Rate of Abnormal Results from Repeated Screening Tests for Gestational Diabetes Mellitus after Normal Initial Tests

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Objective: *To evaluate the rate of abnormal results of repeated screening tests for gestational diabetes mellitus when initial tests were normal and related factors.*
Subjects: *Six hundred women who had clinical risk factors for gestational diabetes mellitus (GDM) who attended the antenatal care clinic at Siriraj Hospital before 24 weeks of gestation, between January and June 2005 were recruited. All had normal screening test.*
Material and Method: *All subjects were followed throughout their pregnancies. All received repeated screening and confirmatory test at 28-32 weeks of gestation. All data of screening and confirmatory test results were collected and analyzed.*
Results: *Six hundred pregnant women who had normal screening test for GDM were enrolled. Eighty-seven cases failed to take the second screening test. Of the remaining 513 cases, 154 (30.0%, 95%CI 28.2%-36.3%) had abnormal results in repeated screening tests. Among them 20 cases (3.9%) were diagnosed as GDM. Pregnant women who were ≥ 30 years old or had result of 50g GCT ≥ 120 mg/dl had significant increased risk for abnormal repeated screening tests.*
Conclusions: *Pregnant women with clinical risk of GDM should receive repeated screening tests when they are 28-32 weeks of gestation. Higher risk was observed among women ≥ 30 years old or those with a result of 50g GCT ≥ 120 mg/dl.*

Keywords: *Gestational diabetes mellitus, Screening test*

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Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance in variable severity with onset or first recognition during pregnancy. It is one of the most common metabolic complications during pregnancy that is associated with an increased risk of maternal and neonatal morbidities and mortality[1-6]. Maternal effects of gestational diabetes include an increased risk of many complications such as infection, preeclampsia, polyhydramnios, postpartum hemorrhage caused by birth canal injury from fetal macrosomia, operative delivery, and increased risk of type 2 diabetes mellitus later in life. Fetal risks can be substantial including fetal macrosomia, birth trauma, fetal anomalies, preterm labor, infectious morbidity, birth asphyxia, neonatal hyperbilirubinemia, hypoglycemia, hypocalcemia, and stillbirth. Long-term fetal effect was childhood obesity and hyperglycemia. Early diagnosis and treatment are important to control maternal blood glucose level and reduce the morbidities and mortalities in pregnant women and her babies.

Since 1986 the American Colleges of Obstetricians and Gynecologist (ACOG) has recommended a glucose screening test for all pregnant women with an average or high risk of gestational diabetes[7]. The prevalence of GDM ranges from 1 to 14% of all pregnancies, depending on the population sample and the diagnostic criteria[1].

In 2000, a clinical practice guideline for gestational diabetes was developed by the Department of Obstetrics and Gynecology, Siriraj Hospital, and currently implemented. A 50-gram glucose challenge test

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(50-g GCT) was used as initial screening test. Among those with abnormal results (> 140 mg/dL), the diagnosis was confirmed with 100-gram oral glucose tolerance test (100-g OGTT). Pregnant women with clinical risk factors are offered these tests at their first visits and repeated tests are offered at 28-32 weeks of gestation if initial tests are normal. Earlier studies of such screening and diagnostic program in Siriraj Hospital revealed that the incidence of GDM was 2.5% in all and 6.2% among high-risk pregnant women[8-10].

However, guideline non-compliance still existed, especially for repeat screening among those with normal initial test results, by either negligence or loss to follow up. The objective of the present study was to determine the rate of abnormal results from repeated screening tests for GDM after normal initial test results. The information from the present study was useful for improving the clinical practice guideline for GDM screening in the future.

Material and Method

The present study consisted of 600 pregnant women who attended antenatal care at Siriraj Hospital before 24 weeks of gestation from January to June 2005. All of these women had at least one clinical risk factor and had a normal initial screening test. Exclusion criteria were pregnant women with overt diabetes mellitus, and pregnant women who first attended antenatal care after 24 weeks of gestation.

The clinical risk factors for GDM were as follows[9,10]: family history of DM, maternal age $\geq$ 30 years, previous unexplained fetal death, previous fetal macrosomia, previous malformed baby, history of previous GDM, obesity (BMI $\geq$ 27 kg/m^2), and history of hypertension or gestational hypertension.

