The Effect of Pre-Pregnancy Weight on Delivery Outcome and Birth Weight in Potential Diabetic Patients with Normal Screening for Gestational Diabetes Mellitus in Siriraj Hospital

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Objective: *To investigate the influence of pre-pregnancy weight on delivery outcome and birth weight in potential diabetic women with normal glucose tolerance.*
Design: *Retrospective Cohort study*
Material and Method: *The medical records of 660 pregnant women, who attended the antenatal clinic and delivered at Siriraj Hospital between January 2003 and December 2005, were reviewed and analyzed. They all had the known pre-pregnancy weight and were at risk of gestational diabetes with the normal glucose tolerance. Any pregnant women without pre-pregnancy weight recorded were excluded from the present study. They were classified into two groups according to the pre-pregnancy BMI, one was the overweight group (BMI $\geq$ 27 kg/m^2) and the other was the normal weight group (BMI 20-25 kg/m^2). Information of the complications of pregnancy, the route of delivery, birth weight, and neonatal outcomes were collected and analyzed.*
Results: *The risks of adverse pregnancy outcomes in overweight women, after adjusting for the confounding factors, were significantly increased, including pre-eclampsia (OR 3.87, 95%CI 2.09-7.25, p < 0.001), cesarean delivery (OR 2.22, 95%CI 1.45-3.39, p < 0.001), cephalopelvic disproportion (OR 2.15, 95%CI 1.35-3.42, p = 0.001), and macrosomia (OR 7.59, 95% CI 1.98-29.09, p < 0.001).*
Conclusion: *Even though the screening test for gestational diabetes mellitus is normal, the overweight women still have several adverse pregnancy outcomes.*

Keywords: *Birthweight, Delivery outcome, Normal glucose tolerance, Overweight, Pregnancy*

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Obesity is a major health care concern[1]. There is a significant association between obesity and diabetes mellitus, heart disease, stroke, and cancer[2,3]. Furthermore, obesity is believed to have an influence on fertility and pregnancy outcome. In women of childbearing age, higher pre-pregnancy weight has been associated with gestational diabetes, pre-eclampsia, eclampsia, cesarean delivery, and infant macrosomia[4-13].

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In 1990, the Institute of Medicine (IOM) recommended that the body mass index (BMI) be used to define maternal weight groups[14]. Body mass index is believed to be superior to weight-for-height as a measure of adiposity. In 1993, the American College of Obstetricians and Gynecologists (ACOG) released its BMI classification of maternal weight and optimal weight gain during pregnancy[15]. Lu et al demonstrated that the incidence of obesity at the first prenatal visit increased from 7.3% to 24.4% in the 20-year time period[16].

In most of the previous studies of pregnancy outcomes and maternal BMI, adjustments had been

made for various confounding factors, including pre-existing diabetes and gestational diabetes mellitus (GDM). However, it has been shown that even minor degrees of glucose intolerance are related to adverse pregnancy outcomes in a continuous and graded fashion[17,18]. Thus, the aim of the present study was to determine the relationship between the pre-pregnancy BMI, delivery outcome, and birth weight in potential diabetic women with a verified normal glucose tolerant test.

Material and Method

A retrospective review was conducted using medical records of the pregnant women who received prenatal care and delivered at Siriraj Hospital between January 2003 and December 2005. All the pregnant women in the present study were at risk for gestational diabetes (GDM), called potential diabetes mellitus. The risks for GDM were described in detail in Table 1[19]. All of them had pre-pregnancy weight recorded; any study pregnant women without their pre-pregnancy weight recorded were excluded from the present study.

Screening method for GDM

Based on the guideline used in the authors' institution[19,20], a 2-step approach was used to screen for and diagnose GDM. The protocol was as follows:

During the first visit, a 50 g glucose challenge test (50 g GCT) was used for screening in each woman. The test was performed by loading 50 g of glucose orally, followed by determination of plasma glucose levels at 1 hour later. The result was considered abnormal if the plasma glucose level was 140 mg/dl or more. An oral glucose tolerance test (OGTT) was used to diagnose GDM only if the result of 50 g GCT was abnormal. Under fasting conditions, 100 g of glucose was loaded orally, followed by plasma glucose level determination at baseline and hourly for 3 hours. GDM was diagnosed when any 2 of 4 plasma glucose levels met or exceeded the value of 105, 190, 165, 145 mg/dl at baseline, 1st, 2nd, and 3rd hour respectively. When the diagnosis of GDM was made, the pregnant women were counseled and treated individually following the treatment guideline as appropriate. Those with normal test results would receive a similar test at 28 weeks of gestation and again at 32 weeks of gestation if the results were still normal.

