≥180 mg/dL for diagnosing GDM and GDM + GIGT using NDDG and CC criteria in all patients.

Criteria	Diagnosis	AUC	95% CI	*P*
NDDG	GDM	0.653	0.604-0.703	<.0001
	GDM + GIGT	0.674	0.627-0.716	<.0001
CC	GDM	0.658	0.613-0.703	<.0001
	GDM + GIGT	0.680	0.635-0.725	<.0001

GCT: Glucose challange test; GDM: gestational diabetes mellitus; GIGT: gestational impaired glucose intolerance; NDDG: National Diabetes Data Group; CC: Carpenter and Coustan; AUC: area under curve; CI: confidence interval.

DISCUSSION

OGTT is designed on the basis that the diabetogenic stress of pregnancy is best recognized in the fed state. OGGT has become established as the gold standard diagnostic test for gestational diabetes. However, it is time consuming, expensive, and unpleasant; therefore, new and easy diagnostic tests need to be validated against OGTT.[5]

Two main criteria, NDDG and CC, are commonly used to examine 3-h OGTT. In 1964, O'Sullivan and Mahan[14] for the first time suggested that pregnancy glucose values obtained during a 100 g 3-h OGTT should be used to diagnose GDM. In 1979, the NDDG recommended new diagnostic thresholds, and most laboratories changed from using venous whole blood samples to using plasma or serum samples.[1] In 2000, the American Diabetes Association (ADA) revised the recommendation for the GDM diagnostic criteria and proposed adoption of CC thresholds, which represented the most accurate conversion of the O'Sullivan and Mahan criteria, rather than the NDDG thresholds, to reduce the risks of adverse perinatal outcomes attributable to GDM.[15] The prevalance rates of GDM have been increased by using CC criteria.[16,17] ACOG and ADA currently recommend the use of CC criteria.[2,3]

In this study, we investigated the PPV of GCT resuts ≥180 mg/dL for diagnosing GDM and both GDM and GIGT according to the NDDG and CC criteria in Turkish pregnant women. The PPV of GCT result between 180 to 189 mg/dL was only 25.4% according to the NDDG diagnostic criteria, and 37.7% according to the CC diagnostic criteria. We reached 100% PPV at the GCT level of 240 mg/dL and greater according to both criteria. When we considered the predictive value of GCT for diagnosing both GDM and GIGT, we reached 100% PPV at the GCT level of 230 mg/dL and greater according to both criteria.

Several studies have been performed in establishing

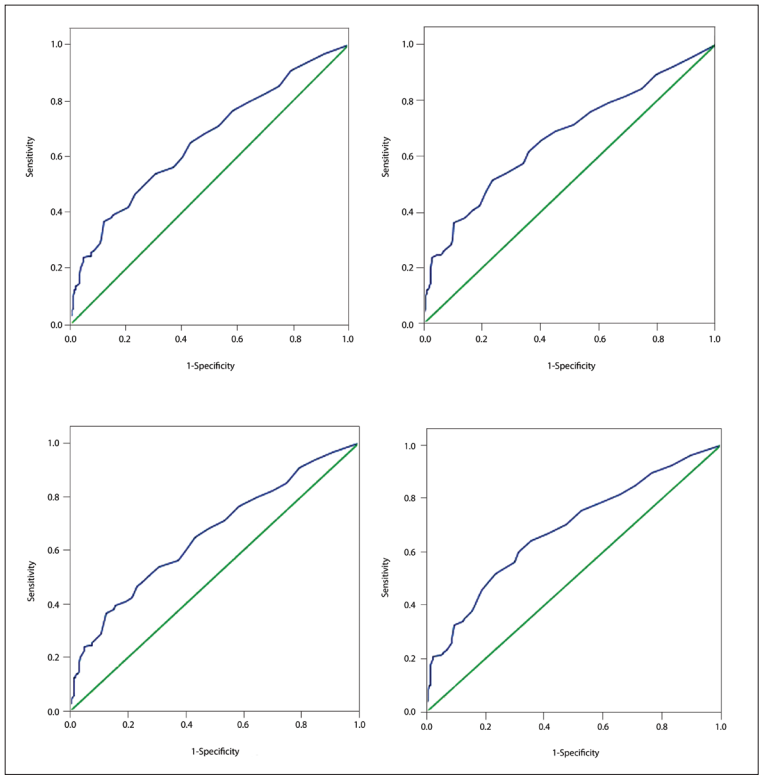

Figure 1. ROC curves for diagnosing GDM and GDM+GIGT using NDDG and CC criteria in all ages.

