
OBSTETRICS

Incidence of Postpartum Glucose Intolerance among Women with Gestational Diabetes in Siriraj Hospital

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ABSTRACT

Objectives: To determine the incidence of postpartum glucose intolerance among women with gestational diabetes (GDM) and its associated factors.

Materials and Methods: A total of 110 GDM women who delivered at Siriraj Hospital were enrolled. A 2-hour 75-gram glucose tolerance test was offered at 6-12 weeks postpartum to determine the incidence of glucose intolerance, which includes impaired glucose tolerance (IGT), and type 2 diabetes (T2DM). Demographic data, GDM risks and diagnosis data, and delivery data were collected. Incidence of glucose intolerance was estimated. Comparison was made between glucose intolerance groups to determine possible associated factors.

Results: Mean age was 33.7 ± 5.1 years, and 46% were nulliparous. According to pre-pregnancy BMI, 45.5% were overweight/obese, and 24.5% gained weight greater than recommendation. Majority was GDM A1 (85.5%), and 63.6% were diagnosed before 20 weeks of gestation. Mean postpartum follow up time was at 6.2 ± 0.9 weeks. Incidence of postpartum IGT and T2DM were 35.5% and 10% respectively. No difference was found between groups in terms of pre-pregnancy BMI, gestational weight gain, weight retention, and severity of GDM. However, HbA1c level was significantly greater among women with postpartum T2DM than IGT and normal results ($6.1 \pm 0.5\%$, $5.6 \pm 0.4\%$, and $5.4 \pm 0.3\%$ respectively, $p < 0.001$). HbA1c level of $\geq 6\%$ significantly increased the chance of T2DM (33.3% vs. 53.4%, $p = 0.001$).

Conclusion: Among GDM pregnant women, incidence of postpartum glucose intolerance was 45.5% (35.5% IGT and 10% T2DM). HbA1c level of $\geq 6\%$ significantly increased the chance of postpartum T2DM.

Keywords: Gestational diabetes, postpartum glucose tolerance test, type 2 diabetes, impaired glucose tolerance test

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อุบัติการณ์ภาวะพร่องความทนทานต่อน้ำตาลหลังคลอดในสตรีที่มีภาวะเบาหวานขณะตั้งครรภ์ในโรงพยาบาลศิริราช

พรพรม อธิธอมรเลิศ, ประเสริฐ ศันสนีย์วิทยกุล, ดิฐกานต์ บริบูรณ์หิรัญสาร

วัตถุประสงค์: เพื่อหาอุบัติการณ์ของภาวะพร่องความทนทานต่อน้ำตาลหลังคลอด ในสตรีที่มีภาวะเบาหวานขณะตั้งครรภ์ และ ศึกษาปัจจัยต่างๆ ที่มีผลต่อภาวะพร่องความทนทานต่อน้ำตาลหลังคลอด

วัสดุและวิธีการ: ทำการศึกษาวิจัยแบบไปข้างหน้า โดยคัดเลือกหญิงซึ่งมีภาวะเบาหวานขณะตั้งครรภ์ที่มาฝากครรภ์และคลอดที่โรงพยาบาลศิริราช จำนวน 110 ราย และนัดมาทำการตรวจด้วย 75-g OGTT ระหว่าง 6-12 สัปดาห์หลังคลอด เพื่อหาอุบัติการณ์ของภาวะพร่องความทนทานต่อน้ำตาลหลังคลอด อันประกอบด้วย ภาวะเบาหวาน และภาวะเสี่ยงต่อเบาหวาน โดยมีการเก็บข้อมูลต่างๆ ของผู้ป่วย ได้แก่ ข้อมูลพื้นฐาน, ปัจจัยเสี่ยงของการเกิดเบาหวานขณะตั้งครรภ์, รายละเอียดการวินิจฉัยเบาหวานขณะตั้งครรภ์, ข้อมูลการคลอดบุตร และผลการตรวจภาวะพร่องความทนทานน้ำตาลหลังคลอด เพื่อนำมาหาอุบัติการณ์การเกิดภาวะพร่องความทนทานน้ำตาลในช่วงหลังคลอด ทำการเปรียบเทียบข้อมูลต่างๆ ระหว่างกลุ่มของภาวะพร่องความทนทานต่อน้ำตาลหลังคลอดเพื่อหาปัจจัยที่อาจจะมีส่วนเกี่ยวข้อง