Data were extracted from the medical record and antenatal record including baseline characteristics, obstetric data, and clinical risk profiles. Data on GDM screening and diagnosis at initial visit and at 28-32 weeks of gestation were abstracted. The diagnosis of GDM are based on the National Diabetic Data Group which requires two or more of four plasma glucose values from OGTT that exceed the value of 105, 190, 165, 145 mg/dL[11].

Descriptive statistics were used to describe patients' baseline characteristics using mean, standard deviation, number and percentage. The rate of abnormal repeat screening test and 95% confidence interval (95% CI) was estimated. Comparison was made between those with normal and abnormal repeated tests. Chi-square test or Fishers' exact test and Student t-test where appropriate were used to determine the differences between groups. A p value of < 0.05 was considered statistically significant.

Results

Between January and June 2005, 600 pregnant women who had at least one clinical risk factor with normal screening test result for GDM before 24 weeks of gestation were enrolled. Baseline characteristics of these pregnant women are shown in Table 1. Mean age of pregnant women in the present study was 30.1 $\pm$ 5.7 years. Gestational age at first ANC was 12.3 $\pm$ 4.3 weeks and 37.8% were nulliparous.

Table 2 shows the clinical risk profile of the pregnant women in the present study. The most common risk factors were age $\geq$ 30 years (65.5%), and family history of DM (42%). Most of the patients had only one risk factor (79.5%).

Eighty-seven cases failed to take the second screening test for GDM when they were 28-32 weeks of

Table 1. Baseline characteristics of the patients (n = 600)

Characteristic	Mean $\pm$ SD
Mean age (years)	30.1 $\pm$ 5.7
Mean gestational age at first ANC ($\pm$ SD) weeks	12.3 $\pm$ 4.3
	Number (%)
Parity	
0	227 (37.8)
1	272 (45.3)
2	88 (14.7)
$\geq$ 3	13 (2.2)

Table 2. Clinical risk factor for GDM (n = 600)

Clinical risk factor	Number (%)
Family history of DM	252 (42)
Age $\geq$ 30 years	393 (65.5)
A previous unexplained fetal death	16 (2.7)
A previous fetal macrosomia	8 (1.3)
A previous malformed baby	3 (0.5)
History of previous GDM	10 (1.7)
History of HT or gestational HT	1 (0.2)
Obesity	54 (9)
Number of risk factor (s)	
1	477 (79.5)
2	108 (18)
$\geq$ 3	15 (2.5)

gestation. Of the 513 cases who received repeated screening test, abnormal results were found in 165 cases (32.2%, 95%CI 28.2%-36.3%). After that, only 154 cases received OGTT. GDM was diagnosed in 20 cases (3.9%), and all were in class A1. These 20 cases of GDM would have been missed if repeated screening test had been neglected.

Table 3 shows the comparison of characteristics between pregnant women who had normal and abnormal repeated screening test results at 28-32 weeks of gestation. Pregnant women with abnormal repeated screening test were significantly older than those with normal results ($p < 0.001$). In addition, mean 50-g GCT results from the initial test were also significantly higher among women with abnormal repeated test results ($p < 0.001$). The rate of abnormal repeated test results was 43.1% when 50-g GCT results from initial test was $\geq$ 120 mg/dL while the rate was only 25.3% when 50-g GCT results from initial test was < 120 mg/dL ($p < 0.001$).

From Table 4, age $\geq$ 30 years is the only risk factor that significantly increased the rate of abnormal repeated test results ($p = 0.022$). Number of clinical risks was not a significant factor.

Discussion

Screening for GDM is controversial. The American Colleges of Obstetricians and Gynecologists (ACOG)[12] recommended screening all pregnant women who had risk factors for GDM by a 2-step

Table 3. Comparison of characteristic between pregnant women who had normal and abnormal repeated screening test at 28-32 weeks of gestation (n = 513)

Characteristic	Repeated screening test results		p-value
	Normal, n = 348 Number (%)	Abnormal, n = 165 Number (%)	
Mean age ($\pm$ SD) (years)	29.48 $\pm$ 5.8	31.28 $\pm$ 5.3	<0.001
Mean gestational age at first ANC ($\pm$ SD) week	12.24 $\pm$ 4.2	12.29 $\pm$ 4.1	0.902
Mean 50 g GCT of initial test ($\pm$ SD)	108.98 $\pm$ 17.3	117.43 $\pm$ 16.6	<0.001
Mean 50 g GCT of initial test			<0.001
< 120 mg/dl	236 (74.7%)	80 (25.3%)	
$\geq$ 120 mg/dl	112 (56.9%)	85 (43.1%)	

