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Risk Factors for Insulin Therapy in Gestational Diabetes Mellitus

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ABSTRACT

Objectives: To determine the factors associated with insulin requirement in patients with gestational diabetes mellitus (GDM) and compare the obstetrics outcomes between those who required insulin therapy and who did not.

Materials and Methods: A case-control study was conducted, including 100 GDM women who required insulin therapy as cases and 400 GDM women who did not require insulin therapy as controls. Data on baseline and obstetric characteristics, antenatal care, GDM risks, screening and diagnostic test results, labor and delivery, and obstetrics outcomes were reviewed from the medical records.

Results: Cases were significantly more likely to be nulliparous, overweight or obese, have DM in family, have had prior GDM, had higher number of GDM risks than controls. Compared with controls, cases had significantly higher plasma glucose level at fasting, 1, and 2 hours, but not at 3 hours after glucose loading and higher rate of abnormal fasting plasma glucose values and higher number of abnormal OGTT values. Logistic regression analysis showed that independent associated factors for insulin requirement were fasting plasma glucose (FPG) at OGTT > 95 mg/dL (adjusted odds ratio (OR) 20.8, 95% confidence interval (CI) 11.4-37.9), overweight or obesity (adjusted OR 1.9, 95%CI 1.1-3.5) and family history of DM (adjusted OR 2.2, 95%CI 1.2-3.9). While other pregnancy outcomes were comparable between the 2 groups, infants of cases were significantly more likely to have neonatal hypoglycemia and need for phototherapy.

Conclusion: Independent associated risks for insulin therapy in GDM women included FPG of > 95 mg/dL at OGTT, overweight or obesity, and family history of DM.

Keywords: gestational diabetes mellitus, insulin, risk factor, pregnancy outcomes.

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ปัจจัยเสี่ยงที่ทำให้ต้องใช้อินสุลินเพื่อควบคุมระดับน้ำตาลในมารดาที่เป็นเบาหวานขณะตั้งครรภ์

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บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาปัจจัยที่เกี่ยวข้องกับการต้องใช้อินสุลินเพื่อควบคุมระดับน้ำตาลในสตรีที่มีภาวะเบาหวานขณะตั้งครรภ์ และเปรียบเทียบผลลัพธ์ของการตั้งครรภ์ระหว่างสตรีที่มีภาวะเบาหวานขณะตั้งครรภ์ที่ใช้และไม่ใช้อินสุลิน*

วัสดุและวิธีการ: *ทำการศึกษาแบบ case-control โดยสตรีที่มีภาวะเบาหวานขณะตั้งครรภ์ที่ต้องใช้อินสุลิน จำนวน 100 คน เป็นกลุ่มศึกษา (case) และ สตรีที่มีภาวะเบาหวานขณะตั้งครรภ์ที่ไม่ต้องใช้อินสุลิน จำนวน 400 คน เป็นกลุ่มควบคุม (control) ทำการค้นข้อมูลจากเวชระเบียน ได้แก่ ข้อมูลพื้นฐานทั่วไป ข้อมูลทางสูติศาสตร์ การฝากครรภ์ ความเสี่ยงของภาวะเบาหวานระหว่างตั้งครรภ์ ผลการตรวจคัดกรองและวินิจฉัย การคลอด และผลลัพธ์ของการตั้งครรภ์*

