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Gestational Diabetes Mellitus in Pregnancy with Single Abnormal Value of 100-Gram Oral Glucose Tolerance Test at a Tertiary Hospital in Thailand

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ABSTRACT

Objectives: To determine the incidence of gestational diabetes mellitus (GDM) in pregnancy with a single abnormal value of the 100-gram oral glucose tolerance test (OGTT) after repeating for 1 month and to compare adverse pregnancy outcomes between pregnant women with a single abnormal value of the 100-gram OGTT and those with a normal 100-gram OGTT.

Materials and Methods: The retrospective cohort study was conducted from 1 August 2018 until 30 May 2021. Three hundred twenty-four pregnant women with a single abnormal value of 100-gram OGTT were recruited into a study group, while 365 pregnant women with normal 100-gram OGTT were recruited into a control group. In the study group, we repeated the second OGTT within one month to determine the incidence of GDM. Maternal and perinatal outcomes were then compared between the two groups.

Results: The incidences of GDMA2 and GDMA1 in pregnancy with a single abnormal test were 7.1% and 25%, respectively. Between the two groups, pregnancies in the study group were older (34.4 ± 7.3 vs. 29.3 ± 6.7, $p < 0.001$). Gestational hypertension (1 (0.3%) and 8 (2.5%), $p = 0.027$) and neonatal hypoglycemia (6 (1.6%) and 18 (5.6%), $p = 0.005$) were the adverse outcome that was higher in the study group with statistical differences.

Conclusion: Pregnant women with a single abnormal value of 100-gram OGTT developed a high incidence rate of GDM, gestational hypertension and neonatal hypoglycemia.

Keywords: 100-gram glucose tolerance test, gestational diabetes mellitus, incidence, one abnormal value, adverse pregnancy outcomes.

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ภาวะเบาหวานที่เกิดขึ้นขณะตั้งครรภ์ที่ตรวจพบค่าน้ำตาลผิดปกติหนึ่งค่าจากการตรวจความทนทานต่อน้ำตาล 100 กรัมที่โรงพยาบาลระดับตติย-ภูมิในประเทศไทย

พิมพ์ชนก พึ่งเสมา, สิริพร ไตรนาค

บทคัดย่อ

วัตถุประสงค์: *เพื่อหาอุบัติการณ์ของภาวะเบาหวานขณะตั้งครรภ์ที่ตรวจความทนทานต่อน้ำตาล 100 กรัม ที่พบค่าผิดปกติหนึ่งค่าหลังจากตรวจซ้ำภายในหนึ่งเดือน และผลการตั้งครรภ์ที่ไม่พึงประสงค์*

วัสดุและวิธีการ: *การศึกษาย้อนหลังตั้งแต่วันที่ 1 สิงหาคม 2561 ถึงเดือน 30 พฤษภาคม 2564 แบ่งหญิงตั้งครรภ์จำนวน 324 คนที่มีพบความผิดปกติจากการตรวจความทนทานต่อน้ำตาล 100 กรัม 1 ค่าเป็นกลุ่มศึกษา และหญิงตั้งครรภ์ 365 คนที่ผลการตรวจความทนทานต่อน้ำตาล 100 กรัมปกติเป็นกลุ่มควบคุม โดยหญิงตั้งครรภ์ในกลุ่มศึกษาจะได้รับการตรวจความทนทานต่อน้ำตาล 100 กรัมซ้ำภายในหนึ่งเดือนเพื่อหาอุบัติการณ์การเกิดภาวะเบาหวาน และเปรียบเทียบภาวะแทรกซ้อนของมารดาและทารกในหญิงตั้งครรภ์ทั้งสองกลุ่ม*

ผลการศึกษา: *อุบัติการณ์ของภาวะเบาหวานชนิด GDMA1 และ GDMA2 ในสตรีตั้งครรภ์ที่ตรวจความทนทานต่อน้ำตาล 100 กรัมและพบความผิดปกติหนึ่งค่าเท่ากับร้อยละ 25 และร้อยละ 7.1 ตามลำดับ กลุ่มศึกษามีอายุมากกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ (34.4 ± 7.3 vs. 29.3 ± 6.7, p < 0.001) ภาวะความดันโลหิตสูงที่ไม่พบโปรตีนในปัสสาวะ (1 (ร้อยละ 0.3) and 8 (ร้อยละ 2.5), p = 0.027) และภาวะน้ำตาลต่ำในเด็กแรกเกิด (6 (ร้อยละ 1.6) and 18 (ร้อยละ 5.6), p = 0.005) เป็นภาวะแทรกซ้อนที่พบในกลุ่มศึกษามากกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ*

