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The Diagnostic Value of the 50-Gram Glucose Challenge Test at Various Cut-off Levels Combined with Clinical Risk Factors in Predicting the Diagnosis of Gestational Diabetes Mellitus

Amontis Chaimongkolpipob, M.D.[1], Supapen Lertvutivivat, M.D.[1], Tongta Nanthakomon, M.D.[1], Chamnan Tanprasertkul, M.D., Ph.D.[1,2], Banthisa Somboon, M.D.[1], Charintip Somprasit, M.D.[1]

[1]Department of Obstetrics and Gynecology, Faculty of Medicine, Thammasat University, Pathumthani 12120, Thailand.

[2]Advanced Clinical Innovative Research in Obstetrics and Gynecology Group, Thammasat University, Pathumthani 12120, Thailand.

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Abstract:

Objective: To evaluate the diagnostic precision of the 50-gram glucose challenge test (50-g GCT) at various levels for the detection of gestational diabetes mellitus (GDM), and to examine its association with clinical risk indicators.

Material and Methods: At Thammasat University Hospital, our retrospective cohort comprised 1,197 pregnant women screened using the 50-g GCT based on risk factors, including a family history of GDM, obesity, and other factors. Out of these, 219 tested positive, with 83 (37.9%) diagnosed with GDM and 136 (62.1%) without GDM. Comprehensive data including baseline characteristics, as well as maternal and neonatal outcomes, were compiled. We assessed the correlations between clinical risk factors and 50-g GCT values to ascertain GDM. The positive predictive value (PPV) and negative predictive value (NPV) for various cut-off levels were determined.

Results: The best cutoff for the 50-g GCT for GDM diagnosis was ≥220 mg/dL with 100% PPV without adding clinical risk. The PPVs reached 75% and 100%, respectively, when combined with maternal age ≥35 years at 50-g GCT thresholds of ≥210 mg/dL and ≥220 mg/dL. A history of diabetes in the family combined with a 50-g GCT provided 100% PPV at 200 mg/dL.

Contact: Supapen Lertvutivivat, M.D.
Department of Obstetrics and Gynecology, Faculty of Medicine,
Thammasat University, Pathumthani 12120, Thailand.
E-mail: supapenl@gmail.com

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Conclusion: A 50-g GCT cut-off value of ≥220 mg/dL is proposed for a definitive GDM diagnosis in certain circumstances, negating the need for this additional test. When a pregnant woman has a family history of diabetes, the 50-g GCT cut-off of 200 mg/dL could be a promising marker for identifying GDM.

Keywords: 50-gram glucose challenge test, 100-gram oral glucose tolerance test, clinical risk factors, gestational diabetes mellitus diagnosis

Introduction

Gestational diabetes mellitus (GDM) is a condition characterized by glucose intolerance first identified or manifesting during pregnancy[1-4]. Factors such as obesity (body mass index (BMI) ≥25 kg/m^2), a significant family history of type 2 diabetes (T2DM), a previous GDM diagnosis, impaired glucose metabolism, or glucosuria are linked to an elevated GDM risk[3,5-8].

The screening and diagnostic protocols for GDM differ globally, with varying strategies leading to debate[9]. The International Association of Diabetes and Pregnancy Study Groups (IADPSG) promotes the use of a single-step 75-gram oral glucose tolerance test (OGTT), while the American College of Obstetricians and Gynecologists (ACOG) advocates for a two-step strategy involving an initial 50-g GCT followed by a 100-gram OGTT if the GCT results are positive[3,10]. Both of these methods are supported by the American Diabetes Association (ADA) and the US Preventive Services Task Force (UPSTF)[1,2].