ผลการศึกษา: อายุเฉลี่ยของสตรีตั้งครรภ์ คือ 33.7 ± 5.1 ปี, เป็นการตั้งครรภ์ครั้งแรก 46% พบว่ามีภาวะอ้วน 45.5%, น้ำหนักขึ้นช่วงตั้งครรภ์เกินกว่าเกณฑ์ 24.5% ผู้เข้าร่วมวิจัยส่วนใหญ่ได้รับการวินิจฉัยเป็น GDMA1 (85.5%) และ 63.3% ได้รับการวินิจฉัยก่อนอายุครรภ์ 20 สัปดาห์ ระยะเวลาเฉลี่ยของการตรวจติดตามหลังคลอด คือ 6.2 ± 0.9 สัปดาห์ อุบัติการณ์การเกิดภาวะเสี่ยงต่อเบาหวาน คือ 35.5% และพบเป็นเบาหวาน 10% ไม่พบความแตกต่างระหว่างกลุ่มในแง่ของค่าดัชนีมวลกาย, น้ำหนักที่เพิ่มขึ้นในช่วงตั้งครรภ์, น้ำหนักที่หลงเหลืออยู่หลังคลอด รวมถึงความรุนแรงของภาวะเบาหวานขณะตั้งครรภ์ เมื่อพิจารณาระดับ HbA1c ที่ตรวจหลังคลอดพบว่า ระดับ HbA1C ในกลุ่มเบาหวานหลังคลอดสูงกว่ากลุ่มเสี่ยงต่อการเกิดเบาหวาน และกลุ่มที่ผลเลือดปกติอย่างมีนัยสำคัญทางสถิติ ($6.1 \pm 0.5\%$, $5.6 \pm 0.4\%$ และ $5.4 \pm 0.3\%$) โดยระดับ HbA1c ที่มากกว่าหรือเท่ากับ 6 จะเพิ่มโอกาสต่อการเกิดเบาหวานในช่วง หลังคลอดอย่างมีนัยสำคัญทางสถิติ (33.4% และ 53.4%, $p=0.001$)

สรุป: ในสตรีที่มีภาวะเบาหวานขณะตั้งครรภ์ พบว่า 35.5% มีภาวะเสี่ยงต่อการเกิดเบาหวานในช่วงหลังคลอด และ 10% เป็นเบาหวานภายหลังการคลอดบุตร ระดับของ HbA1C ที่มากกว่าหรือเท่ากับ 6 เพิ่มความเสี่ยงของการเกิดเบาหวานภายหลังคลอดอย่างมีนัยสำคัญ

Introduction

Gestational diabetes mellitus (GDM), defined as carbohydrate intolerance of variable severity found at the onset or is initially recognized during pregnancy, is among the common complications during pregnancy⁽¹⁾. GDM has been associated with various perinatal and maternal morbidities, including preeclampsia, birth trauma, shoulder dystocia, excessive fetal size, and also increased rate of cesarean section⁽²⁾. The incidence of GDM women was reported to be 2.5% among all pregnant women in Siriraj Hospital⁽³⁾.

Women with GDM are also at increased risk for developing a prediabetic state and type 2 diabetes (T2DM) later in life. Pregnant women with GDM had a 7-fold increase in risk of T2DM in later life and it was estimated that 30-50% of GDM women could develop T2DM in the 10 years after delivery⁽⁴⁾. Previous studies reported that the risk of prediabetic state as 12-36%, and T2DM as 1.2-4.5% among GDM women in the 6-week postpartum period⁽⁵⁾.

