
OBSTETRICS

Incidence and Associated Factors of Gestational Diabetes Mellitus Diagnosed during 24-28 weeks of Gestation

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ABSTRACT

Objectives: To determine incidence and associated factors of gestational diabetes (GDM) diagnosed at 24-28 weeks of gestation.

Materials and Methods: A total of 200 pregnant women at risk for GDM who attended antenatal clinic before 20 weeks of gestation and had negative GDM screening tests were enrolled. All women received a second screening test at 24-28 weeks of gestation, according to institutional guideline. Data was retrieved, including demographic data, GDM risks and diagnosis, weight gain during pregnancy, and labor and delivery data. Incidence of GDM diagnosed by second screening test was estimated and possible associated factors were identified.

Results: Mean maternal age was 31 years, and 51% were nulliparous. Most common GDM risks were age > 30 years (70%) and family history of diabetes (46%). Majority of women had normal pre-pregnancy BMI (63%) and normal weight gain (43.5%), while 38% gained weight greater than recommendation. Incidence of GDM diagnosed at 24-28 weeks of gestation was 15%. Various characteristics were comparable among late-onset GDM and non-GDM group, including age, parity, pre-pregnancy BMI, and gestational weight gain. However, late-onset GDM group had significantly greater second trimester weight gain (7.2 ± 2.8 kg vs. 5.9 ± 2.4 kg, $p=0.01$). Compared to women with normal GCT, abnormal 50-g GCT and abnormal 1 OGTT value at first screening significantly increased the risk of late-onset GDM (9.5%, 18.2%, and 47.4% respectively, $p<0.001$).

Conclusion: Incidence of GDM diagnosed at 24-28 weeks of gestation was 15%. High second trimester weight gain and abnormal first screening results significantly increased the risk of late diagnosed GDM.

Keywords: gestational diabetes, gestational weight gain, abnormal glucose challenge test

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อุบัติการณ์และปัจจัยเสี่ยงของภาวะเบาหวานขณะตั้งครรภ์ที่วินิจฉัยได้ในช่วงอายุครรภ์ 24-28 สัปดาห์

อาทิตยา สิงห์หงษา, ดิฐกานต์ บริบูรณ์หิรัญสาร

วัตถุประสงค์: เพื่อศึกษาอุบัติการณ์และปัจจัยเสี่ยงของการเกิดภาวะเบาหวานขณะตั้งครรภ์ที่วินิจฉัยได้ในช่วงอายุครรภ์ 24-28 สัปดาห์

วัสดุและวิธีการ: ทำการศึกษาสตรีตั้งครรภ์ที่มีความเสี่ยงต่อการเกิดภาวะเบาหวานขณะตั้งครรภ์ ที่มารับการฝากครรภ์ที่โรงพยาบาลศิริราช ก่อนอายุครรภ์ 20 สัปดาห์ และมีผลการตรวจคัดกรองภาวะเบาหวานขณะตั้งครรภ์ครั้งแรกปกติ จำนวน 200 ราย โดยสตรีตั้งครรภ์ดังกล่าวจะได้รับการตรวจคัดกรองซ้ำอีกครั้งเมื่ออายุครรภ์ 24-28 สัปดาห์ ทำการรวบรวมข้อมูลจากการทบทวนเวชระเบียน ได้แก่ ข้อมูลพื้นฐาน, ปัจจัยเสี่ยงของสตรีตั้งครรภ์, น้ำหนักตัวก่อนการตั้งครรภ์, น้ำหนักตัวที่เพิ่มในแต่ละไตรมาส, ข้อมูลการคลอด และผลของการตั้งครรภ์ จากนั้นทำการคำนวณอุบัติการณ์การเกิดภาวะเบาหวานขณะตั้งครรภ์ในช่วงอายุครรภ์ 24-28 สัปดาห์ ทำการเปรียบเทียบข้อมูลต่างๆ ระหว่างกลุ่มที่เกิดเบาหวานขณะตั้งครรภ์ และกลุ่มที่ผลการตรวจปกติ เพื่อประเมินปัจจัยที่เกี่ยวข้อง

