OBSTETRICS

Risk Factors for Large for Gestational age Infants in Pregnant Women with Gestational Diabetes Mellitus

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ABSTRACT

Objective: To examine the risk factors for large for gestational age (LGA) infants in pregnant women with gestational diabetes mellitus (GDM).

Methods: Data were extracted from antenatal records of 282 GDM women who attended the antenatal clinict and delivered at Ramathibodi Hospital, Mahidol University. Risk factors were analyzed and compared between LGA group and control group.

Results: History of previous macrosomia infants, pre-pregnant BMI ≥ 25 kg/m^2, glucosuria on delivery day, fasting plasma glucose (FPG) of oral glucose tolerance test (OGTT) ≥ 95 mg/dl and plasma glucose at 1 hr of OGTT ≥ 180 mg/dl were significant risk factors for LGA infants (P < 0.05). Using multivariate analysis, the remained significant factors were the history of prior macrosomia infants, pre-pregnant BMI ≥ 25 kg/m^2 and FPG of OGTT ≥ 95 mg/dl (OR 4.86, 95%CI 1.66-14.25, OR 1.94, 95%CI 1.08-3.51 and, OR 3.05, 95%CI 1.61-5.77, respectively).

Conclusion: The significant risk factors for LGA infants in GDM women were the history of prior macrosomia infants, pre-pregnant BMI ≥ 25 kg/m^2 and FPG ≥ 95 mg/dl.The most important risk factor for LGA infant was the history of prior macrosomia.

Keywords: gestational diabetes mellitus, risk factors of LGA

Introduction

Gestational diabetes mellitus (GDM) is a common pregnancy complication especially in obese pregnant women. It is well known that infants borned from mother with GDM may be large for gestational age [LGA; defined as birth weight for gestational age above the 95th percentile of fetal weight for gestational age chart of Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University] and macrosomia [defined as birth weight $\geq$ 4,000 g][1]. Babies from GDM mothers may have hypoglycemia, birth injury, small for gestational age and appropriate for gestational age (AGA) infants[2]. Risk factors of having macrosomia or LGA infants in the western countries in GDM mother are prepregnancy weight and obesity[1,3,4]. However, the data in Asian women are limited.

The incidence of macrosomia in our hospital is

5%. GDM correlates with 25% of LGA and macrosomia. The incidence of difficult delivery are approximately 15 cases per month.[5] We need to identify risk factors for LGA in GDM in order to prevent its complicationsimprove pregnancy outcomes. The objective of this study is to evaluate the risk factors of LGA infants in pregnant women with GDM.

Methods

This case controlled study was approved by the Ethical Clearance Committee on Human Rights Related to Researches Involving Human Subjects, Faculty of Medicine Ramathibodi Hospital. The sample size was calculated from the result of our pilot study of 150 GDM women in which 38 of LGA infants were delivered. Eighty GDM with LGA and 160 GDM without LGA were needed to get the number of case : control at a ratio of 1: 2. with a power of 95% at type I alpha error of 0.05 and type II beta error of 0.1.

Data from 437 GDM women who delivered at Ramathibodi Hospital, Mahidol University were reviewed. The inclusion criteria were[1]: attended antenatal care (ANC) and delivered at Ramathibodi Hospital,[2] diagnosis of GDM by Carpenter and Coustan criteria (requires at least two of the following: (i) fasting plasma glucose ≥ 95 mg/dL, (ii) 1-h post load glucose ≥ 180 mg/dL, (iii) 2-h post load glucose ≥ 155 mg/dL, (iv) 3-h post load glucose ≥ 140 mg/dL)[2,3], ultrasonography at the 2nd trimester to confirm GA and detect fetal abnormality[4], singleton[5], no complications of pregnancy such as pregnancy induced hypertension (PIH), fetal growth restriction (FGR)[6], No underlying diseases such as hypertension (HT), diabetes mellitus (DM)[7], term pregnancy (GA ≥ 37 wk). The exclusion criteria of study were: (1) incomplete document, (2) delivery by elective cesarean section (C/S) due to previous C/S, (3) insulin requirement for plasma glucose control. Finally, 282 women with well controlled GDM (defined as FPG < 95 mg/dL or the 2-hour postprandial plasma glucose at < 120 mg/dL)[2] were enrolled and classified to the LGA infant (defined as birth weight for gestational age above the 95th percentile of fetal weight for gestational age chart of Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology,

Faculty of Medicine Chulalongkorn University, Thai version)[6,7] and normal weight infant. Both groups were reviewed for the demographic data and risk factors such as gravida, pre-pregnancy weight and BMI, weight gain during pregnancy, glucosuria on delivery day, family history of diabetes mellitus (DM), previous stillbirth, prior macrosomia, previous GDM, and plasma glucose from OGTT. In this study, we used weight gain ≥ 9 kg as a cut-off for risk factor because weight gain more than 9 kg makes the relative risk of LGA two-fold higher in GDM than in control mother.[8]

Statistical analysis

All analyses were conducted using the SPSS version 11.5. The data were presented as median, mean ± standard deviation (SD) and frequency (%). X^2-test was used for analyzing the data. The significant factors were analyzed by multivariate logistic analysis and presented as p-value, odds ratio and 95% confidence interval. p-value <0.05 was considered statistically significant.