T2DM is a chronic disease which needs lifetime treatment and could lead to many complications such as nephropathy, retinopathy, and many infectious diseases, which adversely affect both patients and families and also the health care system. Early detection of T2DM is the best way to reduce the severity of the disease and risk of complications that might occur. Both the American College of Obstetricians and Gynecologists (ACOG) and the American Diabetes Association (ADA) recommend that women diagnosed with GDM should be screened for persistent glucose abnormality at 6-12 weeks postpartum with fasting plasma glucose (FPG) alone or with 2-hour 75-g oral glucose tolerance test (OGTT)^(1, 6). However, previous studies reported that only 34-73% of women with GDM received these postpartum screenings⁽⁵⁾. The rate of screening is dependent on multiple factors such as patient concern, the policy of each hospital and the health care system of each country.

In Siriraj Hospital, although a clinical practice guideline has been developed and implemented, postpartum screening for glucose intolerance has not been routinely offered to GDM women⁽³⁾. As a result,

evidence on postpartum glucose intolerance is lacking and its importance needs to be addressed.

The primary objective of this study was to estimate the incidence of postpartum glucose intolerance among GDM women. In addition, possible associated risk factors of postpartum prediabetes and T2DM were also evaluated, including pre-pregnancy BMI, gestational weight gain, weight retention, severity of GDM, and timing of diagnosis.

Material and methods

After the study protocol was approved by the Institutional Review Board of Faculty Medicine Siriraj Hospital, Mahidol University, a prospective cohort study was conducted at the Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital during 2014. After informed consent, a total of 110 GDM women who received antenatal care and delivered at Siriraj hospital were enrolled. Women with pre-existing DM, and those who had underlying diseases or were on medications which affect blood glucose level were excluded.

All participants received GDM screening and diagnostic procedures according to institutional guidelines. Risks for GDM include age ≥ 30 years, pre-pregnancy BMI ≥ 25 kg/m², family history of diabetes, hypertension, previous GDM, history of fetal macrosomia, stillbirth, or fetal anomaly. The procedures consisted of 50-g glucose challenge test (GCT) as a screening test, using a cut off value at ≥ 140 mg/dL, followed by 100-g OGTT as a diagnostic test using the criteria of Carpenter and Coustan⁽³⁾. The procedures were offered during their first visit and repeated at 24-28 weeks of gestation if the first screening was normal. All GDM women received either dietary therapy only (GDM A1) or with insulin treatment (GDM A2). Early diagnosis was defined as diagnosis of GDM before 24 weeks of gestation and late diagnosis was those diagnosed after 24 weeks of gestation.

Antenatal, labor, and delivery care were provided according to institutional guidelines. After delivery, all participants were appointed for routine postpartum checkup and glucose intolerance screening at 6-12

weeks. In addition to a pelvic examination and general postpartum counseling, a 2-hour 75-g OGTT were offered to determine glucose intolerance. Interpretation of 2-hour 75-g OGTT was shown in Table 1⁽⁶⁾. In addition, HbA1c was also tested as part of routine care. All the test results were reported to all participants via telephone contact. Participants who had IGT or Type 2 DM were advised and scheduled for further counseling and treatment at the Department of Medicine, Siriraj Hospital or other hospitals as appropriate and by their convenience.

Sample size was estimated based on the incidence of postpartum glucose intolerance of 50% from the pilot study. A sample size of 110 would be adequate to determine the incidence at 95% confidence level with 10% maximum allowable error.

Baseline data, GDM diagnosis and risks, pre-pregnancy BMI, gestational weight gain, and labor and delivery data were collected at the time of delivery. In addition to 2-hour 75-g OGTT and HbA1c test results,

other postpartum characteristics, including weight retention, and timing of glucose tolerance test were recorded, including postpartum weight, postpartum BMI, and weight retention.

Pre-pregnancy BMI category and appropriateness of gestational weight gain was determined according to the IOM recommendation and were classified as less than, within, and greater than recommendation⁽⁷⁾.