ผลการศึกษา: สตรีตั้งครรภ์มีอายุเฉลี่ย 31 ปี เป็นครรภ์แรก 51% ความเสี่ยงต่อภาวะเบาหวานขณะตั้งครรภ์ที่พบบ่อยคือ อายุ >30 ปี (70%), มีประวัติโรคเบาหวานในครอบครัว (46%), ส่วนใหญ่ของสตรีตั้งครรภ์มีค่าดัชนีมวลกายปกติ (63%) น้ำหนักที่เพิ่มขึ้นขณะตั้งครรภ์อยู่ในเกณฑ์ปกติ 43.5% และน้ำหนักตัวเพิ่มเกินเกณฑ์ 38% อุบัติการณ์ของภาวะเบาหวานขณะตั้งครรภ์ที่วินิจฉัยได้ระหว่างอายุครรภ์ 24-28 สัปดาห์คือ 15% พบว่าผู้ป่วยกลุ่มนี้ไม่มีความแตกต่างกับกลุ่มที่ผลการตรวจปกติ ในแง่ของ อายุ, ประวัติการมีบุตร, ดัชนีมวลกาย และ น้ำหนักตัวที่เพิ่มขึ้นตลอดการตั้งครรภ์ แต่พบว่าในกลุ่มที่ภาวะเบาหวานขณะตั้งครรภ์ที่วินิจฉัยได้ระหว่างอายุครรภ์ 24 - 28 สัปดาห์ มีน้ำหนักตัวเพิ่มขึ้นในช่วงไตรมาสที่สอง สูงกว่ากลุ่มที่ไม่ได้เป็นเบาหวานอย่างมีนัยสำคัญทางสถิติ (7.2 ± 2.8 กก. และ 5.9 ± 2.4 กก., $p=0.01$) และพบว่าสตรีตั้งครรภ์ที่มีผลการตรวจในครั้งแรกผิดปกติ คือ กลุ่ม 50-g GCT ผิดปกติ และกลุ่มที่มีค่า 100-g OGTT ผิดปกติ 1 ค่า จะมีความเสี่ยงเพิ่มขึ้นต่อการเกิดภาวะเบาหวานขณะตั้งครรภ์ที่ตรวจพบในช่วง 24-28 สัปดาห์อย่างมีนัยสำคัญทางสถิติ เมื่อเทียบกับกลุ่มที่ผลการตรวจ 50-g GCT ปกติ คือ 47.4%, 18.2%, และ 9.5% ตามลำดับ ($p<0.001$)

สรุป: อุบัติการณ์ของเบาหวานขณะตั้งครรภ์ที่วินิจฉัยได้ขณะอายุครรภ์ 24-28 สัปดาห์ คือ ร้อยละ 15 และปัจจัยเสี่ยงที่สัมพันธ์กับภาวะนี้ คือ น้ำหนักตัวที่เพิ่มขึ้นมากในไตรมาสที่สอง และการมีผลการคัดกรองเบาหวานครั้งแรกที่ผิดปกติ

Introduction

Gestational diabetes mellitus (GDM) is a common medical complication during pregnancy⁽¹⁾. It is a glucose intolerance of variable severity which is first diagnosed during pregnancy. Undiagnosed or poorly-controlled GDM has been associated with maternal and neonatal morbidities, such as preeclampsia, increased cesarean sections, and birth injuries⁽¹⁻⁴⁾. Incidence of GDM in Siriraj Hospital was approximately 2-3% of all pregnant women and 6-7% of women at risk⁽⁵⁾.

The technique and timing for GDM screening and diagnosis are still controversial and recommendations are widely varied. According to institutional clinical practice guideline, GDM screening and diagnosis was offered to all women at risk during their first visit and repeated at 24-28 weeks of gestation. A 50-gram glucose challenge test (GCT) is used as a screening test, using cut off value at ≥ 140 mg/dL, and a 100-gram oral glucose tolerance test (OGTT) is used to diagnose the GDM using the Carpenter and Coustan criteria⁽⁵⁾.

However, non-compliance to the guideline exists, especially in not performing the second tests among those with normal initial tests. This could be due to the negligence of obstetricians or the women themselves. As a consequence, some GDM cases were not diagnosed, which might lead to increased risk of maternal and fetal morbidities.

Therefore, the objective of this study was to determine the incidence of GDM diagnosed during 24-28 weeks of gestation after normal initial tests. In addition, possible associated risk factors were also evaluated. Pregnancy outcomes were also evaluated between normal and late-onset GDM groups. The results would help signifying the importance of the repeated GDM screening later in pregnancy and identify women at higher risk for developing late-onset GDM.

Materials and Methods

After the study protocol was approved from Siriraj Institutional Review Board (SIRB), a retrospective cohort study was conducted at the Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital.

