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Gestational Diabetes: Use of Glucose Challenge Test as a Diagnostic Test

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ABSTRACT

Objective: To evaluate the positive predictive value of 50-g glucose challenge test (50-g GCT) for diagnosis of gestational diabetes (GDM).

Study design: Diagnostic test

Materials and methods: The study was undertaken at the Faculty of Medicine Vajira Hospital, Navamindradhiraj University by reviewing the medical records of pregnant women who had a 50-g GCT value of ≥ 140 mg/dL followed by a 100-g glucose tolerance test (100-g GTT) between October 2010 and September 2013. Results were classified in 10 mg/dL increments. GDM was diagnosed using Carpenter and Coustan criteria.

Results: The current study included 1,886 cases from universal screening of 9,273 pregnant women. The incidence of GDM was 3.6%. A 50-g GCT cut-off value of ≥ 230 mg/dL provided 95% positive predictive value for diagnosis of GDM with 0.1% probability for overdiagnosis. Among population with positive screening who had at least one risk factor of GDM, a 50-g GCT threshold of ≥ 236 mg/dL could be interpreted as GDM without a false positive case and confirmation by 100-g GTT was not required.

Conclusions: For a policy of universal screening of GDM, a 50-g GCT may be employed as a diagnostic test when the value is ≥ 230 mg/dL.

Keywords: gestational diabetes, glucose challenge test, diagnosis

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Introduction

Gestational Diabetes Mellitus (GDM) is a common metabolic complication during pregnancy. Overall, GDM affects 1-14% of pregnant women, depending on population studied as well as diagnostic threshold used[1]. GDM tends to steadily increase concurrent with the increased incidence of diabetes in non-pregnant patients[2]. It is crucial to identify a pregnant woman with this complication since poor glycemic control resulting from untreated GDM carries

a significant risk of perinatal and maternal morbidities, including preeclampsia, unexplained fetal demised, fetal macrosomia, cesarean delivery, postpartum hemorrhage, shoulder dystocia, birth injury and neonatal hypoglycemia[2]. Though there is still controversy regarding the most appropriate diagnostic guideline of GDM, a majority of obstetricians in many parts of the world[3] including in Faculty of Medicine Vajira Hospital identify GDM by a two-step approach using a 50-g GCT as a screening test. Pregnant women with positive screen have to proceed to do the gold standard 100-g GTT; however, this GTT test is cumbersome, time consuming and requires pre-test carbohydrate priming and overnight fasting. Many previous reports have proposed that 100-g GTT may be discarded and GDM can be diagnosed when 50-g GCT results are beyond 180-250 mg/dL[4-11]. Nonetheless, the cut-off level may vary in consequence of the disparity in ethnicity, screening threshold and diagnostic criteria of GDM used. We have previously reported a 3.2% prevalence of GDM following universal screening with a 50-g GCT and using 100-g GTT for diagnosis GDM by National Diabetes Data Group (NDDG) criteria. When a value of 50-g GCT was ≥ 250 mg/dL, 86% positive predictive value for diagnosis of GDM with 0.4% probability for overdiagnosis was demonstrated[11].

Currently, the criteria for diagnosing GDM in our institute's guideline have been changed from NDDG to Carpenter and Coustan (CC) criteria hence the cut-off level may alter. The purpose of the present study was to evaluate the optimal cut-off level of 50-g GCT that should be used to diagnose GDM by CC criteria with high positive predictive value. We also would like to further assess whether 100-g GTT can be withheld if a 50-g GCT value rises above the certain level.