Results

Demographic data of the study population were presented in Table 1. There were no differences in age and gravida between the GDM women with and without LGA. Prepregnant weight and BMI were higher in the study group than in control group (66.4 ± 12.9 kg vs. 58.2 ± 11.9 kg and 26.8 ± 5.5 kg/m² vs. 23.9 ± 4.6 kg/m², respectively). The GDM women with LGA infants had higher rate of cesarean section (OR 2.7, 95% CI 1.53 - 4.77) and forceps extraction (OR 5.15, 95% CI 0.46- 57.65) than in control group.

Table 2 showed the risk factors of LGA by univariate analysis. The history of prior macrosomia, pre-pregnant BMI ≥25 kg/m², glucosuria on delivery day, FPG of OGTT ≥ 95 mg/dl and plasma glucose at 1 hr of OGTT ≥ 180 mg/dl were risk factors.

After multivariate, stepwise logistic analysis, prior macrosomia, pre-pregnant BMI ≥ 25 kg/m² and FPG of OGTT ≥ 95 mg/dl remained significant risk factors for LGA as shown in Table 2.

Table1: Demographic data

Characteristic	LGA (N = 80)	Without LGA (N = 202)
Age(mean ± SD), yr	34.0 (± 4.5)	33.6 (± 5.2)
Gravida (median ; 25,75%tile)	2 (1,3)	2 (1,3)
Pre-pregnant BMI (mean ± SD), kg/m^2	26.8 (± 5.5)	23.9 (± 4.6)
Pre-pregnant weight (mean ± SD),kg	66.4 (± 12.9)	58.2 (± 11.9)
Route of delivery		
- Cesarean section(case),%	73.8 (59)	51 (103)
- Forceps extraction(case),%	2.5 (2)	0.5 (1)
- Vacuum extraction(case),%	-	0.5 (1)
- Normal labor(case),%	23.8 (19)	48 (97)

Discussion

In this study we evaluated the risk factors of LGA in GDM women. The significant risk factors were prior macrosomia, pre-pregnant BMI ≥ 25 kg/m^2 and FPG of OGTT ≥ 95 mg/dl. The most important risk factor was prior macrosomia.

Abnormal FPG of OGTT was found more frequent in GDM women with LGA infants. From the literature review, maternal hyperglycemia caused fetal hyperinsulinemia which was known to be the potent growth hormone during intrauterine development, therefore, the GDM pregnant women had the chance to deliver LGA and macrosomia infants[9]. The quality of plasma glucose control such as FPG during antenatal care and HbA$_1$c were not reviewed in this study so we were not able to conclude the significance of FPG for LGA infants. Abnormal FPG of OGTT was only one of the major risk factors.

The GDM women with LGA infants were more obese than women without LGA infants. Maternal obesity (BMI ≥ 25 kg/m^2) is associated with various complications including insulin resistance, subclinical inflammation, and decreased serum adiponectin[10]. Maternal obesity was found to be the risk factor for large for gestational age infants of GDM mothers[1].

In this study, the most important risk factor for large for gestational age infants in GDM women was prior macrosomia. However, the mechanism is not clear[4]. Prior pregnancy might have not been detected for GDM.

However, this study is the retrospective study, some confounding factors were not recorded such as gestational age of GDM diagnosis, various quality of diabetic control and level of HbA$_1$c. We were not able to conclude the relationship between diabetic control and fetal birth weight. The outcomes of study may be different in a prospective study.

Conclusion

The significant risk factors for LGA infants of GDM women were having prior macrosomia infants, pre-pregnant BMI ≥ 25 kg/m^2 and FPG of OGTT ≥ 95 mg/dl. This data may help the health care provider to reduce the incidence of LGA infants of GDM women by controlling their preprgnancy weight and also have a good FPG control especially in the GDM women who have prior macrosomia babies.