A total of 200 pregnant women were at risk for GDM. They had GDM screening before 20 weeks of gestation and underwent GCT with/without OGTT. The women with negative OGTT were enrolled during 2014. 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. Pregnant women with preexisting chronic illnesses, such as hyperthyroidism, heart disease, or overt DM; and those with documented fetal anomalies were excluded. All participants were offered repeated tests for GDM at 24-28 weeks of gestation. After GDM was diagnosed, intensive dietary counseling was offered by well-trained dietitian nurse. A 2-hour postprandial plasma glucose was used during follow up to determine adequacy of glycemic control and insulin treatment was provided as necessary. Antenatal, intrapartum and postpartum care were provided according to institutional guideline⁽⁵⁾.

Sample size was estimated based on the incidence of late-onset GDM of 12% from pilot study. A sample size of 200 would be adequate to determine the incidence at 95% confidence level with 5% maximum allowable error, including 20% loss.

Data was retrieved from medical records, including demographic data, antenatal care data, GDM risks, diagnosis, and screening and diagnostic test results, labor and delivery data, and pregnancy and neonatal outcomes.

Descriptive statistics, including mean, standard deviation, number, and percentage were used to describe various characteristics as appropriate. Incidence of GDM diagnosed during 24-28 weeks of gestation (late-onset GDM) was estimated. Student t-test and Chi-square test or Fisher's Exact test were used to compare various characteristics between non-GDM and late-onset GDM group. 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.

Results

A total of 200 women at risk for GDM were

included. Baseline characteristics were demonstrated in Table 1. Mean age was 30.9 years, and approximately half were nulliparous (51%). Majority of women had normal pre-pregnancy BMI (63%) and 20.5% were overweight. Mean weight gain during 1st and 2nd trimester were 3.2 and 6.1 kg, respectively. Gestational weight gain was within recommendation in 43.5% and 38% gained weight greater than recommendation.

GDM risks, screening results, and diagnosis were shown in Table 2. Common GDM risks were age >30 years (70%), family history of diabetes (46.5%), and

pre-pregnancy BMI ≥ 25 kg/m² (12.5%). Initial screening was performed at 10.8 weeks of gestation and the results showed that majority had normal 50-g GCT (68.5%), while 22% had abnormal 50-g GCT but normal 100-g OGTT, and 9.5% had abnormal 1 value of 100-g OGTT.

A total of 30 women were diagnosed with GDM during 24-28 weeks of gestation, corresponding to the incidence of 15% (95%CI 10.7 - 20.6%). Mean gestational age at diagnosis was 27.3 weeks.

Table 1. Baseline characteristics of pregnant women at-risk for GDM (N=200).

Characteristics	N (%)
Maternal age (years) mean \pm SD	30.9 \pm 5.8
Parity	
0	102 (51.0)
1	69 (34.5)
≥ 2	29 (14.5)
Pre-pregnancy BMI (kg/m ²) mean \pm SD	22.3 \pm 4.0
Pre-pregnancy BMI category	
Normal	126 (63.0)
Underweight	33 (16.5)
Overweight	41 (20.5)
1 st trimester weight gain (kg) mean \pm SD	3.2 \pm 2.9
2 nd trimester weight gain (kg) mean \pm SD	6.1 \pm 2.5
Gestational weight gain (kg) mean \pm SD	14.9 \pm 4.9
Gestational weight gain category	
Within recommendation	87 (43.5)
Less than recommendation	37 (18.5)
Greater than recommendation	76 (38.0)

Table 2. GDM risks, screening results, and diagnosis (N=200).

Characteristics	N (%)
GDM risk factors	
Age > 30 years	140 (70.0)
Pre-pregnancy BMI ≥ 25 kg/m ²	25 (12.5)
Family history of diabetes	93 (46.5)
Hypertension	6 (3.0)
Previous GDM	4 (2.0)

Table 2. GDM risks, screening results, and diagnosis (N=200). (Cont.)

Characteristics	N (%)
History of fetal macrosomia	4 (2.0)
History of stillbirth or fetal anomaly	7 (3.5)
Number of risks	
1 risk	141 (70.5%)
> 2 risks	49 (29.5%)
Initial GDM screening	
Gestational age at first screening (weeks) mean \pm SD	10.8 \pm 4.2
Normal 50-g GCT	137 (68.5)
Abnormal 50-g GCT, Normal 100-g OGTT	44 (22.0)
Abnormal 1 value of 100-g OGTT	19 (9.5)
GDM diagnosis	
GDM diagnosed at 24-28 weeks	30 (15.0)
Gestational age at diagnosis of GDM (weeks) mean \pm SD	27.3 \pm 2.4

Table 3. Pregnancy and neonatal outcomes (N=200).