Table 4. Comparison of clinical risk factor between pregnant women who had normal and abnormal repeated screening test at 28-32 weeks of gestation

Clinical risk factors	Repeated screening test results		p-value
	Normal, n = 348 Number (%)	Abnormal, n = 165 Number (%)	
Family history of DM	150 (69.4%)	66 (30.6%)	0.506
Age $\geq$ 30 years	215 (64.4%)	119 (35.6%)	0.022
A previous unexplained fetal death	5 (45.5%)	6 (54.5%)	0.090
A previous fetal macrosomia	4 (66.7%)	2 (33.3%)	0.610
A previous malformed baby	3 (100%)	0 (0%)	0.323
History of previous GDM	3 (50%)	3 (50%)	0.279
History of HT or gestational HT	0 (0%)	0 (0%)	-
Obesity	33 (66%)	17 (34%)	0.770
Number of risk factor(s)			0.162
1	286 (69.6%)	125 (30.4%)	
2	57 (63.3%)	33 (36.7%)	
$\geq$ 3	5 (42%)	7 (58%)	

approach. A 50-g GCT should be used as initial screening followed by a 100-g OGTT for those with abnormal 50-g GCT. The diagnosis of GDM was made with 100 g OGTT when any 2 of 4 plasma levels met or exceeded the value of 95, 180, 155, 140 mg/dl (Carpenter and Coustan criteria)[12]. In Siriraj Hospital, a clinical practice guideline has been developed with the use of risk-factor-based selective screening program. Similar 2-step approach as recommended by ACOG was used. However, the cutoff values for OGTT of 105, 190, 165, 145 mg/dL were used as recommended by the National Diabetes Data Group[11].

Normal pregnant women are characterized by mild fasting hypoglycemia, postprandial hyperglycemia, and hyperinsulinemia. This is possibly due to a result of the increased plasma glucose levels (diabetogenic effect) by maternal insulin resistance from many hormones that act as anti-insulin effect (estrogen, progesterone, and human placental lactogen). Because insulin resistance increases with gestational age, these women were still at risk for developing GDM later in their pregnancies. Hence, following the authors' guideline, repeated screening was offered at 28-32 weeks of gestation if their initial test results were normal.

The results of the present study showed that at the second tests, abnormal results were found in 165 of 513 cases (32.2%, 95% CI 28.2%-36.3%), and GDM was eventually diagnosed in 20 cases. The results emphasize the need and importance for repeated screening even when initial tests were normal. From the present study, at least 20 cases of GDM would have been missed if repeated test at 28-32 weeks of gestation were neglected.

However, there were 87 cases who did not receive the second test and another 11 cases who did not receive 100-g OGTT after abnormal second test. Therefore, the actual rate of abnormal repeated test and GDM might be higher than the result suggests. If the rate was applied to those who were lost to follow up, approximately 28 cases would have abnormal second test results (32.2% of 87 cases), and another five cases would have been diagnosed with GDM (13% of 28 and 11 cases).

The present study also demonstrated that age $\geq$ 30 years and higher value of initial 50-g GCT ($\geq$ 120 mg/dL) significantly increased the risk of abnormal results during the second tests. These women might have some degree of diabetogenic effect but was not high enough to show up during initial tests before 24 weeks of gestation. Therefore, pregnant women with such characteristics should receive careful evaluation during their antenatal care. Although the number of clinical risks has been reported to be positively associated with increased risk for GDM, the present study failed to demonstrate its relationship with the rate of abnormal repeated screening tests. Pregnant women with many clinical risks might have already been diagnosed with GDM early in their pregnancy and the risk for GDM for the rest of these women was not so great.

In conclusion, the results of the present study demonstrated that 32.2% of pregnant women who had initial screening tests for GDM before 24 weeks of gestation, would have abnormal tests when repeated at 28-32 weeks of gestation. Increased rate of abnormal tests was found in women $\geq$ 30 years old and those with a higher value of initial 50-g GCT ($\geq$ 120 mg/dL). Repeated screening for GDM among high-risk pregnant women is of value and necessary in detecting GDM that occurs late in pregnancy.