ผลการศึกษา: *กลุ่มศึกษา เป็นสตรีที่คลอดครั้งแรก มีภาวะน้ำหนักเกินหรืออ้วน มีประวัติเบาหวานในครอบครัว เคยมีภาวะเบาหวานระหว่างตั้งครรภ์มาก่อน และมีจำนวนของปัจจัยเสี่ยง มากกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ นอกจากนั้นเมื่อเทียบกับกลุ่มควบคุม กลุ่มศึกษามีค่าระดับน้ำตาลขณะอดอาหารและที่ 1 และ 2 ชั่วโมง หลังกินน้ำตาล ในการตรวจ 100-g Oral glucose tolerance test และมีอัตราความผิดปกติของระดับน้ำตาลขณะอดอาหาร และจำนวนของค่าที่ผิดปกติสูงกว่าอย่างมีนัยสำคัญทางสถิติ จากการวิเคราะห์แบบ logistic regression analysis พบว่าปัจจัยเสี่ยงที่สำคัญของการต้องใช้อินสุลิน ได้แก่ ค่าน้ำตาลหลังอดอาหารมากกว่า 95 มิลลิกรัมต่อเดซิลิตร (adjusted odds ratio (OR) 20.8, 95% confidence interval (CI) 11.4-37.9) ภาวะน้ำหนักเกินหรืออ้วน (adjusted OR 1.9, 95%CI 1.1-3.5) และประวัติโรคเบาหวานในครอบครัว (adjusted OR 2.2, 95%CI 1.3-3.9) ผลลัพธ์ของการตั้งครรภ์ส่วนใหญ่ ไม่มีความแตกต่างกันระหว่าง 2 กลุ่ม แต่พบว่าทารกของมารดากลุ่มศึกษา มีภาวะน้ำตาลต่ำ และภาวะตัวเหลืองที่ต้องส่องไฟรักษา สูงกว่าในกลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ*

สรุป: *ปัจจัยเสี่ยงที่สำคัญของการต้องใช้อินสุลินในสตรีตั้งครรภ์ที่มีภาวะเบาหวานระหว่างตั้งครรภ์ ได้แก่ ค่าน้ำตาลหลังอดอาหารมากกว่า 95 มิลลิกรัมต่อเดซิลิตร ภาวะน้ำหนักเกินหรืออ้วน และประวัติโรคเบาหวานในครอบครัว*

คำสำคัญ: *ภาวะเบาหวานระหว่างตั้งครรภ์ อินสุลิน ปัจจัยเสี่ยง ผลลัพธ์ของการตั้งครรภ์*

Introduction

Gestational diabetes mellitus (GDM) is one of the most common complications in pregnancy. Recent data shows that GDM prevalence has increased over time in association with the increase in prevalence of overweight or obesity in pregnant women[1, 2]. GDM has been associated with short and long-term consequences in both mother and the fetus, including preeclampsia, large for gestational age (LGA), macrosomia, shoulder dystocia, increased risk of caesarean section. In addition, GDM women have a greater risk of developing diabetes of mother and child in the future[3-5].

Initial management in GDM involves counseling, nutritional therapy, behavioral modification, and blood glucose control and monitoring[1, 2]. The goal of blood glucose level is fasting plasma glucose (FPG) of ≤ 95 mg/dL, 1-hour postprandial plasma glucose (1-hr PPG) of ≤ 140 mg/dL, and 2-hour postprandial plasma glucose (2-hr PPG) of ≤ 120 mg/dL. When these initial measures fail to control blood glucose in desirable range, additional pharmacological therapy is required, including various oral antidiabetic drugs and insulin[6-8]. However, insulin therapy is generally recommended as a first-line medication[1, 2, 6-8]. The rate of the need for insulin therapy varies between studies but it is estimated that, in general, approximately 10-20% of GDM women requires insulin therapy[1]. A recent study in Siriraj Hospital showed that insulin therapy was required in 12% of GDM women[9].

Inability to achieve glycemic control and prolonged hyperglycemia in GDM women has been associated with poor pregnancy outcomes, including preeclampsia, large-for-gestational-age (LGA), macrosomia, shoulder dystocia, operative delivery, birth trauma, neonatal hypoglycemia, hyperbilirubinemia, and hypocalcemia. However, early identification of GDM women who need insulin therapy and appropriate interventions could probably reduce such adverse maternal and neonatal outcomes as reported from previous studies[4, 5].

Several factors have been investigated and reported as the possible predicting factors for the need of insulin therapy in GDM women. These included high FPG level, the number of abnormal values of 100-g oral glucose tolerance test (OGTT), overweight or obesity, family history of diabetes mellitus, previous GDM, and early GDM diagnosis[9-15]. However, the results varied between studies, probably due to differences in population characteristics, screening and diagnostic strategies, management guidelines, and physician's preferences and decisions.

Currently, there is still limited information and research about this issue in the Siriraj Hospital. Therefore, this study was primarily aimed to determine factors associated with the need for insulin therapy among GDM women. In addition, pregnancy outcomes were compared between GDM women who required and did not require insulin therapy. Better understanding the associated risks could help predicting the need for insulin therapy among GDM women for better plan of more appropriate care and could help improving pregnancy outcomes.