At Thammasat University Hospital (TUH), we adopt the two-step method advised by the ACOG. This entails a preliminary 50-g GCT with a positive screen defined as ≥140 mg/dL and a confirmatory 100-g OGTT, with carpenter and coustan (CC) thresholds of 95, 180, 155, 140 mg/dL[3,11]. However, this comprehensive method proves cumbersome and challenging for some patients, and it can lead to postponement or inaccuracy in GDM diagnosis if the 100-g OGTT is incomplete. Consequently, delaying the diagnosis results in a slower entry into the treatment process, leading to prolonged hyperglycemia in pregnant women. This, in turn, increases the likelihood of adverse pregnancy outcomes, especially during fetal organogenesis.

Given these difficulties, some have suggested adopting a ≥200 mg/dL cut-off for the 50-g GCT as an indicative diagnostic measure for GDM due to its strong predictive value[8,12-14]. Our literature review noted variances in accuracy across different thresholds; hence, we aimed to determine the diagnostic efficacy of the 50-g GCT at various levels, factoring in clinical risk determinants.

Material and Methods

Study design and subjects

This retrospective cohort investigation involved a review of medical records from the Department of Obstetrics and Gynecology, Faculty of Medicine, TUH, following ethical clearance from the Human Subjects Ethics Committee (MTU-EC-OB-1-007/65) at TUH. We included all eligible singleton pregnant women who received antenatal care and gave birth at TUH between January 2020 and December 2022. The 50-g GCT was routinely administered during the first antenatal visits in high risk pregnancies based on the following risk factors: individuals with a first-degree relative with diabetes, a history of fetal macrosomia, previous GDM, hypertension, impaired glucose tolerance or impaired fasting glucose, conditions associated with insulin resistance, and a history of cardiovascular disease. The threshold of ≥140 mg/dL indicated a positive screen. Women who screened positive subsequently underwent the 100-g OGTT. A

diagnosis of GDM hinged on the presence of two or more elevated glucose readings based on CC criteria.

For those classified as high-risk but who screened negative during the first antenatal care visit, a repeat 100-g OGTT was conducted at gestational age 24-28 weeks. Additionally, for individuals categorized as low-risk initially, the 50-g GCT was also performed as universal screening at 24-28 weeks of pregnancy. We excluded women with pre-existing diabetes or fetal anomalies.

Pregnant individuals diagnosed with GDM received care at the diabetes clinic through collaborative efforts involving obstetricians, endocrinologists and a nutrition team. Initially, they received guidance on dietary control and regular monitoring of blood sugar levels, both fasting and 1-2 hours after meal each day. If there was a trend of elevated sugar levels beyond the specified thresholds, as assessed by fasting blood sugar over 95 mg/dL, 1-hour postprandial over 140 mg/dL and 2-hour postprandial over 120 mg/dL, initiating insulin injections were begun to maintain appropriate blood sugar levels.

The sample size was determined using the research of Lakhananurak et al., and after accounting for attrition, the total number of participants needed was 212[15].

We collected demographic details, including maternal age, BMI, total weight gain, parity, a family history of type 2 diabetes, and past obstetric and pregnancy outcomes. Maternal and neonatal outcomes, such as delivery timing, delivery mode, birth trauma, postpartum hemorrhage, preeclampsia, birth weight, Apgar scores, and neonatal intensive care unit admissions, alongside other complications, were documented and studied.

We employed descriptive statistics to summarize the subjects' baseline characteristics. Continuous variables were expressed as means with standard deviations, while categorical data were shown as frequencies and percentages. To compare characteristics between groups, we utilized student's t-test, Mann-Whitney U test, chi-square test or Fisher's exact test. Logistic regression analyses, both univariate and multivariable, were used to assess associations between clinical risk factors and GDM. After pinpointing potential risk factors via univariate analysis, multivariable analysis gauged the simultaneous influence of various clinical risk factors on the likelihood of GDM. To determine the GDM diagnostic accuracy of the 50-g GCT results, we computed the sensitivity and specificity at incremental cut-off values, targeting a 100% positive predictive value (PPV). These analyses used Statistical Software for Data Science (STATA), version 15.1, with statistical significance assigned to p-values<0.05.

