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Prevalence of Gestational Diabetes Diagnosed before 24 Weeks of Gestation

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ABSTRACT

Objectives: To determine prevalence of gestational diabetes mellitus (GDM) diagnosed before 24 weeks of gestation (early GDM), to evaluate associated risk factors, and to compare pregnancy outcomes between different GDM status.

Materials and Methods: A total of 480 women who started antenatal care before 24 weeks of gestation were included. All women received a universal 2-step approach for GDM screening and diagnosis during first antenatal care visit and repeat at 24 - 28 weeks of gestation. Data were extracted from medical records, including baseline, obstetric and antenatal care data, GDM risks, diagnosis of GDM, and pregnancy outcomes. Prevalence of overall GDM, early and late GDM were estimated. Various characteristics and pregnancy outcomes were compared between women without GDM, early, and late GDM.

Results: Overall prevalence of GDM was 20%. Majority of GDM were diagnosed before 24 weeks of gestation (early GDM) with the prevalence of 14.4% which contributed to 71.9% of all GDM cases. Both early and late GDM were more likely to be overweight and have previous GDM. Early GDM significantly had lower gestational weight gain than those without GDM. Rates of large for gestational age (LGA) and macrosomia were slightly higher in GDM women than those without GDM. The only significant risk factor for early GDM was previous GDM with adjusted odds ratio 5.38, 95% confidence interval 1.16 - 24.92 (p = 0.031).

Conclusion: Prevalence of early GDM was 14.4% which contributed to 71.9% of all GDM cases. Pregnancy outcomes were not significantly different between early, late GDM and those without GDM. The only independent associated factor was previous GDM.

Keywords: gestational diabetes mellitus, early GDM, late GDM, risk factor, pregnancy outcomes.

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ความชุกของภาวะเบาหวานขณะตั้งครรภ์ที่ตรวจพบก่อน 24 สัปดาห์

กานต์กมล ประสิทธิ์, ดิฐกานต์ บริบูรณ์หิรัญสาร

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาความชุกของภาวะเบาหวานขณะตั้งครรภ์ที่ตรวจพบที่อายุครรภ์น้อยกว่า 24 สัปดาห์ และประเมินปัจจัยเสี่ยงที่เกี่ยวข้อง และเปรียบเทียบผลลัพธ์ของการตั้งครรภ์ระหว่างการตรวจพบเบาหวานในลักษณะต่างๆ*

วัสดุและวิธีการ: *เก็บข้อมูลจากสตรีตั้งครรภ์ที่มาฝากครรภ์ก่อน 24 สัปดาห์ จำนวน 480 ราย โดยทุกรายได้รับการตรวจคัดกรองภาวะเบาหวานขณะตั้งครรภ์ตามแนวทางของโรงพยาบาลศิริราช โดยตรวจเมื่อมาฝากครรภ์ครั้งแรกและที่อายุครรภ์ 24 - 28 สัปดาห์ รวบรวมข้อมูลจากบันทึกเวชระเบียน ประกอบด้วย ข้อมูลทั่วไป ข้อมูลทางสูติศาสตร์และการฝากครรภ์ ความเสี่ยงของภาวะเบาหวานขณะตั้งครรภ์ การวินิจฉัยภาวะเบาหวานขณะตั้งครรภ์ และผลลัพธ์ของการตั้งครรภ์ คำนวณหาความชุกของภาวะเบาหวานที่วินิจฉัยก่อนและหลัง 24 สัปดาห์ เปรียบเทียบข้อมูลต่างๆ และผลลัพธ์ของการตั้งครรภ์ระหว่างการตรวจพบเบาหวานในลักษณะต่างๆ*