Materials and Methods

After approval from Siriraj Institutional Review Board, a case-control study was conducted at the Department of Obstetrics and Gynecology, Faculty of Medicine, Siriraj Hospital. According to institutional guideline, GDM screening is offered to all at-risk pregnant women, using a 2-step approach. GDM risks include age > 30 years, pre-pregnancy BMI > 25 kg/m^2, family history of diabetes (DM in first-degree relatives), hypertension, previous GDM, history of fetal macrosomia, stillbirth, or fetal anomaly. A 50-g glucose challenge test (GCT) is used as a screening test at 140 mg/dL cut-off and a 100-g OGTT is used as a diagnostic test using Carpenter and Coustan criteria. The tests are offered at first antenatal visit and repeat during 24-28 weeks of gestation if the first tests are negative[16].

All women diagnosed with GDM initially received individual counseling regarding nutritional therapy and behavioral modification. Fasting and/or 2-hour PPG were used to monitor glycemic control

with the target of < 95 mg/dL and < 120 mg/dL, respectively, either by intermittent testing at each antenatal care visit or self-monitoring blood glucose (SMBG). Insulin therapy was offered if glycemic control within the target value was not achieved after nutritional and behavioral interventions, as appropriate. Generally, failure of nutritional intervention is considered when glycemic targets are not achieved in 3 consecutive antenatal care visits or there are > 70% abnormal glucose values from SMBG records. As of institutional guideline, no oral hypoglycemic agent was used. Management was offered by caring obstetricians and consultation with endocrinologists was done as appropriate.

Sample size was estimated based on the estimated rate of overweight and obesity of 50% and 33.3% among cases and controls. At 95% confidence level and 80% power with 4:1 control to case ratio, at least 90 cases and 360 controls were required. In this study, a total of 500 GDM women diagnosed according to institutional guideline were included. Exclusion criteria included pre-gestational diabetes, multiple pregnancy, fetal anomalies or fetal deaths, GDM diagnosed by other protocols, and GDM women who denied insulin therapy. Cases were 100 GDM women who required insulin therapy and controls were 400 GDM women who did not require insulin therapy. Both cases and controls were selected by simple random sampling procedure from pregnant women diagnosed with GDM.

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. Pre-pregnancy body mass index (BMI) and gestational weight gain were classified according to the Institute of Medicine (IOM) recommendation[17].

Descriptive statistics, including mean, standard deviation, number, and percentage were used to describe various characteristics as appropriate. Student t-test and chi-square test or Fisher's exact test were used to compare various characteristics between cases and controls. Odds ratios (OR) and 95% confidence intervals (CI) were estimated to determine association between the need for insulin therapy and various characteristics. Logistic regression analysis was performed to evaluate independent associated factors for the need for insulin therapy, adjusted for potential confounders. 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 100 cases of GDM women who required insulin therapy and 400 controls who did not need insulin therapy were included. Comparisons of baseline characteristics are shown in Table 1. Cases were more likely to be nulliparous (72% vs. 57.8%, p = 0.009). They had significantly higher BMI than controls (27.2 vs. 24.8 kg/m^2, p < 0.001) and they were significantly more likely to be overweight and obese (OR 3.9 and 3.5, respectively, p < 0.001). Comparison of GDM characteristics showed that GA at diagnosis and proportion of early-onset GDM were comparable. Regarding GDM risks, cases were significantly more likely to have DM in family, be overweight or obese, and have had prior GDM (OR 3.0, 3.6, and 4.9, respectively, p < 0.001). In addition, cases had significantly higher number of GDM risks (OR 2.5 for 2 risks, and 4.7 for > 3 risks, p < 0.001).

Comparison of plasma glucose levels from 100-g OGTT are shown in Table 2. Cases had significantly higher plasma glucose level at fasting, 1, and 2 hours, but not at 3 hours after glucose loading (p < 0.05). Compared with controls, cases were significantly more likely to have abnormal fasting plasma glucose values (81% vs. 13.3%, p < 0.001) while they were less likely to have abnormal 1- and 2-hour plasma glucose value (53% vs. 74.2%, p < 0.001, and 71% vs. 84%, p = 0.002, respectively) and comparable abnormal 3-hour value. Cases were significantly more likely to have higher number of abnormal OGTT values than controls (p < 0.001).