Characteristics	N (%)
Gestational age at delivery (weeks) mean \pm SD	38.1 \pm 1.6
Delivery mode	
Vaginal delivery	100 (50.0)
Primary cesarean delivery	65 (32.5)
Repeat cesarean delivery	35 (17.5)
Neonatal outcomes	
Small for gestational age	18 (9.0)
Large for gestational age	18 (9.0)
Low birth weight	18 (9.0)
Fetal macrosomia	3 (1.5)

Table 3 showed pregnancy and neonatal outcomes of the participants. Mean gestational age at delivery was 38.1 weeks. Half of the women delivered vaginally, while 32.5% delivered by primary cesarean delivery and the rest had repeat cesarean delivery. In terms of neonatal outcomes, SGA, LGA and LBW was found in 9% each and fetal macrosomia was found in 1.5%.

Various characteristics were compared between normal and late-onset GDM groups to evaluate associated factors and the results were shown in Table

4. Both groups were comparable with regard to age, parity, pre-pregnancy BMI, and gestational weight gain. However, late-onset GDM group had significantly greater 2nd trimester weight gain than normal women (7.2 ± 2.8 vs. 5.9 ± 2.4 kg, respectively, $p=0.012$). In addition, the risk of late-onset GDM increased significantly with the degree of abnormal initial test results ($p<0.001$).

Pregnancy and neonatal outcomes were compared between groups and the results were shown in Table 5. Women with late-onset GDM were

significantly more likely to deliver at lower gestational age and had larger infants ($p<0.05$) but the differences were not significant clinically. Primary cesarean delivery was significantly more common among late-onset GDM than normal women (50% vs. 29.4%,

$p=0.026$). In terms of adverse neonatal outcomes, SGA and LBW were less common, while LGA and macrosomia were more common among late-onset GDM women but without statistical significance.

Table 4. Comparison of baseline characteristics between normal women and late-onset GDM.

Characteristics	Normal N=170)	Late GDM (N=30)	P*
Maternal age (years) mean \pm SD	30.8 \pm 5.9	31.7 \pm 4.9	0.425**
Parity			
Nulliparous	83 (81.4%)	19 (18.6%)	0.143
Multiparous	87 (88.8%)	11 (11.2)	
Number of risks			0.171
1 risk	123 (72.4%)	18 (60.0%)	
> 2 risks	47 (27.6%)	12 (40.0%)	
Pre-pregnancy BMI (kg/m ²) mean \pm SD	22.2 \pm 4.0	23.1 \pm 4.4	0.263**
Pre-pregnancy BMI category			0.369
Underweight	29 (87.9%)	4 (12.1%)	
Normal	109 (86.5%)	17 (13.5%)	
Overweight	32 (78%)	9 (22%)	
Weight gain category			0.393
Less than recommendation	29 (78.4%)	8 (21.6%)	
Within recommendation	74 (85.1%)	13 (14.9%)	
Greater than recommendation	67 (88.2%)	9 (11.8%)	
1 st trimester weight gain (kg) mean \pm SD	3.2 \pm 3.1	3.1 \pm 1.9	0.861**
2 nd trimester weight gain (kg) mean \pm SD	5.9 \pm 2.4	7.2 \pm 2.8	0.012**
Initial GDM screening results			<0.001
Normal 50-g GCT	124 (90.5%)	13 (9.5%)	
Abnormal 50-g GCT, Normal 100-g OGTT	36 (81.8%)	8 (18.2%)	
Abnormal 1 value of 100-g OGTT	10 (52.6%)	9 (47.4%)	

* Chi square test

** Student t test

Table 5. Comparison of pregnancy and neonatal outcomes between normal women and late-onset GDM.

Characteristics	Normal N=170)	Late GDM (N=30)	P*
GA at delivery \pm SD (weeks) mean \pm SD	38.2 \pm 1.6	37.5 \pm 1.9	0.037**
Birth weight \pm SD (grams) mean \pm SD	3024.3 \pm 425.9	3212.7 \pm 467.0	0.029**

Table 5. Comparison of pregnancy and neonatal outcomes between normal women and late-onset GDM. (Cont.)

