Thai Journal of Obstetrics and Gynaecology
July 2008, Vol. 16, pp. 147-153

OBSTETRICS

Incidence of Large-for-Gestational Age Newborn among Pregnant Women with One Abnormal Value Oral Glucose Tolerance Test.

Pisutt Srichaikul MD,
Prasert Sunsaneevithayakul MD,
Dittakarn Boriboonhirunsarn MD, M.P.H., Ph.D.

Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand

ABSTRACT

Objectives To evaluate the incidence and risk factors of LGA newborn among pregnant women with one abnormal value OGTT.

Design Retrospective cohort study.

Methods A total of 189 pregnant women who had one abnormal value OGTT were enrolled and followed until delivery. Incidence of LGA was determined as the main outcome. Comparison between LGA and non-LGA was performed with regard to various clinical characteristics to determine associated risk factors. Pregnancy and neonatal outcomes were also evaluated.

Results Incidence of LGA newborn was 19.05% (36/189 cases). The independent associated factors of LGA newborn was multiparity (adjusted OR 5.3, 95%CI 1.2-23.2, p=0.029) and excessive weight gain (adjusted OR 50.2, 95%CI 12.4-203.9, p <0.001). LGA newborn had significant increased rate of cesarean section (83.3% vs 5.9%, p <0.001) and neonatal hypoglycemia (5.6% vs 0%, p=0.035).

Conclusion Pregnant women with one abnormal value OGTT who were multiparous or had excessive weight gain had a significant risk of LGA newborn.

Keywords: one abnormal value oral glucose tolerance test, large-for-gestational age newborn

Introduction

Gestational diabetes mellitus (GDM) is a common clinical condition facing obstetricians and their patients. It complicates approximately 3-7% of pregnancy. Significant perinatal mortality and morbidity, including stillbirth, fetal macrosomia, shoulder dystocia, birth trauma, respiratory distress syndrome, neonatal jaundice, and polycythemia have reportedly occurred where there has been failure to diagnose and treat the condition.[1]

The 100 gm oral glucose tolerance test (OGTT) is currently among the most widely used methods for diagnosing diabetes during pregnancy. These methods are derived from the work of O' Sullivan and colleagues, who were trying to predict the long-term risk of diabetes in women. However

the results of this research were not intended to use for predicting the short-term complication such as macrosomia or large for gestational age (LGA) newborn.[2]

Several studies have demonstrated that the increased glucose intolerance by abnormal one value OGTT during pregnancy was associated with unfavorable fetomaternal outcomes of pregnancy such as macrosomia, cesarean delivery, preeclampsia, neonatal jaundice, and increased length of stay even if criteria for GDM are not reached.[3,4]

This study was, therefore, undertaken to evaluate the incidence of LGA newborns among pregnant women with one abnormal value of OGTT and to identify risk factors associated with LGA newborn in these women.

Materials and Methods

The study design was a retrospective cohort study. Medical records were retrieved from the records of Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital during the period from January, 2005 to December, 2006. Pregnant women who attended the antenatal clinic before 14 weeks of gestation, having one abnormal value of OGTT were eligible. Those women who were known cases of diabetes mellitus before pregnancy or did not follow the screening protocols were excluded.

During first visit, screening test with 50-gm GCT was performed on patients with clinical risk factors for GDM such as a family history of diabetes in first degree relatives, maternal age ≥ 30 years, obesity as defined as pre-pregnancy body mass index(BMI) ≥27 kg/m^2, a past history of GDM or macrosomia (>4000 gm) or unexplained perinatal death or structural congenital abnormalities or preeclampsia. The test scheme was repeated during 24-28 weeks, and 32-34 weeks of gestation if initial test was normal. Those with an abnormal screening test result (50 gm GCT ≥140 mg/dl) were tested for diagnosis of GDM, using 100 gm OGTT. The cut-off values for fasting, 1, 2, 3 hours blood glucose were ≥ 105, 190, 165, 145 mg/dl respectively, followed by National Diabetes Data Group (NDDG) criteria .