สรุป: *การตรวจความทนทานต่อน้ำตาล 100 กรัมขณะตั้งครรภ์ที่พบความผิดปกติหนึ่งค่า มีโอกาสเกิดเบาหวานขณะตั้งครรภ์และภาวะความดันโลหิตสูงที่ไม่พบโปรตีนในปัสสาวะ และการเกิดภาวะน้ำตาลต่ำในเลือดทารกแรกเกิดได้มากขึ้น*

คำสำคัญ: *การตรวจความทนทานต่อน้ำตาล 100 กรัม, ภาวะเบาหวานขณะตั้งครรภ์, อุบัติการณ์, ความผิดปกติหนึ่งค่า, ภาวะแทรกซ้อนของการตั้งครรภ์*

Introduction

Gestational diabetes mellitus (GDM) is a condition of carbohydrate intolerance that develops during pregnancy[1]. In Southeast Asian countries, including Thailand, the highest prevalence of GDM was reported with a median estimate of 29.2%[2]. GDM is associated with several negative maternal and neonatal complications, including hypertension, an increased rate of cesarean section, fetal macrosomia, neonatal hypoglycemia, and shoulder dystocia[3]. Furthermore, half of the women with GDM during pregnancy can develop type 2 diabetes mellitus 5-10 years post-delivery[2].

Diagnostic tests of GDM can be classified as one-step and two-step tests. It is recommended that all pregnant women should be tested for GDM (use patient clinical risk factors). If the 50-g glucose challenge test (GCT) is positive (≥ 140 mg/dL), a 100-g oral glucose tolerance test (OGTT) should be performed. The threshold values used for the OGTT based on the criteria of Carpenter and Coustan are: fasting ≥ 95 mg/dL, 1-hour ≥ 180 mg/dL, 2-hour ≥ 155 mg/dL and 3-hour ≥ 140 mg/dL. At least two abnormal values are required for diagnosis[1,3].

There is currently no consensus on whether pregnant women with a single abnormal value of 100-g OGTT should be retested or treated the same as pregnant women with a normal 100-g OGTT. As a result, the purpose of this study was to find the incidence of GDM and adverse outcomes in pregnant women with a single abnormal value of 100-g OGTT.

Materials and Methods

A retrospective cohort study was conducted at Chonburi Hospital after gaining approval from the institutional review boards. Laboratory records and medical databases from 1 August 2018 to 30 May 2021 were reviewed.

Singleton pregnancy with antenatal care clinic attendance and delivery at Chonburi Hospital, performance of a 50-g GCT at gestational age (GA) 24-28 weeks, pregnancy confirmation before 22 weeks, no underlying diseases, repeat the 100-g OGTT within 1 month, and Asian ancestry were the inclusion criteria. Exclusion criteria included a previous history of GDM during a previous pregnancy, a first degree relative with diabetes mellitus, BMI ≥ 30 kg/m^2, underlying disease with diabetes mellitus and lethal congenital abnormalities.

The data were analyzed using IBM SPSS Statistic 26.0. The sample size was calculated based on a similar study carried out by Kang et al (1997) at Seoul National University Bundang Hospital, which showed the incidence of GDM after repeat 100-g OGTT (28.5%) in pregnant women who were screened for GDM at 24-28 weeks[4]. The number of pregnant women with single abnormal value of 100-g OGTT should be at least 314 with alpha 0.05.

Following Chonburi hospital's clinical practice guideline, screening for GDM is based on risk screening. Pregnant women with severe obesity, a first-degree family history of diabetes mellitus, a prior history of GDM, impaired glucose metabolism, or glucosuria should be tested early at an antenatal visit and reevaluated at GA 24-28 weeks if GDM is diagnosed at first visit.

Pregnant women without risk factors were screened for GDM with 50-g GCT at GA 24-28 weeks based on the inclusion criteria. If the result was abnormal (140 mg/dL), it had to be tested again with a 100-g OGTT within one month. According to Carpenter and Coustan's criteria, the cut-off values for fasting, 1, 2, and 3-hour blood glucose were 95, 180, 155, and 140 mg/dL respectively.

After diagnosis with GDM, the patient was referred to a nutritionist to adjust her diet and calories, an ophthalmologist to rule out diabetic retinopathy, and an endocrine specialist. Pharmacological methods are recommended if diet modification cannot maintain the fasting plasma glucose levels < 95 mg/dL or 2-hour postprandial plasma glucose < 120 mg/dL.

All pregnancies with a single abnormal 100-g OGTT were assigned to a study group, whereas those with an abnormal 50-g GCT but a normal 100-g OGTT were assigned to a control group. To determine the incidence of GDM in a pregnancy with a single abnormal 100-g OGTT, the test must be repeated within one

month.