Materials and Methods

The present study was undertaken in a university hospital serving an urban population, with over 3,000 deliveries each year. After approval by Vajira Institutional Review Board, Navamindradhiraj University, Bangkok, Thailand, a retrospective medical record review was conducted among singleton pregnant women who had a 50-g GCT of ≥ 140 mg/dL pursued by a 100-g GTT between October 2010 and September 2013. A 50-g GCT was universally offered to women during a routine prenatal visit and the result of ≥ 140mg/dL is defined as screen-positive. Pregnant women who had potential risk(s) of GDM were advised to perform 50-g GCT at the first visit and advanced to do the diagnostic test if a screening test was positive. Risk factors of GDM include maternal age ≥ 35 years, obesity (prepregnancy body mass index (BMI) ≥ 30 kg/m^2), family history of diabetes, history of GDM, delivery of a macrosomic infant (birth weight > 4,000 grams) or unexplained fetal demise in prior pregnancy, and glucosuria during current pregnancy[12-16]. If the first glucose screen was negative, a 50-g GCT will be repeated at 24-28 weeks of gestation. For remaining women without potential risk of GDM, 50-g GCT was entirely offered at 24-28 weeks of gestation. The gold standard in diagnosis of GDM was 100-g GTT. GDM was diagnosed using 2 or more abnormal glucose values citing CC criteria (fasting ≥ 95, one hour ≥ 180, two hours ≥ 155, and three hours ≥ 140 mg/dL). Baseline clinical data including age, parity, coexisting medical disease(s), gestational age at screening and risk factor(s) of GDM were retrieved. Preexisting diabetes patients or pregnant women who missed 100-g GTT despite a positive 50-g GCT result or incomplete data were excluded. Results of 50-g GCT were classified in 10 mg/dL increments. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 22.0. The diagnostic performances of 50-g GCT at different cut-offs were computed and validated as sensitivity, specificity, positive predictive value and negative predictive value.

Results

During the study period, a total of 9,273 singleton pregnant women underwent 50-g GCT for screening GDM. Of these, 1,962 (21.1%) had 50-g GCT result ≥ 140 mg/dL. Fifty-seven patients did not carry through the 100-g GTT and the clinical data of 19 cases were incomplete, leaving 1,886 women included in the analysis. The majority of those who did not undergo

100-g GTT were due to late booking and loss of follow-up. Mean values of 50-g GCT in 76 excluded cases were 167.0 ± 20.9 mg/dL (mean ± SD), range from 140 to 212 mg/dL.

Baseline characteristic of study population was shown in Table 1. Mean age of 1,886 recruited cases was 30.3 ± 6.2 years (mean ± SD) and 26.6% of those aged ≥ 35 years. Mean prepregnancy BMI was 23.0 ± 4.7 kg/m^2 (mean ± SD) and 8.8% of those were considered to be obese (BMI ≥ 30 kg/m^2). Fifty-nine percent of women were multiparous. Forty seven patients (2.5%) had coexisting medical disease(s). Chronic hypertension was the most frequent concomitant medical disease and was found in 1.6%. Mean gestational age at screening was 23.3 ± 9.3 weeks (mean ± SD). Mean values of 50-g GCT were 160.1 ± 22.3 mg/dL (mean ± SD), range from 140 to 423 mg/dL. Eighteen percent (339/1,886) of cases with positive screen were diagnosed as GDM after performing 100-g GTT. Mean gestational age at GDM diagnosis was 23.0 ± 9.3 weeks (mean ± SD).

Table 1. Baseline clinical data of study population (N=1,886)

Clinical data	ShD group N = 67
Age (years)	30.3 ± 6.2
< 25	362 (19.2)
25 – 34	1023 (54.2)
≥ 35	501 (26.6)
Parity	
Nulliparous	773 (41.0)
Multiparity	1,113 (59.0)
Prepregnancy BMI (kg/m^2)	23.0 ± 4.7
< 30	1,720 (91.2)
≥ 30	166 (8.8)
Gestational age at screening (weeks)	23.3 ± 9.3
Results of 50-g GCT (mg/dL)	167.0 ± 20.9

Data presented as mean ± SD or n (%)

Concerning about risk factors for GDM, 951 cases (50.4%) with positive 50-gGCT had no risk factor, while 717 cases (38.0%) had 1 risk factor, 196 cases (10.4%) had 2 risk factors and 22 cases (1.2%) had more than 2 risk factors. The most common risk factor found was age ≥ 35 years (26.5%) followed by family history of DM (23.8%), and obesity (8.8%) (Table 2). For those who had 1 or more risk factors, the incidence of GDM was 23.9%. Among these risk factors, prior pregnancy with GDM was found to be at highest opportunity to develop GDM with the risk of 71.4%. However, women with screen-positive who had no risk factor of GDM still have a chance of 12.2% to be diagnosed as GDM. (Table 2).