Selection criteria

In the present study, all the pregnant women had to have their first visit to the antenatal clinic before 29 weeks of gestation. Cases excluded from the study were those in which the screening test for GDM was abnormal, or in which the pregnancy was complicated by preexisting chronic maternal illness (hypertension, diabetes mellitus, human immunodeficiency virus seropositivity, etc.), or in which the elective cesarean delivery was planned, or in which the multifetal gestation was presented. At the time of delivery, the cases of the non-cephalic presentation were also excluded from the present study. The authors restricted the analysis to the pregnant women whose certificate included height and pre-pregnancy weight.

Data collection

Six hundred and sixty pregnant women, who qualified for analysis during the study interval, were divided into two groups according to their pre-pregnancy body mass index (pre-pregnancy BMI). BMI was obtained by dividing weight in kilograms by height in meters squared. Women with pre-pregnancy BMI of 20-25 kg/m^2 were classified as the normal group and those with pre-pregnancy BMI of 27 kg/m^2 or more were in the overweight group. Those with pre-pregnancy BMI 25.1-26.9 kg/m^2 were not included in the present study because this range of BMI may affect the significance of the different outcomes between the overweight and normal groups. However, in the present study, the overweight group was not stratified to categories of overweight and obese, as the effect of the degree of being overweight on the pregnancy outcome was not addressed.

Data were collected from medical records and extracted data were entered into a computerized database for subsequent analysis. Maternal demography, pregnancy complications, mode of delivery, delivery complications, and neonatal birth weight and APGAR score were recorded.

Pre-eclampsia was defined as elevated blood pressure (systolic blood pressure 140 mmHg or greater,

Table 1. Clinical risks for gestational diabetes mellitus in Siriraj Hospital

1. Family history of diabetes mellitus
2. Maternal age of 30 years or more
3. History of macrosomic infant
4. History of congenital fetal anomaly
5. History of unexplained intrauterine fetal death
6. History of preeclampsia
7. Gestational diabetes mellitus in previous pregnancy
8. Obesity (BMI $\geq$ 27 kg/m^2)[20]

or diastolic blood pressure 90 mmHg or greater) at least 6 hours apart, with proteinuria (more than 300 mg/day), after 20 weeks of gestation[21]. Pre-term delivery was defined as delivery before 37 completed weeks. Macrosomia was defined as a birthweight of 4000 g or more[22]. Neonatal jaundice was defined only in cases that required phototherapy. Neonatal hypoglycemia was defined as the condition that intravenous glucose was needed during the first 48 hours of life.

Statistical analysis

All analyses were performed with the statistical program SPSS 13.0. Differences in the frequencies of events between patient-groups were used a Chi-square test, or Fisher's exact test when cases in individual cell numbered less than five. Odds ratio and their 95% confidence intervals were estimated. The student t-test was used for comparison of the mean between patient groups. Data were presented as mean $\pm$ standard deviation. A p-value of < 0.05 was considered to be statistically significant. The effect of pre-pregnancy BMI was analyzed by comparing the frequencies of various outcomes in both groups by multiple logistic regression analysis. Adjustments were made for the confounding factors, such as weight gain during pregnancy, and screening indicators for GDM that are shown in Table 1.

The present study was approved by the Ethical Committee on Human Rights related to Research involving Human Subjects from the authors' institution.

Results

Maternal characteristics are listed in Table 2. Between the overweight and normal weight groups, there was no significant difference in the average maternal age, residence, occupation, education, parity, and gestational age at the first visit and delivery. Maternal weight gain during pregnancy was 9.5 ± 4.92 kg in the overweight group versus 11.63 ± 4.95 kg in the normal weight group, with significant difference ($p < 0.001$).

Regarding the clinical risk factors for gestational diabetes mellitus, the overweight group was characterized by a lower frequency of family history of diabetes mellitus, maternal age at 30 years or more, but a higher frequency of history of macrosomia (as shown in Table 3).