The present study recruited 189 pregnant women who had one abnormal value OGTT from 236 medical records, 80.1%. LGA was defined as birth weight is equal to or greater than 90th percentile for gestational age according to weight-gestational age chart by Department of Pediatrics, Faculty of Medicine Siriraj Hospital. Incidence of LGA was determined as the main outcome. Comparison of LGA and non-LGA group was performed to determine associated risk factor. Excessive weight gain during pregnancy was defined according to the criteria by Institute of Medicine (IOM). Finally, pregnancy and neonatal outcomes were evaluated and compared between 2 groups.

Data collection included baseline characteristics, clinical risk for GDM, pregnancy and neonatal outcomes. Student t test, Chi-square test, and Fisher's Exact test were used in the comparison between the two groups. Multiple logistic regression analysis was also used to determine independent associated factors. Adjusted odds ratio and 95% confidence interval were estimated. P-value of <0.05 was considered statistical significance.

This study has been reviewed and approved by Ethics Committee, Faculty of Medicine Siriraj Hospital, Mahidol University.

Results

During study period, a total of 189 pregnant women with one abnormal value OGTT were enrolled in this study. Table 1 shows demographic data of maternal characteristics. Most of pregnant women delivered at term pregnancy (38.4 ± 1.3 weeks). Clinical risk for GDM was shown in table 2. Maternal age ≥30 years was the most common clinical risk for GDM in this study.

Of 189 pregnant women enrolled, 36 LGA newborns were delivered, therefore, the incidence of LGA newborns among abnormal one value OGTT women in our study was 19.05%.

Table 3 shows risk factors for LGA newborns. There were significantly increased risk of LGA newborns in pregnant women who were multiparous

(RR 3.0, 95% CI 1.2-7.4, p value 0.007), obesity (RR 9.1, 95% CI 5.1-16.4, p value <0.001), excessive weight gain during pregnancy (RR 21.7, 95% CI 9-52.3, p value <0.001). On the other hand, the rest of clinical risk factors were not statistically significant.

Women who had one abnormal OGTT before 24 weeks of gestation were most likely to deliver LGA newborns (RR 1.9, 95% CI 1.03-3.4, p value 0.043), however the frequency of one abnormal value of OGTT did not affect neonatal birth weight as shown in table 4. Multiple logistic regression analysis was used to identify the independent risk factors for LGA and results are shown in table 5. Multiparity (adjusted OR 5.3, 95% CI 1.2-23.2, p value 0.029) and excessive weight gain during pregnancy (adjusted OR 50.2, 95% CI 12.4-203.9, p value<0.001) were the only independent risk factors of LGA newborn delivery.

Neonatal outcomes between LGA and non-LGA groups were shown in table 6. LGA newborns seem to have hypoglycemia at birth (5.6% vs 0%, p value 0.035) and increased rate of cesarean section (83.3% vs 5.9%, p value<0.001). No significant differences were found in the incidence of birth asphyxia and neonatal jaundice.

Table 1. Demographic data.

Maternal characteristics	Mean ± SD
Maternal age (years)	31.9±4.7
Prepregnancy BMI (kg/m^2)	23.1±4.1
Gestational age at first ANC (week)	9.7±2.3
Gestational age at delivery (week)	38.4±1.3
Weight gain during pregnancy (kg)	11.5±4.0

ANC = Antenatal clinic

Table 2. Clinical risk factors for gestational diabetes mellitus.

Clinical risk factors	N (%)
Age≥30 years	132 (69.8%)
Family history of diabetes mellitus	80 (42.3%)
Obesity	34 (18%)
Previous history of preeclampsia	8 (4.2%)
Previous history of congenital anomaly	4 (2.1%)
Previous history of macrosomia	3 (1.6%)
Previous history of unexplained fetal death	3 (1.6%)
Previous history of gestational diabetes mellitus	1 (0.5%)

Table 3. The risk of LGA newborn for various risk factors.