Table 2. Diagnosis of GDM in women with positive 50-g GCT at different risk factors of GDM.

Risk factors of GDM	Number of women at risk		Diagnosis of GDM	
	Number	%*	Number	%**
No risk factor	951	50.4	116	12.2
One or more risk factors	935	49.6	223	23.9
Age ≥ 35 years	500	26.5	128	25.6
Obesity (prepregnancy BMI ≥ 30 kg/m^2)	166	8.8	41	24.7
Family history of DM	449	23.8	108	24.1
History of GDM	7	0.4	5	71.4
Prior delivery of macrosomic infant	23	1.2	14	60.9
History of unexplained fetal demise	15	0.8	6	40.0
Glucosuria in current pregnancy	16	0.8	9	56.3

* the percentage of all 1,886 pregnant women in the study
** the percentage of developing GDM in each risk factor

Overall, GDM affects approximately 3.6% (339/9,273) of the screening population. The diagnostic performance of 50-g GCT to diagnose GDM according to various cut-off values is shown in Table 3. The present data affirmed that when a value of 50-g GCT was ≥ 243 mg/dL, GDM could be diagnosed without possibility for overdiagnosis (100% positive predictive value, 100% specificity, 7.9% sensitivity and 83.1% negative predictive value). If the cut-off at ≥ 230 mg/dL was used, 95.0% probability for diagnosis of GDM with 0.1% liability for overdiagnosis was demonstrated (95% positive predictive value, 99.9% specificity, 10.6% sensitivity and 82.6% negative predictive value). Among women with at least one of the risk factors of GDM, a 50-g GCT threshold of ≥ 236 mg/dL could be interpreted as GDM without a false positive case (Table 4).

Table 3. Diagnosis of GDM and diagnostic performance at various cut-off values of 50-g GCT in pregnant women with positive 50-g GCT.

Cut-off value of 50-g GCT (mg/dL)	Total cases	Diagnosis of GDM N (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
≥ 140	1,886	339 (18.0)	100	0	18.0	-
≥ 150	1,205	271 (22.5)	79.9	39.6	22.5	90.0
≥ 160	730	209 (28.6)	61.7	66.3	28.6	88.8
≥ 170	396	150 (37.9)	44.3	84.1	37.9	87.3
≥ 180	205	103 (50.2)	30.4	93.4	50.2	86.0
≥ 190	124	80 (64.5)	23.6	97.2	64.5	85.3
≥ 200	81	63 (77.8)	18.6	98.8	77.8	84.7
≥ 210	54	45 (83.3)	13.3	99.4	83.3	84.0
≥ 220	42	39 (92.9)	11.5	99.8	92.9	83.7
≥ 230	40	38 (95.0)	10.6	99.9	95.0	82.6
≥ 240	29	28 (96.6)	8.3	99.9	96.6	83.3
≥ 243	27	27 (100)	7.9	100	100	83.1

PPV: positive predictive value; NPV: negative predictive value

Table 4. Diagnostic performance at various cut-off values of 50-g GCT in pregnant women with positive 50-g GCT who had at least one risk factor for GDM.

Cut-off value of 50-g GCT (mg/dL)	Total cases	Diagnosis of GDM N (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
≥ 140	935	223 (23.9)	100	0	23.9	-
≥ 150	607	179 (29.5)	80.3	39.9	29.5	86.6
≥ 160	383	139 (36.3)	62.3	65.7	36.3	84.8
≥ 170	238	108 (45.4)	48.4	81.7	45.4	83.5
≥ 180	124	76 (61.3)	34.1	93.3	61.3	81.9
≥ 190	85	61 (71.8)	27.4	96.6	71.8	81.0
≥ 200	62	49 (79.0)	21.9	98.2	79.0	80.0
≥ 210	41	34 (82.9)	15.3	99.0	82.9	78.9
≥ 220	29	28 (96.6)	12.6	99.9	96.6	78.6
≥ 230	29	28 (96.6)	12.6	99.9	96.6	78.6
≥ 236	24	24 (100)	10.8	100	100	78.2

PPV: positive predictive value; NPV: negative predictive value

Discussion

The 3.6% incidence of GDM in the present study was consistent with the prior reports which diverged from 1 to 14%[1]. The current data may support the universal screening strategy for GDM in our institution since we discovered that for those with positive a 50-g GCT, even low risk women still have a chance of 12.2% to be diagnosed as GDM.

