Incidence of Gestational Diabetes Mellitus among Pregnant Women with One Abnormal Value of Oral Glucose Tolerance Test

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Objective: *To compare the incidence of Gestational Diabetes Mellitus (GDM) between pregnant women with one abnormal value of oral glucose tolerance test (Study group) and those with normal screening test (Control group) and compare their pregnancy outcomes.*
Design: *Retrospective cohort study.*
Setting: *Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital.*
Material and Method: *Two hundred and twenty eight at-risk pregnant women were enrolled from January 2003 to November 2004. They were divided equally with 114 each in study and control group. All received GDM screening before 24 weeks of gestation following the guidelines used at Siriraj Hospital. Data collection included baseline characteristics, data on clinical risks and screening results, final diagnosis, maternal and neonatal complications. Incidence of GDM and pregnancy outcomes was compared between the two groups.*
Results: *Both groups' baseline characteristics and clinical risks were comparable, except that the mean age of women in the study group was significantly greater than in the control group (32.8 $\pm$ 4.9 and 29.7 $\pm$ 5.5 years, $p < 0001$). The incidence of GDM was significantly higher among in study group compared with the control group (21.9% and 1.8% respectively, RR 12.5, 95%CI 3.0-51.5). After adjusting for maternal age, abnormal one OGTT value was the only independent risk for developing GDM (adjusted OR 16.3, 95%CI 3.7-71.9, $p < 0.001$). Infants of the study group had significantly higher birth weight than those of the control group (3203.6 $\pm$ 563.9 and 3050.7 $\pm$ 457.8 g respectively, $p = 0.026$). Rate of primary cesarean section, asphyxia, macrosomia, low birth weight, and other neonatal complications were comparable between the two groups.*
Conclusion: *Pregnant women with one abnormal value of oral glucose tolerance test had a significantly greater risk of developing GDM compared to women with normal screening test. Pregnancy outcomes between the two groups were not significantly different.*

Keywords: *Gestational diabetes mellitus, Incidence, One abnormal value, Oral glucose tolerance test*

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Gestational Diabetes Mellitus (GDM) is defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy. Pregnancy is a diabetogenic condition characterized by insulin resistance with a compensatory increase in B-cell response and hyperinsulinemia. Insulin resistance usually begins in the second trimester and progresses throughout the remainder of pregnancy. Placental secretion of hormones such as progesterone, cortisol, placental lactogen, prolactin and growth hormone is a major cause of the insulin-resistant state. GDM complicates 7% of all pregnancies and can be associated with various maternal and fetal complications[1,2].

The GDM diagnosis is based on criteria originally proposed by O'Sullivan and Mahan and con-

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verted to plasma value by the Nation Diabetes Data Group (NDDG) in 1979[1,2]. Diagnosis of GDM requires that at least two of four glucose levels of the100 g OGTT meet or exceed the upper normal limit. The cut off values for fasting, 1, 2 and 3 hours blood glucose are ≥ 105, 190, 165, and 145 mg/dl respectively[1-3].

Screening program of pregnant women for GDM in Siriraj Hospital has been developed using a selective screening process, based on history and clinical risk factors as shown in Table 1[4]. A 50-g glucose challenge test (50-g GCT) is used as a screening method and 100-g oral glucose tolerance test (100-g OGTT) is used as a confirmatory test.

Several studies have demonstrated that even one abnormal glucose value of diagnostic OGTT was associated with unfavorable fetomaternal outcomes of pregnancy such as macrosomia, pre-eclampsia, eclampsia, and cesarean delivery[5-10]. One abnormal value of OGTT might reflect some degree of carbohydrate intolerance that might be related to increased risk for maternal and neonatal morbidities.

However, no study has demonstrated the risk of developing GDM later in their pregnancy among this group of women. Therefore, the present study was aimed at determining the incidence of GDM among those who had one abnormal OGTT value. In addition, pregnancy outcomes were evaluated in those with normal and abnormal tests.

Table 1. Clinical risk factor for GDM in Siriraj Hospital[4]

Criteria for pregnant women needing selective screening for gestational diabetes
Family history of diabetes mellitus
Age ≥ 30 years
Previous history of macrosomia
Previous history of congenital fetal anomaly
Previous history of unexplained intrauterine fetal death
Previous history of gestational diabetes during previous pregnancy
Hypertension
Obesity (body mass index ≥ 27 kg/m^2)

Material and Method

The retrospective review of data was conducted among women attending antenatal care at Siriraj Hospital between January 2003 and November 2004. Pregnant women, who attended the antenatal clinic before 24 weeks of gestation and had at least 1 clinical risk factor, were eligible. Those who were known cases of DM before pregnancy and those who did not follow the screening guideline were excluded.