Pre-pregnancy body mass index (BMI), maternal age, history of previous cesarean section, and parity were all recorded as baseline characteristics. The primary outcome was the occurrence of GDM in pregnancy after a single abnormal 100-g OGTT that was repeated after one month. Secondary outcomes were maternal and neonatal outcomes. Maternal outcomes included GA at delivery, route of delivery (including cesarean section, spontaneous vertex delivery, vacuum extraction), postpartum hemorrhage, hypertensive disorder of pregnancy (including preeclampsia with a severe feature, gestational hypertension). Preeclampsia with severe features was diagnosed when blood pressure ≥ 160/110 mmHg with proteinuria (urine protein: creatinine ratio ≥ 0.3). Gestational hypertension was defined as blood pressure ≥ 140/90 mmHg without proteinuria[6]. Neonatal outcomes included birth weight, Apgar score at 1 minute, 5 minutes, 10 minutes, birth weight ≥ 4,000 grams, intrauterine growth restriction (IUGR) (birth weight less than 10th percentile for GA at birth), neonatal hypoglycemia, neonatal intensive care unit (NICU) admission, and sick newborn (SNB) admission.

Maternal and neonatal outcomes were compared between the two groups using independent t test and chi square test. A p value < 0.05 was considered statistically significant.

Results

During the study period, 365 pregnant women with one abnormal value of 100-g OGTT were assigned to the study group, while 324 pregnant women with normal 100-g OGTT values were assigned to the control group.

Incidences of GDMA1 and GDMA2 after repeat 100-g OGTT within 1 month were 81 (25%) and 23 (7.1%) respectively, and incidences of normal value and one abnormal value were 140 (43.2%) and 80 (24.7%), respectively.

The maternal demographic characteristics data are shown in Table 1. The mean maternal age of the study group was significantly older than the control group (34.4 ± 7.3 and 29.3 ± 6.7, p < 0.001). The study group also had a previous history of the cesarean section more than the control group with statistically significant (52 (16%) and 38 (10.4%), p = 0.028). Parity and pre-pregnancy BMI were not different.

Table 1. Maternal demographic characteristics.

Characteristics	Control group (n = 365)	Study group (n = 324)	p value
Maternal age (years) ± SD	29.3 ± 6.7	34.4 ± 7.3	< 0.001
Parity			0.031
0	133 (36.4%)	88 (27.2%)	
1	150 (41.1%)	157 (48.5%)	
≥ 2	82 (22.5%)	79 (24.4%)	
Pre-pregnant BMI (kg/m^2)			0.156
< 18.5	4 (1.1%)	5 (1.5%)	
18.5 - 24.9	142 (38.9%)	148 (45.7%)	
25 - 29.9	219 (60%)	171 (52.8%)	
mean ± SD	25.8 ± 3.1	25.2 ± 3.5	0.164
History of previous cesarian section	38 (10.4%)	52 (16%)	0.028

SD: standard deviation, BMI: body mass index

Maternal outcomes are shown in Table 2. The rate of developing gestational hypertension was significantly higher in study group (1 (0.3%) and 8 (2.5%), p = 0.011). Other maternal outcomes including route of delivery, postpartum hemorrhage and preeclampsia with severe feature were not statistically different.

Table 2. Maternal outcomes.

	Control (n = 365)	Study (n = 324)	p value
Route of delivery			0.145
- Cesarian section	108 (29.6%)	105 (32.4%)	
- Spontaneous vertex delivery	254 (69.6%)	211 (65.1%)	
- Vacuum extraction	3 (0.8%)	8 (2.5%)	
Postpartum hemorrhage	4 (1.1%)	3 (0.9%)	0.824
Preeclampsia with severe feature	2 (0.5%)	6 (1.9%)	0.111
Gestational hypertension	1 (0.3%)	8 (2.5%)	0.011

Neonatal outcomes are shown in Table 3. Infants of the study group had a significantly higher rate of hypoglycemia than those with control group (6 (1.6%) and 18 (5.6%), p = 0.005). The study group also had higher rate of birth weight ≥ 4,000 grams (6 (1.6%) and 12 (3.7%), p = 0.091) than study group but no statistical significance. The other neonatal outcomes: Apgar at 1 minute, 5 minutes, 10 minutes, SNB admission, NICU admission, IUGR, and ventilation support were similar in both groups but also not statistically significant, while there was a significant difference of GA at delivery.

Table 3. Neonatal outcomes.