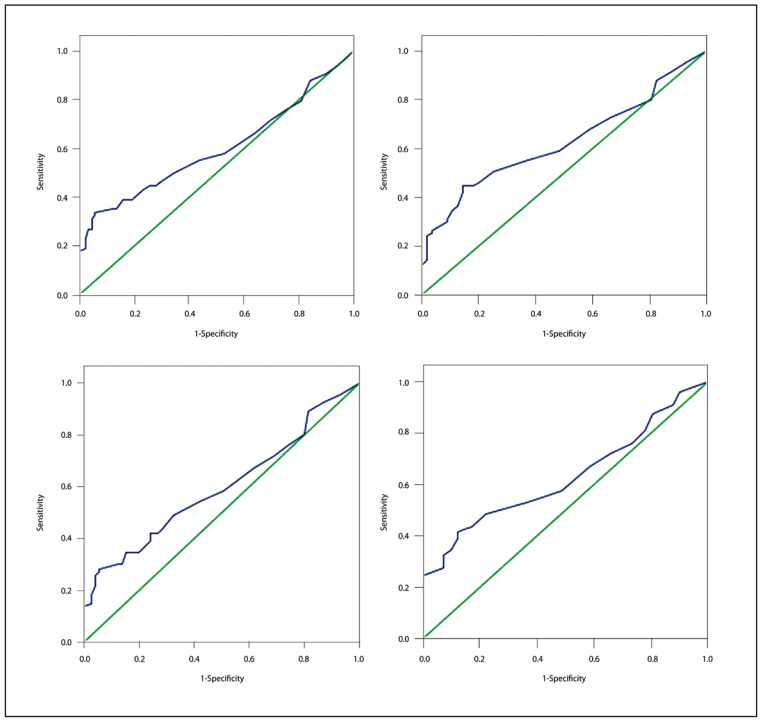

Figure 2. ROC curves for diagnosing GDM and GDM+GIGT using NDDG and CC criteria in patients ≥35 years.

the diagnostic value of markedly elevated GCT levels for gestational diabetes.[7-11] Lanni and Barrett reported that a cutoff value 200 mg/dL predicted only 47% to 54% of GDM cases, so it was inappropriate for GDM to be diagnosed based on the GCT, and this might lead to overdiagnosis.[10] Cheng et al reported 100% PPV for GCT results ≥230 mg/dL for diagnosing GDM according to the CC criteria, which was similar to our findings.[11]

The prevalence of GDM differs depending on the population being screened. In studies conducted in North America, the prevalence was higher in Asian, African American, Native American, and Hispanic compared to non-Hispanic white patients.[16] Because of variations in the prevalence based on ethnicity, it has been suggested that race-specific glucose screening test thresholds should be used.[18] Esakoff et al reported different sensitivity and specificity results for GCT in different ethnic groups.[19] Dooley et al defined a 90% risk of GDM with GCT result ≥200 mg/dL in nonwhite women, but the risk in white women was 66%.[9] Based on these findings, it is logical that different cutoff levels may be accepted in different ethnic groups for diagnosing GDM without performing further OGGT. One of the studies conducted in Turkey reached 100% specificity after a cutoff value of 221 mg/dL, which was lower compared to our findings.[20] Besides ethnicity, one of the major risk factors for GDM is increased maternal age.[16,17] Therefore, we investigated whether the PPV of GCT levels for GDM diagnosis differ in different age groups and we further analyzed our results according to age. After analyzing patients older than 35 years, we reached 100% PPV at the GCT level of 200 mg/dL or greater for diagnosing both GDM and GIGT according to the CC criteria. Our results showed that 100% PPV can be reached with lower GCT results in patients older than 35 years.