Screening test with 50-g GCT was offered at their first visit and those with abnormal results (≥ 140 mg/dl) were confirmed with the diagnosis of GDM with 100-g OGTT. Diagnosis of GDM requires that at least two of four glucose levels of the100-g OGTT meet or exceed the upper limit of normal. The cut off values for fasting 1, 2 and 3 hours blood glucose were ≥ 105, 190, 165, and 145 mg/dl respectively[4]. If GDM was not diagnosed, all the women were retested between 28-32 weeks using the same methods as the first visit[4].

The patients were divided into two groups according to the results of 50-g GCT and 100-g OGTT. The study group was composed those who had abnormal 50-g GCT and one abnormal value on 100-g OGTT. The control group was those who had normal screening test.

A review of medical records, antenatal and labor records were conducted among these women. Data collection included baseline characteristics, clinical risks for GDM, results of screening and diagnostic tests at first visit and at 28-32 weeks of gestation, final diagnosis, labor and delivery data, and maternal and neonatal complications.

The two groups were then compared with regard to various baseline and obstetric characteristics and the development of GDM later in their pregnancy. Relative risk and 95% Confidence Interval (CI) was estimated. Pregnancy and neonatal outcomes were also compared. Descriptive statistics were used to describe patients' characteristics. Student t test and Chi-square test were used in the comparison between the two groups as appropriate. Relative risk and 95%CI were estimated. Multiple logistic regression analysis was used to determine independent associated factors, adjusted for potential confounders. Adjusted Odds Ratio (OR) and 95%CI were estimated. A p value of < 0.05 was considered statistically significant.

The present study was reviewed and approved by the Ethics Committee, Faculty of Medicine Siriraj Hospital, Mahidol University.

Results

During the study period, 228 women were enrolled. Table 2 shows baseline and obstetric characteristics of the women. Mean age of the study group was significantly higher than the control group (29.7 ± 5.5, and 32.8 ± 4.9 years, respectively, $p < 0.001$). Women in the study group attended ANC at a significantly earlier gestational age than the control group (12.1 ±

4.0 and 13.7 ± 4.7 weeks respectively, p = 0.005). Parity in the study group and control group was similar.

Table 3 shows comparison of clinical risk factors for GDM between the 2 groups. Clinical risk factors for developing GDM were comparable, except that the study group was significantly older than the control group (78.1% versus 57.9%; p = 0.001). The most common risk factor was maternal age ≥ 30 years in both groups. The study group had the number of clinical risk factors for GDM slightly more than the control group but not statistically significant.

Table 4 shows the incidence of GDM later in their pregnancy. The study group had a significantly greater incidence of GDM than the control group (21.9% and 1.8%, respectively, RR 12.5, 95%CI 3.0-51.5). All GDM cases were in class A1. Multiple logistic regression analysis was used to determine the association between abnormal 1 value of OGTT and the development of GDM, adjusted for age. The result shows that adjusted OR was 16.3 (95%CI 3.7-71.9). Women in the study group were 16.3 times more likely to develop GDM later in their pregnancy, compared with those in the control group.

Results on pregnancy outcomes are shown in Table 6. In both groups, mean gestational age at delivery and rate of primary cesarean were not significantly different between the 2 groups. Infants of the study group had a significantly higher birth weight

Table 2. Comparison of maternal characteristics (n = 228)

Characteristics	Control group n = 114	Study group n = 114	p-value
Mean maternal age (year) ± SD	29.7 ± 5.5	32.8 ± 4.9	<0.001
Mean gestational age at first ANC (weeks) ± SD	13.7 ± 4.7	12.1 ± 4.1	0.005
Parity			0.09
0	43 (37.7%)	44 (38.6%)	
1	45 (39.5%)	56 (49.1%)	
≥ 2	26 (22.8%)	14 (12.3%)	

Table 3. Comparison of clinical risk factor of GDM

Risk factor	Control group n = 114	Study group n = 114	p-value
Family history of diabetes mellitus	56 (49.1%)	44 (38.6%)	0.109
Age ≥ 30 years	66 (57.9%)	89 (78.1%)	0.001
Previous history of macrosomia	4 (3.6%)	1 (0.9%)	0.366
Previous history of congenital fetal anomaly	0 (0%)	0 (0%)	-
Previous history of unexplained intrauterine fetal death	1 (0.9%)	0 (0%)	1.000
Previous history of gestational diabetes during previous pregnancy	0 (0%)	0 (0%)	-
Hypertension	0 (0%)	1 (0.9%)	0.496
Obesity (body mass index ≥ 27 kg/m^2)	10 (8.8%)	16 (14.0%)	0.211
Number of risk			0.158
1	92 (80.7%)	83 (72.8%)	
≥ 2	22 (19.3%)	31 (27.2%)	