Descriptive statistics, including mean, standard deviation, number and percentage were used to describe various characteristics as appropriate. Incidence of postpartum glucose intolerance was estimated. Various characteristics were compared between normal women and those with IGT and type 2 diabetes to determine possible associated factors. Student t test, ANOVA, and chi-square tests were used in comparison between groups as appropriate. A p-value of <0.05 was considered statistically significant. All analyses were performed using IBM SPSS Statistics for Windows®, Version 21.0. Armonk, NY: IBM Corp.

Table 1. Interpretation of postpartum 2-hour 75-g OGTT.

	Plasma glucose level (mg/dL)		
	Normal	Prediabetes	Type 2 diabetes
Fasting	<110	≥ 110 and <126	≥ 126
2 hours	<140	140-199	≥ 200

Table 2. Baseline characteristic of GDM pregnant women (N=110).

Characteristics	N (%)
Mean maternal age ± SD (years)	33.7 ± 5.1
Nulliparous	51 (46.4)
Mean pre pregnancy BMI ± SD (kg/m ²)	25.3 ± 5.0
Pre-pregnancy BMI category	
Normal	60 (54.5)
Overweight/obese	50 (45.5)
Mean total weight gain ±SD (kg)	10.3 ± 6.4
Weight gain category	
Less than recommendation	45 (40.9)
Within recommendation	38 (34.5)
Greater than recommendation	27 (24.5)

Results

A total 110 GDM women were included in this study and received postpartum glucose intolerance tests. Table 2 shows the baseline characteristics of the participants. Mean maternal age was 33.7 years and 46.4% were nulliparous. Majority had normal pre-pregnancy BMI (54.5%) and only 34.5% gained weight as recommended. GDM risks included maternal age ≥ 30 years (81.8%), family history of diabetes (41.8), pre-pregnancy BMI ≥ 25 kg/m² (60.9%) and previous GDM (2.7%).

Table 3 shows GDM diagnosis characteristics. Most of participants were diagnosed as GDMA1 (85.5%) and 63.6% diagnosed before 20 weeks of gestation.

Table 4 shows pregnancy outcomes. Mean gestational age at delivery was 38.3 weeks. Most of them delivered by cesarean section (62.7%, 40% were primary cesarean) with a mean birth weight of 3,117.6 g. Majority of the newborns (91.8%) were appropriate for gestational age (AGA), 6.4% were large for gestational age (LGA), and only 1.8% were small for gestational age (SGA). Macrosomia was found in 6.4%. Table 5 shows postpartum characteristics of GDM

women and postpartum diagnosis of glucose intolerance. Mean postpartum follow up time was 6.2 ± 0.9 weeks. The results of 75-g OGTT demonstrated that 60 (54.5%) had normal results, 39 (35.5%, 95%CI 27.1-44.7%) had impaired glucose tolerance, and 11 (10%, 95%CI 5.7-17.0%) were diagnosed as type 2 DM. No impaired fasting glucose was found. Mean HbA1c was $5.5 \pm 0.4\%$.

Comparison of various characteristics was made between different postpartum diagnoses and their results are shown in Table 6. No significant differences were found between groups in terms of pre-pregnancy BMI, total weight gain, weight retention, and type and timing of diagnosis of GDM. However, it should be noted that overweight / obese women and those with GDM A2 were slightly more likely to have Type 2 DM than normal weight women and those with GDM A1 (12% vs. 8.3%, and 25% vs. 7.4%, respectively), but without statistical significance.

Women with impaired glucose tolerance and type 2 DM had significantly higher HbA1c level than those with normal OGTT. In addition, women with HbA1c $>6\%$ had significantly higher rate of Type 2 DM (33.3% vs. 5.4%, $p < 0.001$).

Table 2. Baseline characteristic of GDM pregnant women (N=110).

Characteristics	N (%)
Mean maternal age \pm SD (years)	33.7 \pm 5.1
Nulliparous	51 (46.4)
Mean pre pregnancy BMI \pm SD (Kg/m ²)	25.3 \pm 5.0
Pre-pregnancy BMI category	
Normal	60 (54.5)
Overweight/obese	50 (45.5)
Mean total weight gain \pm SD (kg)	10.3 \pm 6.4
Weight gain category	
Less than recommendation	45 (40.9)
Within recommendation	38 (34.5)
Greater than recommendation	27 (24.5)

Table 2. Baseline characteristic of GDM pregnant women (N=110). (Cont.)