Table 2. Maternal characteristics in 660 women with a normal glucose tolerance

Characteristics	Overweight (n = 330) N (%)	Normal (n = 330) N (%)	*p*-value
Maternal age (yr)	29.40 $\pm$ 5.93	29.68 $\pm$ 5.92	0.216
Residence			0.630
- Urban	202 (61.2)	209 (63.3)	
- Rural	128 (38.8)	121 (36.7)	
Occupation			0.137
- None	119 (36.1)	101 (30.6)	
- Employee	174 (52.7)	199 (60.3)	
- Merchant	35 (10.6)	30 (9.1)	
- Student	2 (0.6)	0 (0)	
Education			0.235
- None	13 (3.9)	5 (1.5)	
- Primary	165 (50.0)	161 (48.8)	
- High	127 (38.5)	140 (42.4)	
- University	25 (7.6)	24 (7.3)	
Nulliparous	154 (46.7)	154 (46.7)	1.000
GA at first ANC (wk)	15.84 $\pm$ 6.29	15.86 $\pm$ 6.33	0.961
GA at delivery (wk)	38.81 $\pm$ 1.64	38.74 $\pm$ 1.49	0.569
Weight gain (kg)	9.50 $\pm$ 4.92	11.63 $\pm$ 4.95	<0.001

average maternal age $\pm$ standard deviation
average gestational age at the first antenatal care $\pm$ standard deviation
average gestational age at delivery $\pm$ standard deviation
average weight gain during pregnancy $\pm$ standard deviation

The impact of pre-pregnancy BMI on maternal and neonatal outcomes is summarized in Table 4 and 5 respectively. The overweight group had a significantly higher incidence of pre-eclampsia, cesarean delivery, cephalopelvic disproportion, and macrosomia, whereas the rates of preterm delivery, low birthweight infant, neonatal jaundice and hypoglycemia were similar to the normal weight group. All neonates in the present study had APGAR scores at the 5th minute more than 7, so no complication of birth asphyxia occurred. After adjustment for other factors, an overweight condition was significantly associated

Table 3. Clinical risk factors for gestational diabetes mellitus (GDM)

Clinical risk factors	Overweight (n = 330) N (%)	Normal (n = 330) N (%)	*p*-value
Family history of DM	76 (23.0)	137 (41.5)	<0.001
Maternal age > 30 yr	172 (52.1)	209 (63.3)	0.005
History of macrosomia	10 (3.0)	2 (0.6)	0.041
History of GDM	1 (0.3)	0 (0.0)	1.000
History of preeclampsia	1 (0.3)	1 (0.3)	1.000

Table 4. The impact of weight on maternal outcomes in 660 women with normal glucose tolerance

Maternal outcomes	Overweight (n = 330) N (%)	Normal (n = 330) N (%)	Odds ratio	95%CI	*p*-value
Preeclampsia	74 (22.4)	17 (5.2)	4.35	2.63-7.21	<0.001
Preterm delivery	16 (4.8)	18 (5.5)	0.89	0.46-1.71	0.86
Cesarean delivery	130 (39.4)	86 (26.1)	1.51	1.21-1.89	<0.001
Cephalopelvic disproportion	105 (31.8)	63 (19.1)	1.67	1.27-2.19	0.001

Table 5. The impact of weight on neonatal outcomes in 660 women with normal glucose tolerance

Neonatal outcomes	Overweight (n = 330) N (%)	Normal (n = 330) N (%)	Odds ratio	95% CI	*p*-value
Macrosomia	25 (7.6)	3 (0.9)	8.33	2.54-27.33	<0.001
Low birthweight	12 (3.6)	21 (6.4)	0.57	0.29-1.14	0.15
Neonatal jaundice	17 (5.2)	18 (5.5)	0.94	0.50-1.80	1.000
Hypoglycemia	1 (0.3)	0 (0)			1.000

There was no case of hypoglycemia in the normal weight group, therefore, odds ratio and 95% confidence interval were undefined

Table 6. The impact of weight on maternal and neonatal outcomes in 660 women with normal glucose tolerance

	Overweight (n = 330) N (%)	Normal (n = 330) N(%)	Adjusted odds ratio	95% CI	*p*-value
Preeclampsia	74 (22.4)	17 (5.2)	3.87	2.09-7.25	<0.001
Cesarean delivery	130 (39.4)	86 (26.1)	2.22	1.45-3.39	<0.001
Cephalopelvic disproportion	105 (31.8)	63 (19.1)	2.15	1.35-3.42	0.001
Macrosomia	25 (7.6)	3 (0.9)	7.59	1.98-29.09	<0.001

Multiple logistic regression analysis

with pre-eclampsia, cesarean delivery, cephalopelvic disproportion, and macrosomia (Table 6).