	Control (n = 365)	Study (n = 324)	p value
GA at delivery (weeks)	38.5 ± 1.8	37.3 ± 6.1	0.001
Apgar at 1 min			0.654
> 7	359 (98.4%)	320 (98.8%)	
≤ 7	6 (1.6%)	4 (1.2%)	
Apgar at 5 min			0.288
> 7	365 (100%)	323 (99.7%)	
≤ 7	0 (0%)	1 (0.3%)	
Apgar at 10 min			0.288
> 7	365 (100%)	323 (99.7%)	
≤ 7	0 (0%)	1 (0.3%)	
birthweight	3,122.9 ± 493.3	3,190.0 ± 470.8	0.069
NICU admission	6 (1.6%)	5 (1.5%)	0.916
SNB admission	20 (5.5%)	14 (4.3%)	0.483
birthweight ≥ 4,000 grams	6 (1.6%)	12 (3.7%)	0.091
IUGR	2 (0.5%)	2 (0.6%)	0.905
ventilation support	8 (2.2%)	9 (2.8%)	0.621
hypoglycemia	6 (1.6%)	18 (5.6%)	0.005

GA: gestational age, NICU: neonatal intensive care unit, SNB: sick newborn, IUGR: intrauterine growth restriction.

Discussion

In most cases, the pathophysiology of GDM is similar to that of type 2 diabetes, which is also an inability to achieve an adequate insulin response due to a significant decrease in insulin sensitivity. Pregnant women with single abnormal 100-g OGTT may have

some degree of impair insulin sensitivity so they could develop GDM later.

Another reason why pregnant women with a single abnormal 100-g OGTT develop GDM, according to Ferrara et al, was that a diagnosis of GDM based on Carpenter and Coustan criteria resulted in a 50% increase in the prevalence of GDM[11].

Nowadays, the current guidelines for the diagnosis of GDM in pregnancy are mainly classified as universal screening and selective screening based on risk factors. Selective screening based on risk factors performs poorly as a screening tool, with up to one-sixth of women with GDM diabetes being missed[12]. This may affect the primary outcome of this study.

Francesco et al reported that hypertensive disorders (preeclampsia and pregnancy-induced hypertension) were more common in pregnancy with a single abnormal value of 100-g OGTT[10]. While this study found that gestational hypertension was significantly higher in the study group, preeclampsia with severe features did not differ statistically. It is possible that the previous study did not perform a subgroup analysis, which explains the discrepancy.

Prior studies have shown that adverse pregnancy outcomes with a single abnormal value of 100-g OGTT represented adverse neonatal outcomes; macrosomia had a higher rate in pregnancy with a single abnormal value of 100-g OGTT[7, 9-10] as well as a higher mean birth weight[7, 8]. The study group, on the other hand, had a higher birth weight of 4,000 grams, but the difference was not statistically significant.

There may be various reasons for the disparity in outcomes. First and foremost, this study was conducted in a moderate risk pregnancy group, and the study population was diverse. Second, because the sample size was calculated primarily for the primary outcomes (incidence of GDM in pregnancy with one abnormal value 100-g OGTT after repeat within 1 month), the sample size may be insufficient to represent the true adverse maternal and neonatal outcomes. Third, previous research has linked a single abnormal 100-g OGTT value to an increase in adverse neonatal outcomes, particularly macrosomia[7, 9-10]. Physicians have paid attention to and provided intensive counseling to this group, as they did to the GDM group. This emphasizes the importance of pregnant women getting adequate exercise and a diet plan in order to reduce the negative outcomes. Even though one-third of pregnant women with a single abnormal value of 100-g OGTT developed GDM, it seemed to have no clinical significance because the adverse outcomes of this group were not different from those with normal OGTT. Several biases may have affected the outcomes of this study.

The retrospective design study was the study's limitation. As a result of the previously hospital records' information, the data could be inaccurate and out of date. The strength of this study was the first interested in the incidence of GDM in the average-risk pregnancy group with one abnormal value after repeating within one month.

According to the result of this study, the incidences of GDMA1 and GDMA2 were 25% and 7.1% respectively. It showed a high incidence of GDM in pregnant women who had a single abnormal 100-g OGTT and then repeated it within one month. This could be used to develop clinical practice guidelines for the early detection of GDM in pregnancy at other hospitals. It may also reduce the adverse consequences of GDM.

This study suggested that pregnancy with a single abnormal 100-g OGTT value after repeating within one month tended to develop into GDM, particularly GDMA1, and increased the likelihood of pregnancy-induced hypertension, particularly gestational hypertension. As a result, obstetricians should be concerned about the planned diet program for this group and monitor their blood pressure during the antepartum and intrapartum periods.

Conclusion

Pregnant women with a single abnormal value of 100-gram OGTT developed a high incidence rate of GDM, gestational hypertension and neonatal hypoglycemia.

Potential conflicts of interest

The authors declare no conflicts of interest.

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