Risk factors		LGA (%)	RR (95%CI)	p-value
1. Multiparity	No	5/62 (8.1%)	1.0	0.007
	Yes	31/127 (24.4)	3.0 (1.2-7.4)	
2. Age≥30 years	No	7/57 (12.3%)	1.0	0.12
	Yes	29/132 (22%)	1.8 (0.8-3.8)	
3. Obesity	No	12/155 (7.7%)	1.0	<0.001
	Yes	24/34 (70.6%)	9.1 (5.1-16.4)	
4. Excessive weight gain	No	5/147 (3.4%)	1.0	<0.001
	Yes	31/42 (73.8%)	21.7 (9-52.3)	
5. Family history of DM	No	22/109 (20.2%)	1.0	0.643
	Yes	14/80 (17.5%)	0.9 (0.5-1.6)	
6. History of macrosomia	No	34/186 (18.3%)	1.0	0.093*
	Yes	2/3 (66.7%)	3.6 (1.6-8.6)	
7. History of preeclampsia	No	33/181 (18.2%)	1.0	0.179*
	Yes	3/8 (37.5%)	2.1 (0.8-5.3)	
8. History of congenital anomaly	No	35/185 (18.9%)	1.0	0.574*
	Yes	1/4 (25%)	1.3 (0.2-7.4)	
9. History of unexplained fetal death	No	36/186 (19.4%)	-	1.00*
	Yes	0/3 (0%)		
10. History of GDM	No	35/188 (18.6%)	1.0	0.19*
	Yes	1/1 (100%)	5.4 (4.0-7.2)	

* Fisher's Exact test

Table 4. Frequency and timing of abnormal one value of OGTT and the risk of LGA newborn.

One abnormal value of OGTT	LGA (%)	RR (95%CI)	p-value
1. Frequency			0.135*
1 time	29/168 (17.3%)	1.0	
≥2 times	7/21 (33.3%)	1.9 (0.9-3.8)	
2. Timing			0.043
≥24 weeks	23/145 (15.9%)	1.0	
<24 weeks	13/44 (29.5%)	1.9 (1.03-3.4)	

* Fisher's Exact test

Table 5. Results of multiple logistic regression analysis.

Variables	Adjusted OR	95% CI	p-value
Multiparity	5.3	1.2-23.2	0.029
Excessive weight gain	50.2	12.4-203.9	<0.001
Obesity	3.3	0.9-12.8	0.08
Time of 1st abnormal OGTT <24 weeks	1.8	0.5-6.4	0.391

Table 6. Comparison of pregnancy outcomes between LGA and non-LGA newborns.

Pregnancy outcomes	LGA (%)	Non-LGA (%)	p-value
Hypoglycemia	2 (5.6%)	0 (0%)	0.035*
Birth asphyxia	0 (0%)	4 (2.6%)	1.00*
Neonatal jaundice	4 (11.1%)	32 (20.9%)	0.178
Cesarean section	30 (83.3%)	9 (5.9%)	<0.001

* Fisher's Exact test

Discussion

Several studies have shown that the incidence of LGA newborns in mild gestational hyperglycemia varied, range from 13.2-53.9%, depending on race, pre-pregnancy body mass index, maternal age, multiparity, educational status, and dietary control.[5,6] In this study, the incidence of LGA newborns among one abnormal value OGTT women was 19.05%, comparing with 1-11.6% in normal population.[5,7] These results demonstrated that minor abnormalities of glucose metabolism even though without GDM are a significant risk factor for fetal overgrowth.

Excessive weight gain during pregnancy in LGA group was found in 73.8%, reflecting poor dietary control in the present population. Previous studies have shown that increasing carbohydrate intolerance in women without gestational diabetes mellitus was associated with a significantly increased incidence of cesarean section, macrosomia, preeclampsia, and neonatal jaundice, as well as an increased length of stay of both mother and infant.[3,4] However, treatment with dietary control and insulin therapy significantly decrease the prevalence of macrosomia.[8] However, the authors' institution did not have diet counseling program in this group and the authors hope that intensive dietary control might decrease the incidence of LGA newborns.

Similar to previous studies, maternal obesity, and women who gained weight more than recommendation of IOM were also more likely to have infant with macrosomia.[9-12] From the present study, multiparous women or having weight gain over normal recommendation were more likely to deliver LGA infants but no statistical significance was found in obese women when multiple logistic regression analysis was used. The inconsistence may be from the definition of obesity in pregnant women that was different (>27 kg/m^2 in our study vs >30 kg/m^2 in previous study).[10,11]

Insulin resistance which is the cause of GDM is known to begin in the second trimester and increase with gestational age.[13] It is possible that women who have an abnormal OGTT earlier are more likely to have serious glucose intolerance later and tend to have poor pregnancy outcomes. In this study it was found that women who had an abnormal

OGTT before 24 weeks of gestation were 1.9 times more likely to have a LGA newborn. This may be from the authors' institution did not have a guideline for diet therapy in this abnormal one value of OGTT. However, after adjustment by multiple logistic regression analysis, this association was not statistical significance. Incidence of LGA newborn was similar between early and late detection of abnormal one value OGTT. Further study is needed to verify the effect of dietary control among this group of pregnant women to decrease incidence of LGA.