Discussion

In the past, several studies addressed the influence of maternal pre-pregnancy body mass index (BMI) on pregnancy outcome[4-13]. Many pregnancy complications have been linked to obesity ranging from increased risk of gestational diabetes mellitus (GDM) and hypertension to increased risk of cesarean delivery and macrosomia[9-12]. The present study confirms that higher pre-pregnancy BMI is associated with a number of adverse pregnancy outcomes. However, the authors have shown that this relationship is independent of maternal glucose levels by selecting the pregnant women who had normal glucose tolerance. It could be argued that the normal-weight group did not represent the general population since all cases had at least one risk factor for GDM. These factors would theoretically increase the risk of complications. This bias will mean that if the whole population of pregnant women had been investigated, it seems to be that the risk of adverse outcome in overweight women would have increased even more, compared to the normal population.

In the authors' institution, the selective screening program for GDM has been recommended and reported to be a reasonable approach to identify the disease. Moreover, it has been reported to be more cost-effective than a universal screening program. Common risk factors for GDM previously reported from the authors' institution were maternal age of 30 years or more (69.1%), family history of DM (40.3%), and obesity (10.0%)[19]. The distribution of risk factors in the present study was comparable to the previous report. Therefore, it is reasonable that the prevalence of maternal age of 30 years or more and with a family history of DM in the normal-weight group were significantly more than those of the overweight group. In addition, possibly due to the small sample size of the present study, there are neither cases of a previous history of congenital fetal anomaly nor cases of a previous history of unexplained intrauterine fetal death.

Maternal weight gain, like pre-pregnancy BMI, has been associated with adverse pregnancy outcomes. The overweight women should restrict diet during pregnancy more than the normal weight women. Therefore, the guidelines recommended lower weight gains for women with higher BMI and higher weight gains for women who begin pregnancy with lower BMI[15]. As in the research by Edwards et al[23], the present study found that the overweight women gained less weight during pregnancy compared to the normal weight women. Pre-pregnancy BMI in the present study was calculated using maternal memory of pre-pregnancy weight, therefore weight gain revealed bias results. However, BMI is a better indicator of body composition than weight alone and no less predictive than weight alone for many other outcomes[24].

Reports on Confidential Enquiries into maternal deaths in the United Kingdom have shown that hypertensive complication remains among the most common causes of maternal death[25]. In a recent study, Erez et al reported that elevated pre-pregnancy BMI was a risk factor for the development of pre-eclampsia[26]. The presented data also revealed a higher frequency of hypertensive complication in the overweight group ($p < 0.001$). Sibai et al noted a significant difference in the incidence of pre-eclampsia for women with an early second trimester BMI < 20 kg/m^2 (4.3%) compared to those with a BMI score of 34 kg/m^2 or more (12.6%, $p < 0.001$)[27]. The mechanism is still unknown. Current hypothesis suggests that the pathophysiological changes may be insulin resistant and association with obesity-related cardiovascular risk is responsible for an increased incidence of pre-eclampsia in obese women[28]. A preliminary study was conducted to explore the relationship of polymorphism of the beta3-adrenergic receptor (beta-AR) gene and the risk of pre-eclampsia in the obese women. Further studies are needed to confirm these findings[29].

Pre-pregnancy BMI plays an important role in determining infant birth weight. Mathew et al[12], LaCoursiere et al[30] and Grossetti et al[31] showed that the obese gravida was at an increased risk for delivering a high birth weight infant, a conclusion in concert with the present findings. Obesity is associated with higher fasting plasma triglyceride levels and greater leucine turnover[32-34]. Triglycerides are energy rich and placental lipases can cleave triglycerides and transfer free fatty acids to the fetus[35]. The increased energy flux to the fetus may explain the increased frequency macrosomia seen in the overweight group.

Although macrosomia was more common in infants of the overweight group, the risk of neonatal jaundice and hypoglycemia did not increase. However, serious long-term consequences of macrosomia may develop later[36]. Murtaugh et al has reported that high birth weight is associated with insulin resistance and higher fat mass in adolescents[37].