Characteristics	N (%)
Risk factor	
Family history of diabetes	46 (41.8)
Age \geq 30 years	90 (81.8)
Pre-pregnancy BMI \geq 25 kg/m ²	67 (60.9)
Previous GDM	3 (2.7)

Table 3. GDM diagnosis characteristics (N=110).

Diagnosis characteristics	N (%)
Type of GDM	
GDM A1	94 (85.5)
GDM A2	16 (14.5)
Early diagnosis	70 (63.6)
Mean GA at diagnosis \pm SD	
Early diagnosis	11.5 \pm 5.1
Late diagnosis	29.9 \pm 3.9

Table 4. Pregnancy outcomes (N=110).

Outcomes	N (%)
Mean GA at delivery \pm SD (weeks)	38.3 \pm 1.6
Route of delivery	
Vaginal route	41 (37.3)
Primary C/S	44 (40)
Repeat C/S	25 (22.7)
Mean fetal birthweight \pm SD (g)	3117.6 \pm 505.9
Fetal birthweight category	
SGA	2 (1.8)
LGA	7 (6.4)
AGA	101 (91.8)
Fetal macrosomia	7 (6.4)

Table 5. Postpartum characteristic of GDM women and diagnosis (N=110).

Characteristics	N (%)
Mean postpartum follow up \pm SD (weeks)	6.2 \pm 0.9
Mean weight retention \pm SD (kg)	1.1 \pm 5.4
Postpartum Diagnosis	
Postpartum GTT	
Mean FBS \pm SD (mg/dL)	88.7 \pm 16.9
Mean 2-hour 75-g OGTT \pm SD (mg/dL)	140.9 \pm 43.9
Mean HbA1C \pm SD (%)	5.5 \pm 0.4
Postpartum Diagnosis	
Normal	60 (54.5)
IGT	39 (35.5)
DM	11 (10.0)

Table 6. Comparison of characteristics between different postpartum diagnoses.

Characteristics	Normal (N=60)	IGT (N=39)	DM (N=11)	P
Mean pre pregnancy BMI \pm SD (Kg/m ²)	25.1 \pm 5.5	25.0 \pm 3.9	27.7 \pm 6.0	0.274
Pre pregnancy BMI category				0.259
Normal	37 (61.7)	18 (30.0)	5 (8.3)	
Overweight/obese	23 (46.0)	21 (42.0)	6 (12.0)	
Mean total weight gain \pm SD (kg)	10.4 \pm 6.1	9.9 \pm 7.2	11.0 \pm 5.1	0.876
Weight gain category				0.711
Less than recommendation	23 (60.5)	13 (34.2)	2 (5.3)	
Within recommendation	24 (53.3)	15 (33.3)	6 (13.3)	
Greater than recommendation	13 (48.1)	11 (40.7)	3 (11.1)	
Type of GDM				0.073
GDM A1	54 (57.4)	33 (35.1)	7 (7.4)	
GDM A2	6 (37.5)	6 (37.5)	4 (25.0)	
Time of GDM diagnosis				0.396
Early diagnosis	35 (50)	28 (40)	7 (10)	
Late diagnosis	25 (62.5)	11 (27.5)	4 (10)	
Mean weight retention \pm SD (kg)	0.9 \pm 5.5	0.8 \pm 5.2	2.6 \pm 5.9	0.626
Mean HbA1C \pm SD (%)	5.4 \pm 0.3	5.6 \pm 0.4 (0.035)*	6.1 \pm 0.5 (<0.001)*	<0.001
HbA1c level				0.001
< 6%	55 (59.8)	32 (34.8)	5 (5.4)	
\geq 6%	5 (27.8)	7 (38.9)	6 (33.3)	