Results

During the study period, out of 1,197 pregnant women screened using the 50-g GCT, 219 (18.3%) were identified as positives. Among these, GDM was diagnosed in 83 (37.9%) women, while the remaining 136 (62.1%) were not diagnosed with GDM.

Comparison of baseline characteristics between the two groups indicated significant differences as shown in Table 1. All respectively, women with GDM had a higher mean age than those without (34.2±5.3 years versus 31.3±5.7 years, p-value<0.001) and were more likely to be of advanced maternal age (over 35 years) (48.2% versus 34.6%, p-value=0.045). Pre-pregnancy BMI was notably higher in the GDM group (24.2±4.7 versus 22.7±4.4, p-value=0.018) and a family history of diabetes was more prevalent (22.9% versus 12.5%, p-value=0.044). The GDM group also had a higher average 50-g GCT value (181.5±36.6 mg/dL versus 160±18.2 mg/dL, p-value<0.001).

Table 1 Comparison of baseline characteristics between study GDM and non-GDM pregnant women

Characteristic	GDM (n=83)	Non-GDM (n=136)	p-value
Maternal age±S.D. (years)	34.2±5.3	31.3±5.7	<0.001
Age ≥35 years	40 (48.2%)	47 (34.6%)	0.045
Nulliparity	31 (37.3%)	57 (41.9%)	0.500
Pre-pregnancy BMI±S.D. (kg/m^2)	24.2±4.7	22.7±4.4	0.018
BMI ≥25 kg/m^2	30 (36.1%)	34 (25.0%)	0.079
Weight gained±S.D. (kg)	10.9±8.5	12.5±5.7	0.100
50-g GCT result±S.D. (mg/dL)	181.5±36.6	160±18.2	<0.001
GA at having 50-g GCT±S.D. (weeks)	21.6±7.8	23.2±8.7	0.170
GA at having 100-g OGTT±S.D. (weeks)	24.7±6.6	26.6±4.8	0.014
Family history of DM	19 (22.9%)	17 (12.5%)	0.044
Previous pregnancy with GDM	6 (7.2%)	4 (2.9%)	0.140
Previous fetal macrosomia	3 (1.6%)	7 (3.8%)	0.200

number are mean±S.D., or n (%), BMI=body mass index, GCT=glucose challenge test, GA=gestational age, OGTT=oral glucose tolerance test, DM=diabetes mellitus, GDM=gestational diabetes mellitus

Table 2 Comparison of maternal and neonatal outcomes between study GDM and non-GDM pregnant women

Pregnancy outcome	GDM (n=83)	Non-GDM (n=136)	p-value
Maternal outcome			
GA at delivery±S.D. (weeks)	38.5±1.3	38.5±1.3	1.00
Delivery at GA≥37 weeks	76 (91.6%)	128 (94.1%)	0.47
Delivery at GA 34-36+6 weeks	6 (7.2%)	7 (5.1%)	0.53
Route of delivery			
Normal vaginal delivery	44 (53.0%)	67 (49.3%)	0.73
Cesarean delivery	37 (44.6%)	67 (49.3%)	
Operative vaginal delivery	2 (2.4%)	2 (1.5%)	
Shoulder dystocia	1 (1.2%)	2 (1.5%)	0.87
OASIS	1 (1.2%)	4 (2.9%)	0.40
Preeclampsia			
Without severe features	1 (1.2%)	4 (2.9%)	0.39
With severe features	1 (1.2%)	5 (3.7%)	

Table 2 (continued)

Pregnancy outcome	GDM (n=83)	Non-GDM (n=136)	p-value
Neonatal outcome			
Birthweight±S.D. (grams)	3075.3±478.8	3053.1±457.7	0.73
Macrosomia	15 (18.1%)	19 (14.0%)	0.42
Growth restriction	3 (3.6%)	3 (2.2%)	0.54
Hypoglycemia	7 (8.4%)	1 (0.7%)	0.003
Jaundice	22 (26.5%)	17 (12.5%)	0.009
Respiratory distress syndrome	10 (12.0%)	13 (9.6%)	0.56
Stillbirth	1 (1.2%)	1 (0.7%)	0.72
HR/NICU admission	12 (14.5%)	17 (12.5%)	0.68

number are mean±S.D., or n (%), GA=gestational age, OASIS=obstetric anal sphincter injuries, EBL=estimated blood loss, HR=high-risk, NICU=neonatal intensive care unit