Regarding the utility of the obviously elevated level of a 50-g GCT as a diagnostic test for GDM, many preceding researches have reported a probability of GDM of nearly 100% when a glucose screen result was in the range of 180-200 mg/dL[4,5,8,9]. In addition, Canadian Diabetes Association Clinical Practice Guidelines Expert Committee 2013 also suggested that GDM diagnosis can be made when a 50-g GCT cut-off value was ≥ 200 mg/dL[6]. However, the current results did not agree with those findings since a probability of GDM was revealed of only 77.8% when 50-g GCT result was above 200 mg/dL. These discrepant findings may stem from the variation in ethnicity, incidence of GDM among populations, screening modalities, screen positive threshold and diagnostic criteria used. In Canadian Diabetes Association Clinical Practice Guidelines Expert Committee 2013, the 5.9% incidence of GDM was quoted which was higher than the incidence in our study. A universal screening by a 50-g GCT was recommended and screen positive threshold was established at ≥ 140 mg/dL that was similar to ours. However, the gold standard in diagnosis of GDM, using a 75-g glucose tolerance test was different from the present study[6].

For women with positive screening who had risk factor(s) for GDM, the present evidence revealed 23.9% incidence of GDM and a 50-g GCT threshold of ≥ 236 mg/dL provided 100% positive predictive value for diagnosis of GDM without the need for a diagnostic test. This cut-off value was comparable to the conclusion of the recent study from Faculty of Medicine Siriraj Hospital, Thailand[7]. Thirty-five percent incidence of GDM following risk-based screening with a 50-g GCT and using 100-g GTT for diagnosis GDM by NDDG criteria was published from Siriraj Hospital's study[7]. With a 50-g GCT threshold of ≥ 240 mg/dL, the positive predictive value of GDM was 100% without false positive case[7].

Although the present evidence demonstrated that when a 50-g GCT cut-off value of ≥ 243 mg/dL could provide 100% positive predictive value for diagnosis of GDM without possibility for overdiagnosis, a threshold of ≥ 230 mg/dL might be more appropriate. The reason was that if a value of 50-g GCT of ≥ 243 was adopted

as a diagnostic test, only 1.4% of study population would advantage from initiating GDM treatment immediately without further testing while nearly twice more cases (2.1%) would benefit if a threshold of ≥ 230 mg/dL was applied. At such cut-off value provided as high as 95% positive predictive value for diagnosis of GDM with very low chance for overdiagnosis (0.1%). The important impact from overdiagnosis was unnecessary intervention; nevertheless, dietary modification did not cause serious harm to women. In addition, the prior literatures have reported that women with false positive 50-g GCT results were still at increased risk of adverse perinatal outcomes related to diabetic mothers[17,18].

The advantage of this study was that a confirmatory 100-g GTT can be withheld in a number of pregnant women if a 50-g GCT value markedly elevated above the certain level. Consequently, this group of women can promptly commence dietary modification and blood glucose monitoring, omitting an inconvenient testing as a 100-g GTT. However, the present study had some limitations due to the nature of retrospective study. In addition, there was a small sample size in higher cut-off values that might cause the estimation of positive predictive value less accurate as well as the women who would benefit from this assumption were not in large numbers. It is difficult to anticipate the outcomes if 100-g GTT in the seventy-six excluded patients were comprised for analysis. Besides, the proportion of hidden pregestational diabetes women in the present study could not be estimated (despite known cases of preexisting diabetes were eliminated by exclusion criteria); accordingly, the 50-g GCT results of those patients probably affected the cut-off value.