ผลการศึกษา: *พบความชุกของภาวะเบาหวานในระหว่างตั้งครรภ์ร้อยละ 20 โดยร้อยละ 71.9 ตรวจพบก่อนอายุครรภ์ 24 สัปดาห์ หรือคิดเป็นร้อยละ 14.4 จากหญิงตั้งครรภ์ทั้งหมด กลุ่มที่ตรวจพบภาวะเบาหวานขณะตั้งครรภ์ทั้งก่อนและหลัง 24 สัปดาห์ มีน้ำหนักตัวที่เพิ่มขึ้นน้อยกว่ากลุ่มที่ไม่เป็นเบาหวานอย่างมีนัยสำคัญทางสถิติ และพบอัตราการเกิดทารกมีน้ำหนักตัวมากกว่าอายุครรภ์ และทารกที่มีน้ำหนักเกิน 4,000 กรัม สูงกว่ากลุ่มที่ไม่เป็นเบาหวานอย่างมีนัยสำคัญทางสถิติ ปัจจัยเสี่ยงที่สัมพันธ์กับภาวะเบาหวานในระหว่างการตั้งครรภ์ที่ตรวจพบก่อน 24 สัปดาห์ ได้แก่ การมีประวัติเบาหวานขณะตั้งครรภ์ในครรภ์ก่อน (adjusted odds ratio 5.38, 95% confidence interval 1.16 - 24.92, p = 0.031)*

สรุป: *ความชุกของภาวะเบาหวานขณะตั้งครรภ์ที่พบก่อนอายุครรภ์ 24 สัปดาห์เท่ากับร้อยละ 14 โดยคิดเป็นร้อยละ 71.9 ของภาวะเบาหวานขณะตั้งครรภ์ทั้งหมด ไม่พบความแตกต่างอย่างมีนัยสำคัญระหว่างผลลัพธ์ของการตั้งครรภ์ระหว่างการตรวจพบเบาหวานในลักษณะต่างๆ ปัจจัยเสี่ยงที่สัมพันธ์กับภาวะเบาหวานในระหว่างตั้งครรภ์ที่ตรวจพบก่อน 24 สัปดาห์ ได้แก่ การมีประวัติเบาหวานขณะตั้งครรภ์ในครรภ์ก่อน*

คำสำคัญ: *ภาวะเบาหวานขณะตั้งครรภ์, อายุครรภ์ที่วินิจฉัย, ปัจจัยเสี่ยง, ผลลัพธ์ของการตั้งครรภ์*

Introduction

Gestational diabetes mellitus (GDM) is a condition in which carbohydrate intolerance develops during pregnancy[1, 2], incidence of GDM has increased as a result of worldwide increase in overweight and obese women[1-3]. As previously reported in many studies, GDM has been associated with increased risk of maternal and neonatal morbidities, including large for gestational age (LGA) fetus or fetal macrosomia, cesarean delivery, birth injuries, preeclampsia, and future risk for diabetes mellitus[1-3].

A recent report from Siriraj Hospital, prevalence of GDM was 13.9% from a risk-based screening and, among which, 9.2% was diagnosed before 24 weeks of gestation, accounted for 65.9% of all GDM[4]. The results were similar to another study from the same institution that of 10.2% GDM prevalence, 5.3% of which was diagnosed before 20 weeks of gestation[5]. A systematic review reported that, among GDM, 15-70% can be detected early in pregnancy before 24 weeks of gestation, depending on the setting, criteria used and screening strategy[6].

GDM diagnosed early in pregnancy were reported to be at increased risk of adverse maternal and neonatal outcomes, including preeclampsia, insulin therapy, LGA, macrosomia, neonatal hypoglycemia, perinatal morbidities and mortality[6-13]. In a meta-analysis of 13 cohort studies, increased risk of perinatal mortality, neonatal hypoglycemia, and insulin use were observed, compared to late-onset GDM women, despite treatment[6]. However, factors associated with early GDM and the benefit of early treatment were still not clear.

After decades of risk-based GDM screening, a universal screening is currently adopted as an institutional guideline that all pregnant women are offered GDM screening during their first visit and repeat during 24 - 28 weeks of gestation. However, the prevalence of GDM as well as those diagnosed early in pregnancy have not been evaluated. Therefore, the objectives of this study were to determine prevalence of GDM diagnosed before 24 weeks of gestation (early GDM). In addition, associated risk factors were evaluated and pregnancy outcomes between different GDM status were compared.