As shown in Table 2, maternal and neonatal outcomes were compared. The average gestational age at the time of delivery was identical in both groups, standing at 38.5 weeks. A higher, yet non-significant, incidence of preterm birth was noted in the GDM group (7.2% versus 5.1%, respectively, p-value=0.53). There were no notable differences in delivery method or preeclampsia incidence. While birth weights were similar across groups, a slight increase in fetal macrosomia (birth weight over 4,000 grams) was seen in the GDM group, although not statistically significant (18.1% versus 14%, respectively, p-value=0.42). Significantly, neonatal hypoglycemia and jaundice occurred more frequently in babies born to women with GDM (8.4% versus 0.7%, p-value=0.003 and 26.5% versus 12.5%, respectively, p-value=0.009).

Table 3 delineates the analysis of each clinical risk factor's association with GDM. A 50g-GCT value greater than 200 mg/dL indicates a significantly increased risk of developing GDM (odds ratio [OR] 4.657, 95% confidence interval [CI] 1.686-12.863). A notable finding was that a strong family history of diabetes substantially elevated the likelihood of a GDM diagnosis (OR 2.252, 95% CI 1.070-4.738). Additionally, maternal age of 35 or more noticeably increased GDM risk (OR 1.468, 95% CI 0.813-2.649). While an association was detected between a BMI of 25 kg/m^2 or above and GDM diagnosis, this did not achieve statistical significance.

In Table 4, the diagnostic performance of the 50-g GCT, when combined with clinical risk factors, is compared with that of the 100-g OGTT, the gold standard test. Using the 50-g GCT values alone at various cut-off points, it was discerned that a threshold of ≥220 mg/dL diagnosed GDM with a PPV of 100%. At cut-off values of ≥210 mg/dL and ≥200 mg/dL, the PPVs were 81.3% and 71.4%, respectively.

Table 3 Multivariable logistic regression of clinical risk factors associated with GDM

Risk factors	OR (95% CI)	p-value
50-g GCT ≥200 mg/dL	4.657 (1.686-12.863)	0.003
Family history of DM	2.252 (1.070-4.738)	0.032
Age ≥35 years	1.468 (0.813-2.649)	0.203
BMI ≥25 kg/m^2	1.543 (0.829-2.875)	0.171

GCT=glucose challenge test, DM=diabetes mellitus, BMI=body mass index, GDM=Gestational diabetes mellitus, OR=odd ratio, CI=confedence interval

When considering individuals with a clinical risk factor alongside various 50-g GCT threshold levels, maternal age ≥35 years with cut-offs ≥210 mg/dL and ≥220 mg/dL showed accurate GDM diagnosis with PPVs of 75% and 100%, respectively, yielding statistically significant outcomes. A BMI of ≥25 kg/m^2 combined with 50-g GCT thresholds of ≥210 mg/dL and ≥220 mg/dL had PPVs of 60% and 100%, respectively, although these findings were statistically inconclusive. Lastly, a strong family history of diabetes combined with 50-g GCT cut-off values of ≥200 mg/dL, ≥210 mg/dL, and ≥220 mg/dL all conferred a PPV of 100%, but these results all lacked statistical significance.