Characteristics	Normal N=170)	Late GDM (N=30)	P*
GA at delivery \pm SD (weeks) mean \pm SD	38.2 \pm 1.6	37.5 \pm 1.9	0.037**
Birth weight \pm SD (grams) mean \pm SD	3024.3 \pm 425.9	3212.7 \pm 467.0	0.029**
Delivery mode			
Vaginal delivery	88 (51.8%)	12 (40.0%)	0.235
Primary cesarean delivery	50 (29.4%)	15 (50.0)	0.026
Repeat cesarean delivery	32 (18.8%)	3 (10.0)	0.241
Neonatal outcomes			
Small for gestational age	16 (9.4%)	2 (6.7%)	1.0***
Large for gestational age	13 (7.6%)	5 (16.7%)	0.157*
Low birth weight	16 (9.4%)	2 (6.7%)	1.0***
Fetal macrosomia	1 (0.6%)	2 (6.7%)	0.059***

* Chi square test

** Student t test

*** Fisher exact test

Discussion

Gestational diabetes is the most common complications during pregnancy which could result in various maternal and neonatal morbidities. Benefits of early diagnosis and intervention among GDM women in reducing maternal and neonatal morbidities have been demonstrated^(1, 6-8).

In this study, incidence of late-onset GDM was 15% among women at risk who had normal initial tests. As pregnancy advances, the impact of hormonal changes on insulin resistance increases, resulting in late-onset GDM. However, the incidence in this study was greater than previous report from the same institution (7%)⁽⁹⁾. The difference might be due to the change in GDM diagnostic criteria from those of National Diabetes Data Group (NDDG) to Carpenter and Coustan⁽¹⁰⁾, which use lower cut off values of 100-g OGTT results⁽¹¹⁾.

In addition, a significant trend was observed that the risk of late-onset GDM increased with the degree of initial test abnormality. Even among women with normal 50-g GCT, the incidence was 9.5%. The incidence was greatest among women with 1 abnormal OGTT value (47.4%). Insulin resistance has been

reported to be of similar severity in women with 1 elevated OGTT value⁽¹²⁾. The importance of 1 abnormal OGTT value has been consistently reported. These women were at increased risk of various maternal and neonatal morbidity, including preeclampsia, cesarean delivery, macrosomia, and birth asphyxia⁽¹³⁻¹⁵⁾. However, benefit of treating these women have not been established⁽¹⁶⁾.

These results signify the importance of second screening at 24-28 weeks of gestation to identify late-onset GDM, even those with normal initial tests. Omission from the repeat tests would result in considerable number of undiagnosed GDM that could lead to undesirable maternal and neonatal outcomes.

Pre-pregnancy BMI and gestational weight gain has been associated with increased risk of GDM^(17, 18). However, most of the studies focused on total weight gain over the entire pregnancy, thus also including weight gained after the diagnosis of GDM. The study had examined in details of weight gain before diagnosis of GDM. A previous study reported that first trimester weight gain was a significant predictor of GDM⁽¹⁹⁾. However, our results demonstrated that women with late-onset GDM had greater second trimester weight

gain than those without GDM. Higher weight gain may lead to greater maternal fat deposition, which may impair insulin sensitivity.

As weight gain is a modifiable risk factor, women at risk for GDM including those with normal initial tests should aware of their weight gain during pregnancy. A recent study has reported that behavioral intervention and weight gain control since early pregnancy can reduce GDM risk by 39% among high-risk women⁽²⁰⁾. Therefore, appropriate counseling regarding dietary and behavioral modification, as well as regular weight gain monitoring should be provided in these women in order to reduce GDM risk and related health consequences. Some limitations of this study should be addressed. Some data might be inaccurate due to the retrospective nature of the data. However, this was minimized by verification of data from both antenatal care and admission record. In addition, all women at risk also received dietary counseling but actual effects of dietary control and behavioral risks could not be measured. In addition, the results can only be applied to pregnant women without other underlying diseases as excluded from this study.

In conclusion, the incidence of late-onset GDM among women at risk for GDM with normal initial tests was 15%. Second trimester weight gain and degree of abnormality of first GDM screening results were associated with late-onset GDM. This emphasizes the importance of repeat GDM screening at 24-28 weeks of gestation, especially among high-risk women. Appropriate behavioral modification, including dietary and weight gain control could possibly reduce the risk of late-onset GDM.

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