With regard to maternal and fetal outcomes, a previous study has shown that macrosomia is associated with higher rate of cesarean birth, postpartum hemorrhage, birth trauma (such as brachial plexus injuries, clavicular, and humeral fractures), birth asphyxia, hypoglycemia, meconium aspiration syndrome, and prolonged hospital stays.[7] In our study, the LGA newborn group was only shown a significant increase in rate of cesarean section, and neonatal hypoglycemia but not birth asphyxia or neonatal jaundice.

Various limitation of this study should be noted. Our study had a small sample size and there might be unable to detect some uncommon morbidity in neonatal outcomes such as neonatal jaundice, meconium aspiration syndrome, etc. Moreover, other important confounding factor such as the dietary control that seem to be an important impact on the pregnancy outcomes could not be assessed. Further study should be mainly focused on this topic.

In conclusion, pregnancy with abnormal one value OGTT, who was multiparity or had excessive weight gain during pregnancy had a significant increased risk of LGA newborn. More attention should be paid to this group and intensive counseling for appropriate dietary control program should be advised.

References

1. Hackman R, Jame R, Green CO, Ferber A, Barnhard Y, Divon M. The impact of maternal age, body mass index, and maternal weight gain on the glucose challenge test in pregnancy. J Matern Fetal Neonatal Med 2007; 20: 253-7.
2. Ouzilleau C, Roy MA, Leblanc L, Carpentier A, Maheux P. An observational study comparing 2-hour-75-g oral glucose tolerance with fasting plasma glucose in pregnant women: both poorly predictive of birth weight. Can Med Assoc J 2003; 168: 403-9.
3. Sermer M, Naylor CD, Gare DJ, Kenshole AB, Ritchie JW, Farine D, et al . Impact of increasing carbohydrate intolerance on maternal fetal outcomes in 3637 women without gestational diabetes. The Toronto Tri-hospital gestational diabetes project. Am J Obstet Gynecol 1995; 173: 146-56.
4. Berkus MD, Langer O. Glucose tolerance test: degree of glucose abnormality correlates with neonatal outcome. Obstet Gynecol 1993; 83: 344-8.
5. Tina MS, Anna MS, Linda SA, David AS, John MT, Jr. The association between impaired glucose tolerance and birth weight among black and white women in Central North Carolina. Diabetes care 2003; 26: 656-61.
6. Vambergue A, Nuttenst MC, Verier-Mine O, Dognin C, Cappoen JP, Fontaine P. Is mild gestational hyperglycemia associated with maternal and neonatal complications? The diagest study. British Diabetic Association. Diabet Med 2000; 17: 203-8.
7. Elizabeth J. Lawrence. A matter of size: part 2: evaluating the large for gestational age neonate. Adv Neonatal Care 2007; 7: 187-97.
8. Bevier WC, Fischer R, Jovanovic L. Treatment of woman with an abnormal glucose challenge test (but a normal oral glucose tolerance test) decreases the prevalence of macrosomia. Am J Perinatol 1999; 16: 269-75.
9. Jain NJ, Denk CE, Kruse KK, Dandolu V. Maternal obesity: can pregnancy weight gain modify risk of selected adverse pregnancy outcomes? Am J Perinatol 2007; 24: 291-8.
10. Catalano PM. Management of obesity in pregnancy. Obstet Gynecol 2007; 109: 419-33.
11. Rode L, Hegaard HK, Kjaergaard H, Moller L, Tabor A, Ottesen B. Association between maternal weight gain and birth weight. Obstet Gynecol 2007; 109: 1309-15.
12. Hedderson MM, Weiss NS, Sacks DA, Pettitt DJ, Selby JV, Quesenberry CP, Ferrara A. Pregnancy weight gain and risk of neonatal complications: macrosomia, hypoglycemia, and hyperbilirubinemia. Obetet Gynecol 2006; 108: 1153-61.
13. Cunningham FG, Leveno KJ, Bloom SL, Hault JC, Gilstrap LC, Wenstrom KD. Williams obstetrics. 22nd ed. New York: McGraw-Hill; 2005: 1170-84.
14. Sunsaneevithayakul P, Boriboonhirunsarn D, Sutanthavibul A, Ruangvutilert P, Kanokpongsakdi S, Singkiratana D, et al. Risk factor based selective screening program for gestational diabetes mellitus in Siriraj hospital: a result from clinical practice guideline. J Med Assoc Thai 2003; 86: 708-14.