Acknowledgement

Table 2: Risk factors of LGA in GDM

Characteristic	LGA (n = 80)	Without LGA (n = 202)	Univariate analysis			Multivariate logistic analysis		
			P-value	Odd Ratio	95% CI	P-value	Odd Ratio	95% CI
Age ≥ 35 years	40 (50%)	108 (55.5%)	0.69	0.87	0.52 - 1.46	-	-	-
Gravida > 1	58 (72.5%)	132 (65.4%)	0.26	1.40	0.79 - 2.47	-	-	-
Pre-pregnant BMI ≥ 25 kg/m^2	42 (52.5%)	59 (29.2%)	< 0.001	2.68	1.57 – 4.57	0.028	1.94	1.08 – 3.51
Weight gain ≥ 9 kg	54 (67.5%)	134 (66.3%)	0.889	1.54	0.61 – 1.83	-	-	-
Glucosuria on delivery day	7 (8.8%)	4 (2.0%)	0.014	4.75	1.35 – 16.69	0.123	3.00	0.74 - 12.15
Family History of DM	32 (40.0%)	93 (46.0%)	0.357	0.78	0.46 – 1.32	-	-	-
Previous stillbirth*	1 (1.7%)	4 (3.0%)	1.000	0.56	0.06 – 5.14	-	-	-
Prior Macrosomia*	13 (22.4%)	6 (4.6%)	< 0.001	6.07	2.18 – 16.92	0.004	4.86	1.66 - 14.25
Previous GDM*	10 (17.2%)	13 (9.9%)	0.156	1.91	0.78 – 4.64	-	-	-
OGTT 1 ≥ 95 mg/dl	35 (43.8%)	30 (14.9%)	< 0.001	4.46	2.48 – 8.03	0.001	3.05	1.61 – 5.77
OGTT 2 ≥ 180 mg/dl	72 (90.0%)	160 (79.2%)	0.038	2.36	1.06 – 5.29	0.167	1.82	0.78 – 4.24
OGTT 3 ≥ 155 mg/dl	76 (95.0%)	191 (94.6%)	1.000	1.09	0.34 – 3.54	-	-	-
OGTT 4 ≥ 140 mg/dl	46 (57.5%)	110 (54.5%)	0.691	1.13	0.67 – 1.91	-	-	-

95% CI = 95% Confidence Interval

* Exclude G1; LGA group, n = 58 cases, Without LGA group, n = 132 cases

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ปัจจัยเสี่ยงของการเกิดทารกน้ำหนักมากในสตรีที่มีภาวะเบาหวานขณะตั้งครรภ์

ณัฐภรณ์ พรประเสริฐสุข, พัญญ์ พันธ์บูรณะ, ณัฐพงศ์ อิศรางกูร ณ อยุธยา

วัตถุประสงค์ *: เพื่อศึกษาปัจจัยเสี่ยงของการเกิดทารกน้ำหนักมาก (Large for gestational age, LGA) ในสตรีที่มีภาวะเบาหวานขณะตั้งครรภ์*

วัสดุและวิธีการ *: ข้อมูลจากเวชระเบียนของสตรีที่มีภาวะเบาหวานขณะตั้งครรภ์ทั้งหมด 282 ราย ที่มาฝากครรภ์และคลอดที่โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล จะนำมาทบทวนและแยกกลุ่มผู้ป่วยออกเป็น 2 กลุ่มได้แก่กลุ่มที่คลอดทารกน้ำหนักมากและกลุ่มที่คลอดทารกน้ำหนักปกติเป็นกลุ่มควบคุม ปัจจัยเสี่ยงทั้งหมดจะนำมาวิเคราะห์ทางสถิติและเปรียบเทียบกันระหว่างทั้ง 2 กลุ่ม*

ผลการศึกษา *: ประวัติการคลอดทารกน้ำหนักมากในครรภ์ก่อน, ดัชนีมวลกายก่อนการตั้งครรภ์มากกว่าหรือเท่ากับ 25 กก/ม², การตรวจพบน้ำตาลในปัสสาวะในวันที่คลอด, ปริมาณน้ำตาลในกระแสเลือดหลังงดน้ำงดอาหาร (Fasting plasma glucose of OGTT) มากกว่าหรือเท่ากับ 95 มก/ดล และปริมาณน้ำตาลในกระแสเลือด 1 ชั่วโมงหลังรับประทานน้ำตาล 100 ก 1 ชั่วโมง (plasma glucose at 1 hr of OGTT) มากกว่าหรือเท่ากับ 180 มก/ดล เป็นปัจจัยเสี่ยงที่จะทำให้คลอดทารกน้ำหนักมากกว่าปกติอย่างมีนัยสำคัญทางสถิติ (P < 0.05) การวิเคราะห์ทางสถิติโดยวิธี Multivariate logistic analysis พบว่าปัจจัยเสี่ยงที่ยังมีความสำคัญทางสถิติได้แก่ ประวัติการคลอดทารกน้ำหนักมากในครรภ์ก่อน, ดัชนีมวลกายก่อนการตั้งครรภ์มากกว่าหรือเท่ากับ 25 กก/ม2และปริมาณน้ำตาลในกระแสเลือดหลังงดน้ำงดอาหารมากกว่าหรือเท่ากับ 95 มก/ดล (OR 4.86, 95%CI 1.66-14.25, OR 1.94, 95%CI 1.08-3.51 และ OR 3.05, 95%CI 1.61-5.77 ตามลำดับ)*

สรุป *: ปัจจัยเสี่ยงของการเกิดทารกน้ำหนักมากในสตรีที่มีภาวะเบาหวานขณะตั้งครรภ์ได้แก่ ประวัติการคลอดทารกน้ำหนักมากในครรภ์ก่อน, ดัชนีมวลกายก่อนการตั้งครรภ์มากกว่าหรือเท่ากับ 25 กก/ม2 และปริมาณน้ำตาลในกระแสเลือดหลังงดน้ำงดอาหารมากกว่าหรือเท่ากับ 95 มก/ดล โดยปัจจัยที่มีความสำคัญมากที่สุด คือ ประวัติการคลอดทารกน้ำหนักมากในครรภ์ก่อน*