Table 4. Comparison of incidence of GDM later in pregnancy

Group	GDM	Normal	RR (95%CI)
Control group (n = 114)	2 (1.8%)	112 (98.2%)	1.0
Study group (n = 114)	25 (21.9%)	89 (78.1%)	12.5 (3.0-51.5)

Table 5. Results of multiple logistic regression analysis

Variables	Adjusted Odds ratio	95%CI	p-value
Abnormal 1 value of OGTT	16.3	3.7-71.9	<0.001
Age > 30 years	0.8	0.3-2.2	0.841

Table 6. Comparison of pregnancy outcomes

Outcomes	Control group n = 114	Study group n = 114	p-value
Mean gestational age at delivery (weeks) SD	38.7 ± 1.6	38.5 ± 1.6	0.204
Mean birth weight (grams) SD	3050.7 ± 457.8	3203.6 ± 563.9	0.026
Primary cesarean	29 (25.4%)	30 (26.3%)	0.420
Male infant	57 (50.0%)	57 (50.0%)	0.893
Large for gestational age	3 (2.6%)	8 (7.0%)	0.122
Low birth weight	12 (10.5%)	10 (8.8%)	0.654
Birth asphyxia	0 (0%)	0 (0%)	-
Phototherapy	4 (3.5%)	6 (5.2%)	0.518

than those of the control group (3203.6 ± 563.9 and 3050.7 ± 457.8 g respectively, p = 0.026). Other neonatal outcomes were relatively good and comparable between the groups, including LGA, low birth weight, birth asphyxia, and need for phototherapy.

Discussion

From the present study, one abnormal value of OGTT from initial screening test was independently associated with the development of GDM later in pregnancy (adjusted OR 16.3, 95%CI 3.7-71.9). This group of pregnant women demonstrated the risk for developing GDM later in their pregnancy exceeded those who had normal screening test. No previous study has demonstrated such an association. It is possible that pregnant women with one abnormal value of OGTT had impaired glucose tolerance to some degree that increased the risk for GDM later in pregnancy when placental hormones further increased insulin resistance.

Insulin resistance, which is the cause of GDM is known to increase with age[11]. It is, thus, possible that the study group had greater risk because they were significantly older than the control group. After adjusting for maternal age, such association existed. The older women were 16.3 times more likely to develop GDM than those with a normal screening test.

The diagnosis of gestational diabetes mellitus in the present study was based on criteria of National Diabetes Data Group (NDDG)[1]. These cutoff values were higher than the thresholds recommended by the Carpenter and Coustan modification. These defined the cutoffs at 95, 180, 155, and 140 mg/dl at fasting, 1, 2, and 3 hours respectively[2]. Ferrara A et al reported that the prevalence of GDM increased on average by 50% with the use of the Carpenter and Coustan thresholds[12]. So, if such diagnostic criteria were used, pregnant women might benefit from early diagnosis and treatment to prevent adverse outcomes. However, Pennison and Egerman[13] compared perinatal outcomes in 130 women with GDM diagnosed using the NDDG criteria with 43 women diagnosed using the Carpenter and Coustan criteria and concluded that such benefits of the latter criteria were unclear.

The number of abnormal OGTT values related to the severity of disease and several studies demonstrated that even one abnormal value at the diagnostic OGTT is associated with an unfavorable feto-maternal outcome of pregnancy[5] Many studies have reported that one abnormal value of OGTT had a significant impact on the maternal and perinatal outcomes in relation to the increased incidence of LGA infants and possibly on the incidence of pre-eclampsia and eclampsia[5-10].

However, no serious adverse maternal outcomes were reported in the present study. With regard to fetal outcomes, both groups showed comparable rate of adverse outcomes. Infants of women in the study group weighed significantly more than those of the

control group, but the incidence of LGA was only slightly higher among the study group. This might be the result of effective screening and counseling programs in our institution. Such programs were offered to all at-risk women regardless of testing results. In addition, more intensive counseling and follow-up were given to those diagnosed with GDM.

In summary, the risk for developing GDM increased significantly among women with one abnormal OGTT value. This emphasizes the importance for early antenatal care and early screening and diagnosis of GDM. Greater attention should be paid to this group of women even if they had only one abnormal OGTT value. Intensive counseling regarding their risk as well as an appropriate diet control program should be advised. Such measures could prevent adverse pregnancy outcomes in both the mothers and their newborn infants.