Table 4 Diagnostic performance of 50-g GCT and various clinical risk factors for the diagnosis of GDM

50-g GCT	PPV	NPV
Cut-off		
≥200 mg/dL	71.4 (65.5-77.4)	65.7 (59.4-72.0)
≥210 mg/dL	81.3 (76.1-86.4)	65.5 (59.2-71.8)
≥220 mg/dL	100.0	64.8 (58.4-71.1)
Age ≥35 years with 50-g GCT		
≥200 mg/dL	64.3 (54.2-74.4)	57.50 (47.2-67.9)
≥210 mg/dL	75.0 (65.9-84.1)	58.70 (48.3-69.0)
≥220 mg/dL	100.0	58.80 (48.4-69.1)
BMI ≥25 kg/m^2 with 50-g GCT		
≥200 mg/dL	71.4 (60.4-82.5)	56.10 (44.0-68.3)
≥210 mg/dL	60.0 (48-72)	54.20 (42.0-66.4)
≥220 mg/dL	100.0	54.80 (42.7-67.0)
Family history of DM with 50-g GCT		
≥200 mg/dL	100.0	50.0 (33.7-66.3)
≥210 mg/dL	100.0	50.0 (33.7-66.3)
≥220 mg/dL	100.0	48.6 (32.2-64.9)

GCT=glucose challenge test, PPV=pulse pressure variation, NPV=net present value, BMI=body mass index, DM=diabetes mellitus

Discussion

The development of GDM has been linked to adverse pregnancy outcomes, as indicated in the Hyperglycemia and Adverse Pregnancy Outcome study and subsequent research[4,16,17]. The ideal approach for GDM screening and diagnosis is debated with various institutions devising differing strategies.

Consistent with previous findings our investigation found no significant differences between the GDM and non-GDM groups in outcomes such as preterm delivery, cesarean or operative birth or preeclampsia[5]. However, GDM was associated with more frequent cases of neonatal hypoglycemia and jaundice, echoing other studies results[16,17].

Our analysis corroborated higher maternal age, particularly over 35, a significant family history of diabetes, and increased BMI as substantial clinical risk indicators for GDM, in agreement with other research[3,5-8]. The presence of a family history of diabetes was demonstrated to double the risk of GDM, while a 50g-GCT ≥200 mg/dL increased the risk by nearly 5 times of developing GDM.

This study's results emphasize the association between higher 50-g GCT values and an increased GDM risk, aligning with expectations and earlier studies[8,18,19]. The diagnostic use of the 50-g GCT cut-off at 220 mg/dL provided a PPV of 100%, contrasting with other studies proposing different cut-off values[8,19]. However, our lower cut-off of 200 mg/dL, as endorsed by some research, led to an overdiagnosis of GDM by almost 30%[8,19]. Adding age and BMI stratification to the 50-g GCT did not aid in diagnosis. Notwithstanding its strong association, a family history of diabetes coupled with a 200 mg/dL cut-off did not achieve statistical significance concerning PPV enhancement.

Previous research indicated that combining maternal risk factors with the 50-g GCT provided better PPV and NPV. However, our findings suggest that combining clinical risk factors with the 50-g GCT does not support lowering its cut-off value for diagnosing GDM[8,18]. Variations in population, GDM prevalence, timing of assessment, and

the limited size of our subject pool could have influenced this discrepancy. Moreover, the small number of cases (21 women) with 50-g GCT values above 200 mg/dL might have impeded the evaluation of clinical risk factors' efficacy in reducing the cut-off value. Additional research in this domain would be beneficial.

In summary, the 50-g GCT is a common universal screening tool for pregnant women, independent of clinical risk factors. Our study proposes the ≥220 mg/dL cut-off value for a decisive GDM diagnosis, eliminating the need for the 100-g OGTT in certain scenarios, such as late prenatal visits or when a woman cannot complete the OGTT. For patients with a family history of diabetes, the 50-g GCT cut-off of 200 mg/dL is a potential diagnostic marker for GDM. This approach facilitates early diagnosis and treatment, potentially enhancing pregnancy outcomes, and underscores the need for future research to establish proper cut-off values and ascertain the optimal timing for the 50-g GCT, as well as its effects on pregnancy outcomes.

Conflict of interest

There are no potential conflicts of interest to declare.

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