Materials and Methods

The cross-sectional study was conducted in 480 pregnant women who received universal GDM screening at Siriraj Hospital after approval from Institutional Review Board. Women with singleton pregnancy who started antenatal care before 24 weeks of gestation were included, while those with pre-existing diabetes and those with severe fetal anomalies or fetal death were excluded. Sample size was calculated based on the prevalence of GDM diagnosed before 24 weeks of 10% from a pilot study. At 95% significance level and 3% acceptable error, at least 470 women are required, including 20% loss.

According to current institutional guideline, a universal 2-step approach is used for GDM screening and diagnosis to all pregnant women during first antenatal care visit. A 50-g glucose challenge test (GCT) is used as a screening test with 140 mg/dL cut-off value. A 100-g oral glucose tolerance test (OGTT) was used to diagnose GDM, using Carpenter and Coustan criteria. The tests are repeated during 24 - 28 weeks of gestation if initial tests were normal. After GDM diagnosis, dietary counseling and nutritional therapy were offered. A 2-hour postprandial plasma glucose was used to evaluate glycemic control during follow-up was by either intermittent test or self-monitoring with a glucose meter. Insulin therapy was initiated as necessary. GDM that is diagnosed before 24 weeks of gestation is considered “early GDM” and those diagnosed during 24 - 28 weeks are defined as “late GDM”.

Data were extracted from medical records, including baseline, obstetric and antenatal care data, GDM risks, diagnosis of GDM, and pregnancy outcomes. GDM risks included age ≥ 30 years, DM in family, body mass index (BMI) ≥ 25 kg/m^2, previous GDM, previous macrosomia, previous congenital anomaly or intrauterine fetal death, and hypertension. Pre-pregnancy BMI and gestational weight gain (GWG) were classified according to Institute of Medicine (IOM)

recommendation[14]. Data on pregnancy outcomes were collected, including delivery data, GWG, preeclampsia, birth weight, birth weight for gestational age, birth asphyxia, neonatal hypoglycemia, and neonatal intensive care unit (NICU) admission. Prevalence of overall GDM, early and late GDM were estimated. Various characteristics and pregnancy outcomes were compared between women without GDM, early, and late GDM.

Descriptive statistics were used to describe various characteristics, including mean, standard deviation, number, and percentages as appropriate. Chi-square test and one-way analysis of variance (ANOVA) with post-hoc comparison were used to compare characteristics between the 3 groups as appropriate. Logistic regression analysis was used to determine independent associated factors for early and late GDM, adjusted for potential confounders, including parity, age, BMI, previous GDM, and hypertension. A p value of < 0.05 was considered statistically significant.

Results

The study included 480 pregnant women who received early universal GDM screening and baseline characteristics are described in Table 1. Mean age was 30.4 years and 50.6% were nulliparous. Mean BMI was 22.8 kg/m^2, 17.7% were overweight and 7.9% were obese. Common GDM risk factors were age of ≥ 30 years (55%), BMI of ≥ 25 kg/m^2 (25%), and history of DM in first degree relatives (18.1%). While 31.5% of the women did not have any GDM risks, 40% had 1 risk and 28.5% had 2 or more risks.

Table 1. Baseline characteristics of the study population (n = 480).

Characteristics	
Mean age ± SD (years)	30.4 ± 5.9
Mean BMI ± SD (kg/m^2)	22.8 ± 4.6
Nulliparous, n (%)	243 (50.6)
BMI category, n (%)	
Normal (18.5-24.9 kg/m^2)	290 (60.4)
Underweight (< 18.5 kg/m^2)	67 (14)
Overweight (25-29.9 kg/m^2)	85 (17.7)
Obese (≥ 30 kg/m^2)	38 (7.9)
GDM risk factors, n (%)	
Age ≥ 30 years	264 (55)
DM family	87 (18.1)
BMI ≥ 25 kg/m^2	120 (25)
Previous GDM	10 (2.1)
Previous macrosomia	6 (1.3)
Previous anomaly/fetal death	12 (2.5)
Hypertension	5 (1)
Number of GDM risks, n (%)	
No risk	151 (31.5)
1	192 (40)
≥ 2	137 (28.5)