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อุบัติการณ์การเกิดภาวะเบาหวานขณะตั้งครรภ์ที่ตรวจพบค่า Oral Glucose Tolerance Test ผิดปกติหนึ่งค่าในโรงพยาบาลศิริราช

ศรลดา ธเนศวร, ดิฐกานต์ บริบูรณ์หิรัญสาร

วัตถุประสงค์: เพื่อเปรียบเทียบอุบัติการณ์การเกิดภาวะเบาหวานขณะตั้งครรภ์ในสตรีตั้งครรภ์ที่ตรวจพบค่า Oral Glucose Tolerance Test ผิดปกติหนึ่งค่า (กลุ่มศึกษา) และสตรีตั้งครรภ์ที่ผลการตรวจกรองปกติ (กลุ่มควบคุม) และเปรียบเทียบผลของการตั้งครรภ์ระหว่างสตรีสองกลุ่มดังกล่าว

วัสดุและวิธีการ: Retrospective cohort study

สถานที่ทำการศึกษา: ภาควิชาสูติศาสตร์-นรีเวชวิทยา คณะแพทยศาสตร์ศิริราชพยาบาล

กลุ่มตัวอย่าง: สตรีตั้งครรภ์ที่มีปัจจัยเสี่ยงของภาวะเบาหวานขณะตั้งครรภ์จำนวน 228 คนโดยแบ่งเป็นกลุ่มศึกษาและกลุ่มควบคุมกลุ่มละ 114 คน ซึ่งมาฝากครรภ์ตั้งแต่ช่วงเดือนมกราคม พ.ศ. 2546 ถึงเดือนพฤศจิกายน พ.ศ. 2547 โดยสตรีทั้งหมดได้รับการตรวจกรองภาวะเบาหวานขณะตั้งครรภ์ก่อนอายุครรภ์ 24 สัปดาห์และทำตามขั้นตอนของแนวทางการดูแลรักษาในโรงพยาบาลศิริราช

วัสดุและวิธีการ: ทำการเก็บข้อมูลต่าง ๆ ของกลุ่มตัวอย่าง ได้แก่ ข้อมูลพื้นฐาน, ข้อมูลเกี่ยวกับปัจจัยเสี่ยงของภาวะเบาหวานขณะตั้งครรภ์, ผลของการตรวจกรอง, การวินิจฉัยสุดท้าย และภาวะแทรกซ้อนของมารดาและทารก, เปรียบเทียบอุบัติการณ์การเกิดภาวะเบาหวานขณะตั้งครรภ์และผลของการตั้งครรภ์ระหว่างสตรีสองกลุ่ม

ผลการศึกษา: กลุ่มตัวอย่างทั้งสองกลุ่มมีข้อมูลพื้นฐานที่คล้ายคลึงกันยกเว้นอายุเฉลี่ยในกลุ่มศึกษามากกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ (32.8 $\pm$ 4.9 และ 29.7 $\pm$ 5.5 ปี, $p < 0.001$) อุบัติการณ์การเกิดภาวะเบาหวานขณะตั้งครรภ์ในกลุ่มศึกษาสูงกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ (ร้อยละ 21.9และร้อยละ1.8 ตามลำดับ, RR 12.5, 95%CI 3.0-51.5) พบว่าค่า OGTT ที่ผิดปกติ 1 ค่า เป็นปัจจัยเสี่ยงที่สำคัญต่อการเกิดภาวะเบาหวานขณะตั้งครรภ์ (adjusted OR 16.3, 95%CI 3.7-71.9, $p < 0.001$) ทารกในกลุ่มศึกษามีน้ำหนักแรกคลอดสูงกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ (3203.6 $\pm$ 563.9 และ 3050.7 $\pm$ 457.8 กรัม, $p = 0.026$) อัตราการผ่าตัดคลอด, ภาวะขาดออกซิเจนในทารก, ทารกน้ำหนักตัวมากกว่าปกติ, ทารกน้ำหนักน้อยและภาวะแทรกซ้อนอื่นของทารกไม่แตกต่างกันในทั้งสองกลุ่ม

สรุป: สตรีตั้งครรภ์ที่ตรวจพบค่า OGTT ผิดปกติหนึ่งค่ามีความเสี่ยงที่จะเกิดภาวะเบาหวานในขณะตั้งครรภ์มากกว่าสตรีตั้งครรภ์ที่ตรวจกรองเบาหวานปกติอย่างมีนัยสำคัญทางสถิติและผลของการตั้งครรภ์ในทั้งสองกลุ่มไม่มีความแตกต่างกันทางนัยสำคัญทางสถิติ