Table 1. Comparison of baseline characteristics between the 2 groups.

Characteristics	Controls N = 400	Cases N = 100	OR (95%CI)	p value
Mean age ± SD (years)	33.4 ± 5.2	32.6 ± 5.6		0.173
Mean BMI ± SD (kg/m^2)	24.8 ± 5.0	27.2 ± 5.2		< 0.001
Mean GA at diagnosis ± SD (weeks)	17.1 ± 9.2	15.5 ± 8.5		0.109
Nulliparous	231 (57.8%)	72 (72%)	1.9 (1.2-3.0)	0.009
BMI category				< 0.001
Normal	221 (55.3%)	26 (26%)		
Underweight	22 (5.5%)	4 (4%)	1.6 (0.5-4.8)	0.691
Overweight	99 (24.8%)	46 (46%)	3.9 (2.3-6.7)	< 0.001
Obese	58 (14.5%)	24 (24%)	3.5 (1.9-6.6)	< 0.001
Early-onset GDM (< 24 weeks)	260 (65%)	72 (72%)	1.4 (0.8-2.2)	0.185
GDM risks				
Age ≥ 30 years	315 (78.8%)	72 (72%)	0.7 (0.4-1.2)	0.149
Family history of DM	83 (20.8%)	44 (44%)	3.0 (1.9-4.8)	< 0.001
BMI ≥ 25 kg/m^2	157 (39.3%)	70 (70%)	3.6 (2.3-5.8)	< 0.001
Previous GDM	16 (4.0%)	17 (17%)	4.9 (2.4-10.1)	< 0.001
Previous fetal death	6 (1.5%)	2 (2%)	1.3 (0.3-6.7)	0.663
Previous macrosomia	6 (1.5%)	4 (4%)	2.7 (0.7-9.9)	0.119
Hypertension	40 (10%)	10 (10%)	1.0 (0.5-2.1)	1.00
Number of GDM risks				< 0.001
1 risk factor	219 (54.8%)	27 (27%)	1.0	
2 risk factors	121 (30.3%)	38 (38%)	2.5 (1.5-4.4)	< 0.001
≥ 3 risk factors	60 (15%)	35 (35%)	4.7 (2.7-8.4)	< 0.001

OR: odds ratio, CI: confidence intervals, SD: standard deviation, BMI: body mass index, GA: gestational age, DM: diabetes mellitus, GDM: gestational diabetes mellitus

Table 2. Comparison of baseline characteristics between the 2 groups.

Plasma glucose level of 100-g OGTT	Controls N = 400	Cases N = 100	p value
Mean fasting plasma glucose ± SD (mg/dL)	84.5 ± 13.0	126.0 ± 39.4	< 0.001
Mean 1-hour plasma glucose ± SD (mg/dL)	191.1 ± 26.3	216.8 ± 50.4	0.015
Mean 2-hour plasma glucose ± SD (mg/dL)	171.1 ± 21.2	197.2 ± 58.4	0.029
Mean 3-hour plasma glucose ± SD (mg/dL)	137.1 ± 27.5	155.3 ± 52.2	0.087
Abnormal plasma glucose values	N (%)	N (%)	
Fasting plasma glucose >95 mg/dL	53 (13.3)	81 (81)	< 0.001
1-hour plasma glucose >180 mg/dL	297 (74.3)	53 (53)	< 0.001
2-hour plasma glucose >155 mg/dL	336 (84)	71 (71)	0.002
3-hour plasma glucose >140 mg/dL	180 (45)	42 (42)	0.589
Number of abnormal values			< 0.001
Abnormal 2 values	153 (63.2)	55 (55)	
Abnormal 3 values	134 (33.5)	21 (21)	
Abnormal 4 values	13 (3.3)	24 (24)	

OGTT: oral glucose tolerance test, SD: standard deviation.

Pregnancy and neonatal outcomes were compared and the results are shown in Table 3. Maternal outcomes were comparable between cases and controls regarding gestational weight gain (GWG), GA at delivery, route of delivery, and preeclampsia. For neonatal outcomes, infants of cases were significantly more likely to have neonatal hypoglycemia and need for phototherapy. Both groups have comparable indications for cesarean section. Common indications for primary cesarean sections among cases and controls included cephalo-pelvic disproportion (23.6% vs. 25.7%), non-reassuring fetal heart rate (20.7% vs. 22.9%), and failed labor induction (9.3% vs. 11.4%).