SD: standard deviation, BMI: body mass index, GDM: gestational diabetes

Table 2 shows characteristics of GDM diagnosis. Overall prevalence of GDM from early universal screening was 20%. Majority of GDM were diagnosed before 24 weeks of gestation (early GDM) with the

prevalence of 14.4% and mean GA at diagnosis of 10 weeks of gestation. Prevalence of late GDM, diagnosed after 24 weeks of gestation, was 5.6% with mean GA at diagnosis of 26.6 weeks of gestation. Early GDM contributed to 71.9% of all GDM cases. Of all GDM women, insulin use was required in 9.4%.

Various characteristics were compared between different GDM diagnosis and the results are shown in Table 3. While other characteristics were comparable between groups, BMI of ≥ 25 kg/m^2 and previous GDM were significantly more common in both early and late GDM than those without GDM (p = 0.029 and < 0.001, respectively).

Table 2. Diagnosis of GDM (n = 480).

Diagnosis of GDM	n (%)
No GDM	384 (80)
Early GDM	69 (14.4)
Mean GA at diagnosis ± SD (weeks)	10.0 ± 4.0
Late GDM	27 (5.6)
Mean GA at diagnosis ± SD (weeks)	26.6 ± 2.5

SD: standard deviation, GDM: gestational diabetes, GA: gestational age

Table 3. Comparison of characteristics between different GDM diagnosis.

Characteristics	No GDM (n = 384)	Early GDM (n = 69)	Late GDM (n = 27)	p value
Mean age ± SD (years)	30.2 ± 5.8	31.5 ± 5.3	32.3 ± 5.6	0.052[a]
Mean BMI ± SD (kg/m^2)	22.7 ± 4.6	23.1 ± 4.2	23.5 ± 4.0	0.600[a]
Nulliparous	181 (47.1%)	43 (62.3%)	13 (48.1%)	0.067[b]
BMI category				0.386[b]
Normal (18.5-24.9 kg/m^2)	225 (58.6%)	47 (68.1%)	18 (66.7%)	
Underweight (< 18.5 kg/m^2)	61 (15.9%)	4 (5.8%)	2 (7.4%)	
Overweight (25-29.9 kg/m^2)	67 (17.4%)	13 (18.8%)	5 (18.5%)	
Obese (≥ 30 kg/m^2)	31 (8.1%)	5 (7.2%)	2 (7.4%)	
GDM risk factors				
Age ≥ 30 years	203 (52.9%)	44 (63.8%)	17 (63%)	0.17[b]
DM family	96 (25%)	17 (24.6%)	7 (25.9%)	0.991[b]
BMI ≥ 25 kg/m^2	61 (15.9%)	20 (29%)	6 (22.2%)	0.029[b]
Previous GDM	3 (0.8%)	5 (7.2%)	2 (7.4%)	< 0.001[b]
Previous macrosomia	5 (1.3%)	1 (1.4%)	0 (0%)	0.83[b]
Previous anomaly	9 (2.3%)	1 (1.4%)	2 (7.4%)	0.221[b]
Hypertension	4 (1.0%)	1 (1.4%)	0 (0%)	0.821[b]
Number of GDM risks				0.119[b]
No risk	126 (32.8%)	18 (26.1%)	7 (25.9%)	
1	159 (41.4%)	23 (33.3%)	10 (37%)	
≥ 2	99 (25.8%)	28 (40.6%)	10 (37%)	