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อัตราการตรวจพบความผิดปกติในการตรวจคัดกรองซ้ำภาวะเบาหวานขณะตั้งครรภ์หลังผลการตรวจครั้งแรกปกติ

ดิฐกานต์ บริบูรณ์หิรัญสาร, วิบูลย์ จุติมงคลกุล

วัตถุประสงค์*: เพื่อศึกษาอัตราการตรวจพบความผิดปกติ ในการตรวจคัดกรองซ้ำภาวะเบาหวานขณะตั้งครรภ์หลังการตรวจครั้งแรกปกติ และปัจจัยที่เกี่ยวข้อง*

กลุ่มตัวอย่าง*: สตรีตั้งครรภ์ที่มารับการฝากครรภ์ที่โรงพยาบาลศิริราช ที่มีปัจจัยเสี่ยงต่อการเกิดโรคเบาหวานระหว่างตั้งครรภ์ และพบการตรวจคัดกรองครั้งแรกปกติ ในช่วงตั้งแต่มกราคม – มิถุนายน พ.ศ. 2548 จำนวน 600 คน*

วัสดุและวิธีการ*: ทำการคัดเลือกกลุ่มตัวอย่างตามเกณฑ์ที่กำหนด ติดตามการตั้งครรภ์ของสตรีตั้งครรภ์โดยเก็บข้อมูลของการตรวจคัดกรองและวินิจฉัยโรคเบาหวานระหว่างตั้งครรภ์ เมื่อมาฝากครรภ์ครั้งแรก และเมื่อตรวจคัดกรองซ้ำและวินิจฉัย ที่อายุครรภ์ 28-32 สัปดาห์ และทำการรวบรวมข้อมูลต่าง ๆ และนำข้อมูลที่ได้ไปวิเคราะห์ตามขั้นตอน*

ผลการศึกษา*: เก็บรวบรวมข้อมูลจากหญิงตั้งครรภ์ จำนวน 600 ราย มีหญิงตั้งครรภ์ไม่มารับการตรวจคัดกรองซ้ำตามนัด จำนวน 87 ราย คิดเป็น14.5% คงเหลือ 513 รายที่มารับการตรวจคัดกรองซ้ำ ในจำนวนนี้มีผลการตรวจคัดกรองซ้ำผิดปกติของโรคเบาหวานระหว่างตั้งครรภ์ จำนวน 165 ราย คิดเป็น 32.2% (95% CI 28.2% – 36.3%) และมีหญิงตั้งครรภ์ที่มารับการตรวจยืนยันด้วยวิธี 100 g OGTT 154 ราย ในกลุ่มนี้พบว่ามีหญิงตั้งครรภ์ที่ได้รับการวินิจฉัย เป็นโรคเบาหวานจำนวน 20 ราย คิดเป็น 3.9% และพบว่าถ้ามารดาอายุตั้งแต่ 30 ปีขึ้นไปหรือผลการตรวจ 50-g GCT ครั้งแรกมากกว่าหรือเท่ากับ 120 มก./ดล. จะเพิ่มความเสี่ยงในการพบความผิดปกติของการตรวจคัดกรองโรคเบาหวานขณะอายุครรภ์มากกว่า 24 สัปดาห์ อย่างมีนัยสำคัญทางสถิติ*

สรุป*: หญิงตั้งครรภ์ที่มีปัจจัยเสี่ยงต่อการเกิดโรคเบาหวานและมารับการตรวจคัดกรองขณะอายุครรภ์ต่ำกว่า 24 สัปดาห์ แล้วมีผลการตรวจคัดกรองโรคเบาหวานปกติ จะมีอุบัติการณ์การพบความผิดปกติของการตรวจคัดกรองซ้ำโรคเบาหวาน ขณะอายุครรภ์ 28-32 สัปดาห์เท่ากับร้อยละ 30.2 โดยเฉพาะถ้ามีอายุมากกว่า 30 ปีหรือ ผลการตรวจ 50 g GCT มากกว่าหรือเท่ากับ 120 มก./ดล. ดังนั้นหญิงตั้งครรภ์ดังกล่าว ควรที่ได้รับการตรวจคัดกรอง และการวินิจฉัยภาวะเบาหวานขณะตั้งครรภ์ เมื่อมาฝากครรภ์ครั้งแรกและตรวจซ้ำขณะอายุครรภ์มากกว่า 28-32 สัปดาห์*