An important limitation regarding GCT results is low reproducibility. Only 83% of abnormal results were reproducible the next day in a study by Espinosa de los Monteros et al.[21] This was attributed to the fact that the reproducibility of the test would rely on the timing since the last meal. In pregnancy, plasma glucose concentrations after GCT were higher if administered in the fasting state compared with the postprandial state, and this effect might alter the test characteristics.[22] Therefore, it is important to be cautious in using GCT for diagnostic purposes.

Accuracy is measured by the area under the ROC curve, which summarizes the discriminative ability of a test and provides a measure of the overall performance of a diagnostic test. The greater the value of AUC, the

Table 3. Rate of GDM and GDM + GIGT diagnosed according to GCT results using NDDG criteria and Carpenter and Coustan criteria in patients ≥35 years.

National Diabetes Data Group									
	GDM					GDM+GIGT			
		+	-	Total			+	-	Total
GCT	≥220	12 (100%)	0	12	GCT	≥220	12 (100%)	0	12
	<220	73 (42.3%)	99 (57.7%)	172		<220	111(64.5%)	61 (35.5%)	172
	Total	85 (46.1%)	99 (53.9%)	184		Total	123 (66.8%)	61 (33.2%)	184
Carpenter and Coustan criteria									
	GDM					GDM+GIGT			
		+	-	Total			+	-	Total
GCT	≥220	12 (100%)	0	12	GCT	≥200	32 (100%)	0	32
	<220	94 (54.6)	82 (45.4%)	172		<200	128 (84.2%)	24 (15.8)	152
	Total	106 (57.2%)	82 (42.8%)	184		Total	160 (87.8%)	24 (12.2%)	184

GDM: Gestational diabetes mellitus; GIGT: Gestational impaired glucose intolerance.

better would be the test.[23] In this study, for GCT values ≥180 mg/dL, we generated ROC curves and calculated AUC. The best value was 0.680 in the curve of GDM + GIGT diagnoses using CC criteria, which provided low accuracy. This is the first study analyzing PPVs of GCT results for diagnosing both GDM and GIGT. Although, women with one elevated glucose tolerance test value are not diagnosed with GDM, they may still be at risk of adverse perinatal outcomes, and dietary counseling and glucose monitoring is recommended to decrease perinatal morbidity.[24] Women with one elevated glucose tolerance test value have an increased likelihood of developing an abnormal glucose tolerance later in life, which is similar to the risk in women with gestational diabetes.[25] Since most clinicians offer glucose monitoring for GIGT, we analyzed the predictive value of GCT results for diagnosing GDM and both GDM and GIGT.

The major limitation of our study is its retrospective design, but it would be difficult to include a large cohort in a prospective study. We could not analyze the effect of other risk factors like maternal weight, positive family history of diabetes, and personal history of previous gestation diabetes. Also, we did not assess the reproducibility of GCT results and obstetric outcomes. However, we focused on the impact of age for the diagnostic utility of GCT results for diagnosing GDM and GIGT. Our data suggest that we may omit OGTT in pregnant women with GCT results ≥230 mg/dL. A cutoff value of 200 mg/dL can be used in patients older than 35 years. This approach may prevent overdiagnosis, and unnecessary interventions can be avoided.

Table 4. Receiver-operator characteristic curve analysis of GCT results ≥180 mg/dL for diagnosing GDM and GDM + GIGT using NDDG and CC criteria in patients ≥35 years.

Criteria	Diagnosis	AUC	95% CI	*P* value
NDDG	GDM	0.599	0.509-0.690	.0293*
	GDM + GIGT	0.629	0.544-0.713	.0070
CC	GDM	0.597	0.511-0.684	.0331*
	GDM + GIGT	0.630	0.542-0.718	.0127

GCT: Glucose challange test; GDM: gestational diabetes mellitus; GIGT: gestational impaired glucose intolerance; NDDG: National Diabetes Data Group; CC: Carpenter and Coustan; AUC: area under curve; CI: confidence interval.

*Not significant because of Bonferrroni corrections.

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