Table 3. Comparison of pregnancy and neonatal outcomes between the 2 groups.

Outcomes	Controls N = 400	Cases N = 100	p value
Maternal outcomes			
Mean GWG ± SD (kg)	11.8 ± 5.3	11.2 ± 6.4	0.342
GWG category			0.514
Normal	142 (35.5%)	37 (37%)	
Inadequate	131 (32.8%)	27 (27%)	
Excessive	127 (31.8%)	36 (36%)	
Mean GA at delivery ± SD (weeks)	37.70 ± 1.78	37.53 ± 1.29	0.376
Route of delivery			0.835
Vaginal	182 (45.5%)	43 (43%)	
Primary C/S	140 (35%)	35 (35%)	
Repeat C/S	78 (19.5%)	22 (22%)	
Preeclampsia	62 (15.5%)	16 (16%)	0.902
Neonatal outcomes			
Mean birth weight ± SD (g)	3059.9 ± 525.8	3174.1 ± 577.9	0.058
Fetal LGA	102 (25.5%)	34 (34%)	0.088
Macrosomia	14 (3.5%)	7 (7%)	0.119
Apgar < 7 at 1 minute	22 (5.5%)	6 (6%)	0.846
Neonatal hypoglycemia	39 (9.8%)	17 (17%)	0.040
Phototherapy	80 (20%)	32 (32%)	0.010

GWG:, SD: standard deviation, GA: gestational age, C/S: cesarean section, LGA: large for gestational age.

Logistic regression analysis was performed to determine independent associated factors for the need of insulin therapy as shown in Table 4. After adjusted for age, parity, timing of GDM diagnosis, number of GDM risks, and number of abnormal OGTT values, independent associated risks for insulin therapy were FPG at OGTT > 95 mg/dL (adjusted OR 20.8, 95%CI 11.4-37.9, p < 0.001), overweight or obesity (adjusted OR 1.9, 95%CI 1.1-3.5, p = 0.029) and family history of DM (adjusted OR 2.2, 95%CI 1.2-3.9, p = 0.012).

Table 4. Logistic regression analysis to determine independent associated factors for insulin use, adjusted for potential confounders.

Factors	Adjusted OR	95% CI	p value
FPG at OGTT > 95 mg/dL	20.8	11.4 - 37.9	< 0.001
Overweight or obesity	1.9	1.1 - 3.5	0.029
Family history of DM	2.2	1.2 - 3.9	0.012

Adjusted for age, parity, timing of GDM diagnosis, number of GDM risks, and number of abnormal OGTT values

OR: odds ratio, CI: confidence intervals, FPG: fasting plasma glucose, OGTT: oral glucose tolerance test, DM: diabetes mellitus, GDM: gestational diabetes mellitus

Discussion

GDM women with poor glycemic control are associated with various adverse maternal and neonatal outcomes. Nutritional therapy and behavioral modification are commonly prescribed as initial treatment. However, when these measures fails, additional pharmacological treatment is needed for appropriate glycemic control and insulin is the first-line treatment of choice[1, 2, 6]. Identifying the factors related to the insulin requirement among GDM women is important in improving care process. This will help physician in identifying high-risk women who need close glycemic monitoring and can also aid in insulin treatment decision.

The results of this study showed that independent associated risks for insulin therapy were FPG of > 95 mg/dL at OGTT, overweight or obesity, and family history of DM. Abnormal FPG at the time of OGTT (> 95 mg/dL) showed the strongest association with adjusted OR of 20.8. Many previous studies have also reported that abnormal or high FPG level at the time of GDM diagnosis was related to the risk of insulin requirement[10, 11, 13-15]. A previous study reported that FPG of > 89.5 mg/dL had 72.7% sensitivity, 62.6% specificity, and 73% positive predictive value for insulin requirement[13]. While another study reported that FPG of >105 mg/dL at OGTT had a high specificity of 91.89% and positive predictive value of 80.64%[11].