[a] Analysis of variance, [b] Chi-square

SD: standard deviation, BMI: body mass index, GDM: gestational diabetes

Table 4 shows comparison of pregnancy outcomes between different GDM diagnosis. GWG was significantly higher among those without GDM (p = 0.011), and post hoc analysis showed that early GDM significantly had lower GWG than those without GDM (11.9 vs. 14.1 kg, p = 0.011). In addition, early GDM also had significantly lower proportion of excessive weight gain than the other 2 groups (p = 0.03). Among GDM, insulin was required only among early GDM women (13%). Mean GA at delivery, route of delivery, mean birth weight, and preeclampsia were comparable between the 3 groups. However, it should be noted that LGA was slightly higher in GDM women than those without GDM (26.1% in early GDM, 29.6% in late GDM, and 18.8% in no GDM) but without statistical significance. Rates of macrosomia also increased among both early and late GDM but also without statistical significance (7.2% in early GDM, 7.4% in late GDM, and 2.1% in no GDM). Other neonatal outcomes were comparable between the 3 groups.

Table 4. Comparison of pregnancy outcomes between different GDM diagnosis.

Characteristics	No GDM (n = 384)	Early GDM (n = 69)	Late GDM (n = 27)	p value
Mean GA at delivery ± SD (weeks)	38.1 ± 1.3	37.8 ± 1.7	37.8 ± 1.8	0.182[a]
Mean gestational weight gain ± SD (kg)	14.1 ± 5.8	11.9 ± 5.9*	12.9 ± 5.7	0.011[a]
GWG category				0.03[b]
Normal	127 (33.1%)	26 (37.7%)	5 (18.5%)	
Less than recommendation	95 (24.7%)	25 (36.2%)	11 (40.7%)	
Excessive weight gain	162 (42.2%)	18 (26.1%)	11 (40.7%)	
Insulin use		9 (13%)	0 (0%)	0.057[b]
Route of delivery				0.485[b]
Vaginal delivery	220 (57.3%)	42 (60.9%)	13 (48.1%)	
Primary cesarean section	104 (27.1%)	13 (18.8%)	9 (33.3%)	
Repeat cesarean section	60 (15.6%)	14 (20.3%)	5 (18.5%)	
Birth weight ± SD (g)	3,067.0 ± 434.8	3,104.2 ± 562.7	3,227.4 ± 614.3	0.205[b]
Birth weight category				0.255[b]
AGA	291 (75.8%)	46 (66.7%)	19 (70.4%)	
SGA	21 (5.5%)	5 (7.2%)	0 (0%)	
LGA	72 (18.8%)	18 (26.1%)	8 (29.6%)	
Macrosomia	8 (2.1%)	5 (7.2%)	2 (7.4%)	0.032[b]
Preeclampsia	14 (3.6%)	4 (5.8%)	0 (0%)	0.394[b]
Apgar at 1 min < 7	14 (3.6%)	5 (7.2%)	1 (3.7%)	0.384[b]
Apgar at 5 min < 7	1 (0.3%)	0 (0%)	0 (0%)	0.882[b]
Phototherapy	60 (15.6%)	10 (14.5%)	4 (14.8%)	0.968[b]
Hypoglycemia	10 (2.6%)	5 (7.2%)	1 (3.7%)	0.141[b]
NICU admission	9 (2.3%)	3 (4.3%)	1 (3.7%)	0.607[b]

* Significant different from women without GDM, p = 0.01 [a] Analysis of variance, [b] Chi-square

SD: standard deviation, GA: gestational age, GDM: gestational diabetes, GWG: gestational weight gain, SGA: small for gestational age, AGA: appropriate for gestational age, LGA: large for gestational age, NICU: neonatal intensive care unit

Logistic regression analysis was performed to determine independent risk factors associated with early GDM and the results are shown in Table 5. After adjusting for potential confounders, the

only significant risk factor for early GDM was previous GDM with adjusted odds ratio (OR) 5.38, 95% confidence interval (CI) 1.16 - 24.92 (p = 0.031).

Table 5. Logistic regression analysis to determine independent risk of early GDM.