* p value compared to normal OGTT group by LSD post-hoc comparison

Discussion

GDM, defined as any degree of glucose intolerance with onset or first recognition during pregnancy is partly a result of progressive insulin resistance during pregnancy. Although insulin resistance is generally restored to the pre-pregnancy level shortly after delivery, such dysfunction could persist^(8, 9). Women with a history of GDM have a greatly increased risk of conversion to type 2 diabetes over time with as much as 7-fold increased risk of T2DM has been reported. Cumulative incidence of T2DM increased markedly in the first 5 years after delivery and appeared to plateau after 10 years^(4, 6, 10). Appropriate counseling regarding lifestyle changes could lower the risk of the progression to T2DM in the future by as much as 50%^(11, 12).

The results of this study show that 45.5% of GDM women had glucose intolerance, of which 10% had T2DM. The rates varied among previous studies, which was possibly due to differences in population risks, criteria for GDM diagnosis, and time of follow up^(5, 10, 13-15). Similar to other studies, the rate of postpartum glucose intolerance might be under- or overestimated. Contamination of pre-existing diabetes was possible and status of women who were failed to follow up or were unable to return for postpartum testing could not be determined. Nonetheless, the results of this study demonstrated and signify the importance of postpartum screening for glucose intolerance among GDM women. ADA and ACOG recommended that women with GDM should be screened for persistent diabetes or prediabetes at 6-12 weeks postpartum using 75-g OGTT with non-pregnancy criteria and every 1-3 years thereafter depending on other risk factors^(1, 6).

However, non-adherence to the guidelines is common. Previous studies have shown that rate of postpartum screening among GDM women was relatively low. The rate has been reported to be 34-73% during 6-12 weeks and 16-58% within the first year postpartum, with only a part of these women receiving an OGTT^(5, 15).

The barriers to postpartum diabetes testing are multifactorial. Women with GDM may have limited

knowledge of the significance of postpartum follow up and do not realize their risk of T2DM after delivery. In addition, health care providers themselves may also have limited information on the importance of the increased risk of future T2DM among these women and did not offer appropriate counseling and postpartum testing⁽¹⁶⁾.

The results of this study also showed that HbA1c was significantly higher among T2DM and IGT women than non-DM women. Moreover, women whose HbA1c level was $\geq 6\%$ had a significantly increased risk of having T2DM. Some previous studies have evaluated the use of FPG alone and/or HbA1c for postpartum glucose intolerance screening but the results were conflicting with sensitivity of 60–83% and 83–90%, respectively. But the use of HbA1c alone demonstrated a low sensitivity of 22–65% compared to OGTT^(15, 17).

Possible associated factors for postpartum glucose intolerance were examined but no significant relationship was observed among various variables. However, it should be noted that women with T2DM had higher pre-pregnancy BMI and overweight/obese women were more likely to have T2DM than other groups. GDM women who required insulin treatment (GDM A2) were also at increased risk for T2DM, but without statistical significance. Frequently reported clinical risk factors included maternal age, ethnicity, parity, family history of T2DM, pre-pregnancy weight, weight gain during pregnancy, a previous history of GDM, early diagnosis of GDM, requirement of insulin during pregnancy, and elevated FPG during pregnancy^(10, 14, 15).

Some limitations of this study need to be addressed. The incidence of postpartum glucose intolerance might be under or overestimated due to possible contamination of women with pre-existing DM and incidence among those who did not agree to participate was not determined. The study also had limited power to evaluate significant associated factors. In addition, effects of dietary control among these women could not be determined. Future large-scale studies are needed to determine the long-term risk of T2DM among this group of women and identify

significant risk factors in order to understand more about the nature of the progression of GDM.

In conclusion, postpartum glucose intolerance was common among GDM women. Both health care providers and pregnant women should realize the importance of postpartum testing. A routine 75-g OGTT should be scheduled, not only to detect T2DM that has rapidly progressed after GDM but also to detect women with pre-existing DM. This information would help in timely diagnosis and treatment of T2DM and provide women their baseline risk for future pregnancy and T2DM later in life. Moreover, dietary and behavioral intervention could then be offered to women to decrease their T2DM risk in the future.

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