Not only that overweight and obesity are among important risks for GDM[1, 2, 6, 16], they have been reported to be another significant risk for the need of insulin therapy similar to the results of this study[10, 12, 14]. A previous study in Siriraj Hospital also reported that overweight and obesity significantly increased the risk of insulin therapy as well[9]. Overweight and obese women might have higher degree of glucose intolerance and insulin resistance that increase the chance of nutritional therapy failure and consequently increase the risk for insulin therapy.

In this study, family history of DM also significantly increased the risk of insulin therapy among GDM women. A recent systematic review has reported that family history of DM was an important risk for development of GDM with odds ratio of 3.46[18]. In addition, another systematic review also reported that family history of DM significantly increased the risk of future type-2 DM as well[19]. Association between family history of DM and insulin requirement has been previously reported by a few previous studies[10, 12]. Genetic susceptibility for glucose intolerance and insulin resistance among women with family history of DM could have some roles in these observed results. However, exact underlying mechanism is still unknown and further studies regarding this specific issue are needed.

Many previous studies have reported association between HbA1c at the time of diagnosis and insulin therapy among GDM women[12, 13, 15, 20]. However, as HbA1c is not included as a routine test according to institutional guideline, such association could not be evaluated. Further studies might be required to determine if HbA1c is of value in predicting insulin requirement in GDM women. Other associated factors for insulin therapy that have been reported include maternal age, prior GDM[10], number of abnormal OGTT values[12], and gestational age at diagnosis[14]. These factors were also evaluated in this study but did not reach statistical significance level in multivariate analysis.

In terms of pregnancy outcomes, the results showed that infants of GDM women who required insulin therapy only increased the risk of neonatal hypoglycemia and the need for phototherapy, but not associated with other adverse outcomes. Awareness of both conditions, especially on neonatal hypoglycemia, should be raised when caring these infants after delivery. Previous studies have reported comparable pregnancy outcomes between the 2 groups that cesarean delivery, preterm birth, birth asphyxia, and NICU admission did not significantly increase with insulin therapy[11, 14]. However, increased birth weight and birth weight percentile have been reported[11]. Birth weight, LGA, and macrosomia only slightly higher in GDM women with insulin therapy, but without statistical significance. The absence of

significant association between some of the adverse pregnancy outcomes and insulin therapy may be partially due to the mitigating effects of GDM treatment.

Variations in the results between studies might be due to differences in population characteristics and risks, screening and diagnostic strategies, and management guidelines. While some studies used 75-g OGTT[13-15, 20], others used 100-g OGTT[9, 11, 12] for GDM diagnosis. Rates of insulin requirement in different settings also varied from 12% to 50% which partly reflects differences in population characteristics, risks and management scheme. However, some common risks were observed, e.g., high plasma glucose level at OGTT, pre-pregnancy overweight and obesity, etc., that might be useful to identify women at higher risk for insulin therapy.

The strengths of this study included the uniform screening and diagnosis and management guideline of GDM according to institutional guideline, and all GDM-related data were routinely recorded and collected systematically. Nonetheless, some deviations might exist from physicians' preference and judgment about insulin therapy. However, the issue should result only the delay in starting insulin and should not substantially alter the results. With regard to pregnancy outcomes, the study might have limited power to detect the differences between groups. In addition, effects of GDM treatments, both from nutritional and insulin therapy, on pregnancy outcomes could not be measured objectively. Further larger studies are needed to evaluate associated risks for insulin therapy as well as to determine if insulin therapy relates to adverse pregnancy outcomes in more details.

Nevertheless, the results of this study provide more insights on GDM management that are applicable into clinical practice. Understanding the significant risk factors will help caring physicians identify GDM women who are at higher risk for insulin therapy. Glycemic control of high-risk women should be closely monitored and decision on starting insulin therapy can be made in a timely manner. This might help GDM women to better achieve their glycemic target and minimize some related adverse pregnancy outcomes.

Conclusion

Independent associated risks for insulin therapy in GDM women included FPG of > 95 mg/dL at OGTT, overweight or obesity, and family history of DM. Infants of GDM women who required insulin therapy were significantly at higher risk of neonatal hypoglycemia and the need for phototherapy.

Potential conflicts of interest

The authors declare no conflict of interest.

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