Risk factors	Adjusted OR	95%CI	p value
Nulliparous	1.55	0.89-2.69	0.12
Age ≥ 30 years	1.39	0.79-2.42	0.24
BMI ≥ 25 kg/m^2	0.8	0.43-1.50	0.501
Family history of DM	1.75	0.92-3.31	0.085
Previous GDM	5.38	1.16-24.92	0.031

BMI: body mass index, GDM: gestational diabetes, OR: odds ratio, CI: confidence interval

Discussion

The results of this study showed that overall prevalence of GDM was 20% and prevalence of GDM diagnosed before 24 weeks of gestation (early GDM) was 14.4% with mean GA at diagnosis of as early as 10 weeks of gestation. The prevalence of both overall GDM and early GDM increased from previous reports from the same institution[4, 5]. This is due to the change in screening protocol from risk-based to universal screening protocol. Contribution of early GDM also increased from 50 - 65% to as many as 71.9% as shown in this study. Previous studies reported variations in prevalence of early GDM, ranging from 1-20% of all pregnant women[9, 10]. A systematic review also reported the prevalence of 15-70% of all GDM cases[6]. Differences of the results between studies were due to variations in study population as well as screening and diagnostic strategies and criteria in each setting.

In terms of risk factors for early GDM, the results showed that BMI of ≥ 25 kg/m^2 and previous GDM were significantly more common in early GDM than those without GDM in univariate analysis. However, after adjusting for potential confounders, the only significant risk factor for early GDM was previous GDM (adjusted OR 5.38, 95%CI 1.16 - 24.92, p = 0.031). Previous GDM was an important risk for GDM in subsequent pregnancy as previously reported[15, 16]. Women who had GDM in previous pregnancies might have carbohydrate intolerance to some degree that not only they were at higher risk for GDM but also that GDM could be diagnosed early in pregnancy. Previous reported associated risk factors for early diagnosis of GDM included older age, higher BMI, and family history of diabetes[9, 10]. Different findings might probably be due to different in risk criteria for early GDM screening in each setting.

GWG among early GDM women was significantly lower than those without GDM and they were also less likely to gain weight greater than recommendation. The findings were similar to the results from other studies[8, 13] This could probably be due to early nutritional and behavioral interventions provided to this group of women as the result of early diagnosis. Although rate of insulin requirement has been reported to increase among early GDM[7, 10, 12], the result of this study showed that while 13% of early GDM required insulin therapy, none of late GDM did, with borderline significance (p = 0.057) probably due to limited number of cases.

Many adverse outcomes associated with early diagnosis of GDM have been reported, including hypertensive disorders, perinatal mortality, neonatal hypoglycemia, asphyxia, NICU admission[6-10]. However, in this study, many GDM-related pregnancy outcomes were comparable between the 3 subgroups, but it should be noted that, although rates of both LGA and macrosomia were similar between early and late GDM, they seem to be higher than those without GDM. Significant increase in LGA and macrosomia among early GDM have been observed in some previous

studies[12, 13].

Some limitations of this study should be noted. Although all the women diagnosed with GDM received uniform counseling and management, the effects of both nutritional and pharmacological therapy could not be assessed. In addition, the degree to which those interventions affect pregnancy outcomes could not be evaluated. A specific screening and diagnostic strategies used in this study were also different from those of other studies that the results could not be compared directly. There might be some contaminations of women with unknown pre-pregnancy diabetes in the study samples due to the nature of a 2-step approach for GDM screening. However, the proportion of this group should be minimal and would not deviate the results significantly. Samples in subgroup analyses were also limited that there might be limited power to determine significant differences between groups.

The results of this study showed that majority of GDM could be diagnosed early in pregnancy, which supported the use of early universal GDM screening. However, further studies are needed to evaluate the use of screening protocol in other aspects, as well as its benefits in reducing adverse pregnancy outcomes.

Conclusion

In conclusion, prevalence of early GDM was 14.4% which contributed to 71.9% of all GDM cases. Pregnancy outcomes were not significantly different between early, late GDM and those without GDM. Both early and late GDM had slightly increase in rates of LGA and macrosomia. Previous GDM was the only independent factor associated with early GDM.

Potential conflicts of interest

The authors declare no conflicts of interest.

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