อุบัติการณ์การคลอดทารกน้ำหนักมากกว่าอายุครรภ์ในสตรีที่ตรวจพบค่า Oral Glucose Tolerance Test ผิดปกติหนึ่งค่า

พิสุทธิ์ ศรีชัยกุล, ประเสริฐ ศันสนีย์วิทยกุล, ดิฐกานต์ บริบูรณ์หิรัญสาร

วัตถุประสงค์ *: เพื่อศึกษาอุบัติการณ์และปัจจัยเสี่ยงของการคลอดทารกน้ำหนักมากกว่าอายุครรภ์ในสตรีที่ตรวจพบค่า Oral Glucose Tolerance Test ผิดปกติหนึ่งค่า*

วัสดุและวิธีการ *: ศึกษาสตรีตั้งครรภ์ที่ตรวจพบค่า Oral Glucose Tolerance Test ผิดปกติหนึ่งค่าจำนวน 189 คนจนกระทั่งคลอดบุตร เพื่อคำนวณหาอุบัติการณ์การคลอดทารกน้ำหนักมากกว่าอายุครรภ์ในสตรีที่ตรวจพบค่า Oral Glucose Tolerance Test ผิดปกติหนึ่งค่า, เปรียบเทียบระหว่างสตรีที่คลอดบุตรน้ำหนักมากกว่าอายุครรภ์กับสตรีที่ไม่ได้คลอดบุตรน้ำหนักมากกว่าอายุครรภ์เพื่อหาปัจจัยเสี่ยงของการคลอดทารกน้ำหนักมากกว่าอายุครรภ์, ศึกษาผลลัพธ์ของการตั้งครรภ์และภาวะแทรกซ้อนของมารดาและทารกเปรียบเทียบระหว่างสตรีสองกลุ่ม*

ผลการศึกษา *: อุบัติการณ์การคลอดทารกน้ำหนักมากกว่าอายุครรภ์ในสตรีที่ตรวจพบค่า Oral Glucose Tolerance Test ผิดปกติหนึ่งค่าคือ 19.05%, ปัจจัยเสี่ยงที่สำคัญของการคลอดทารกน้ำหนักมากกว่าอายุครรภ์ ได้แก่ เคยคลอดบุตรมากกว่าหนึ่งครั้ง (adjusted OR 5.3, 95%CI 1.2-23.2, p=0.029) และน้ำหนักตัวเพิ่มมากกว่าเกณฑ์มาตรฐานระหว่างตั้งครรภ์ (adjusted OR 50.2, 95%CI 12.4-203.9, p <0.001), ทารกที่มีน้ำหนักมากกว่าอายุครรภ์เพิ่มอัตราการผ่าตัดคลอด (83.3% และ 5.9%, p <0.001) และระดับน้ำตาลในเลือดต่ำแรกเกิด (5.6% และ 0%, p=0.035)*

สรุป *: สตรีตั้งครรภ์ที่ตรวจพบค่า Oral Glucose Tolerance Test ผิดปกติหนึ่งค่าร่วมกับมีปัจจัยเสี่ยงได้แก่ เคยคลอดบุตรมากกว่าหนึ่งครั้งหรือน้ำหนักตัวเพิ่มมากกว่าเกณฑ์มาตรฐานระหว่างตั้งครรภ์มีความเสี่ยงที่จะคลอดบุตรน้ำหนักมากกว่าอายุครรภ์*