Future effort should focus on the prospective studies which investigate the impacts of employing the proposed threshold of ≥ 230 mg/dL for diagnosis of GDM; furthermore, the pregnancy outcomes of implementing the suggested cut-off of ≥ 236 mg/dL for diagnosis of GDM in women at high risk for GDM should also be investigated.

In conclusion, for a strategy of universal screening of GDM in the population with relatively low prevalence of GDM, if glucose challenge test is to be used as the diagnostic test, a threshold of ≥ 230 mg/dL would be recommended.

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การใช้การตรวจคัดกรองเบาหวานในการวินิจฉัยเบาหวานขณะตั้งครรภ์

นุกูล ปุ้ยสูงเนิน, วราลักษณ์ ยมะสมิต, สุมนมาลย์ มนัสศิริวิทยา

วัตถุประสงค์ *: เพื่อประเมินค่าทำนายผลบวกของการตรวจคัดกรองเบาหวานโดยใช้กลูโคส 50 กรัม เพื่อใช้ในการวินิจฉัยเบาหวานขณะตั้งครรภ์*

วัสดุและวิธีการ *: ทำการศึกษา ณ คณะแพทยศาสตร์วชิรพยาบาล มหาวิทยาลัยนวมินทราธิราช โดยการทบทวนเวชระเบียนของสตรีตั้งครรภ์ตั้งแต่ เดือนตุลาคม พ.ศ.2553 ถึง เดือนกันยายน พ.ศ.2556 โดยคัดเลือกรายที่มีผลการตรวจคัดกรองเบาหวานโดยใช้กลูโคส 50 กรัม ≥ 140 มก./ดล. และได้รับการตรวจต่อโดยใช้กลูโคส 100 กรัม การวินิจฉัยเบาหวานขณะตั้งครรภ์ใช้เกณฑ์ของ Carpenter และ Coustan และวิเคราะห์ข้อมูลโดยแบ่งค่าการตรวจคัดกรองเบาหวานโดยใช้กลูโคส 50 กรัมเป็นขั้น ๆ ขั้นละ 10 มก./ดล.*

ผลการศึกษา *: จากการตรวจคัดกรองเบาหวานในสตรีตั้งครรภ์แบบครอบคลุมทุกรายจำนวน 9,273 ราย พบสตรีตั้งครรภ์ที่มีค่าการตรวจคัดกรองเบาหวานโดยใช้กลูโคส 50 กรัม ≥ 140 มก./ดล. ซึ่งถูกคัดเข้าในการศึกษานี้มีจำนวนทั้งหมด 1,886 ราย พบอุบัติการณ์การเกิดเบาหวานขณะตั้งครรภ์ร้อยละ 3.6 หากค่าการตรวจคัดกรองเบาหวานโดยใช้กลูโคส 50 กรัม ≥ 230 มก./ดล. จะสามารถวินิจฉัยเบาหวานขณะตั้งครรภ์ได้ร้อยละ 95 และมีโอกาสที่จะวินิจฉัยเกินจริงร้อยละ 0.1 สำหรับสตรีตั้งครรภ์รายที่การตรวจคัดกรองเบาหวานเป็นบวกและมีความเสี่ยงอย่างน้อย 1 ปัจจัยต่อการเกิดเบาหวานขณะตั้งครรภ์ หากตรวจพบค่าการตรวจคัดกรองเบาหวานโดยใช้กลูโคส 50 กรัม ≥ 236 มก./ดล. จะสามารถให้การวินิจฉัยเบาหวานขณะตั้งครรภ์ได้โดยไม่จำเป็นต้องทำการตรวจยืนยันโดยใช้กลูโคส 100 กรัม*

สรุป *: สำหรับแนวทางการตรวจคัดกรองเบาหวานขณะตั้งครรภ์แบบครอบคลุมทุกราย การตรวจคัดกรองเบาหวานโดยใช้กลูโคส 50 กรัมอาจใช้วินิจฉัยเบาหวานขณะตั้งครรภ์ได้หากตรวจพบค่าที่ ≥ 230 มก./ดล.*