In most studies, the cesarean section rate increased along with maternal BMI[4,38,39]. There are

several confounding variables increasing the cesarean section rate, such as abnormal presentation of the fetus and medical complications of pregnancy. Garbaciak et al found obese women at increased risk for delivery by cesarean section even in the absence of any pregnancy complications[40]. The presented data represented only glucose-tolerant women and even when women with abnormal fetal presentations or elective cesarean delivery were excluded from the analysis, there was a convincing impact of pre-pregnancy BMI on the cesarean rate. The increase in cesarean sections may have been a result of an increased rate of macrosomic infants leading to disproportion during labor, the uterine contractility may be suboptimal in the overweight women, or there may be increased fat deposition in the soft tissue of the pelvis. Determining the indication of the cesarean rate, the authors found that the most common indication was cephalopelvic disproportion, supporting a higher incidence of dysfunctional labor pattern among overweight women. The cesarean delivery in the overweight women is associated with numerous perioperative concerns, including anesthetic problems, infections, blood loss, and prolonged hospitalization[41-44]. The present study did not address the perioperative morbidity.

As in most previous studies, perinatal mortality has been zero and morbidity, determined by Apgar scores, has been very low without any differences related to pre-pregnancy BMI[45-47].

There is a trend towards substantial increases in BMI during the reproductive years. From the present study, the overweight women with normal glucose tolerance also represented a high-risk group, not only those with glucose intolerance. The early identification of individuals affected by high pre-pregnancy BMI and ongoing counseling, education, and intervention are essential to prevent adverse pregnancy outcomes. Moreover, further studies are needed to describe in detail the pathophysiological relationship between obesity and adverse pregnancy outcomes.

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ผลของน้ำหนักก่อนการตั้งครรภ์ต่อการคลอดและน้ำหนักทารกแรกเกิดในสตรีตั้งครรภ์ที่มีความเสี่ยงต่อการเกิดภาวะเบาหวานขณะตั้งครรภ์ซึ่งมีผลการตรวจคัดกรองโรคเบาหวานปกติในโรงพยาบาลศิริราช

นิศารัตน์ พิทักษ์วัชระ, วิทยา ถิฐาพันธ์

วัตถุประสงค์*: เพื่อเปรียบเทียบความสัมพันธ์ระหว่างน้ำหนักก่อนการตั้งครรภ์ต่อการคลอดและน้ำหนักทารกแรกเกิดในสตรีตั้งครรภ์ที่มีความเสี่ยงต่อการเกิดภาวะเบาหวานขณะตั้งครรภ์ซึ่งมีผลการตรวจคัดกรองโรคเบาหวานปกติ*

ชนิดของการวิจัย*: การวิจัยแบบ Retrospective Cohort*

วัสดุและวิธีการ*: ทบทวนเวชระเบียนของสตรีตั้งครรภ์ที่มีความเสี่ยงต่อการเกิดภาวะเบาหวานขณะตั้งครรภ์ (ซึ่งผลการตรวจคัดกรองภาวะเบาหวานขณะตั้งครรภ์ในสตรีตั้งครรภ์เหล่านี้เป็นปกติ) ที่มาฝากครรภ์และคลอดที่โรงพยาบาลศิริราช จำนวน 660 คน ในช่วงเวลาตั้งแต่ เดือน มกราคม พ.ศ. 2543 จนถึง เดือน ธันวาคม พ.ศ. 2548 สตรีทุกราย ที่นำมาศึกษา ต้องมีบันทึกน้ำหนักตัวก่อนตั้งครรภ์ในเวชระเบียนชัดเจน ถ้าไม่มีบันทึกไว้ก็คัดออกจากการศึกษา โดยแบ่งเป็น 2 กลุ่ม กลุ่มศึกษาได้แก่ สตรีตั้งครรภ์ที่มีค่าดรรชนีมวลกาย 27 กิโลกรัมต่อตารางเมตรขึ้นไป จำนวน 330 คน และกลุ่มควบคุมได้แก่สตรีตั้งครรภ์ที่มีค่าดรรชนีมวลกาย 20 ถึง 25 กิโลกรัมต่อตารางเมตร จำนวน 330 คน ทำการรวบรวมข้อมูลต่าง ๆ เกี่ยวกับ ข้อมูลทั่วไป ข้อมูลการคลอด ผลการคลอด และบันทึกข้อมูลในแบบบันทึกข้อมูลที่จัดทำขึ้น จากนั้นจึงนำข้อมูลที่ได้ไปวิเคราะห์*

ผลการศึกษา*: พบว่าเมื่อเทียบกับกลุ่มควบคุม ในกลุ่มศึกษามีอัตราการเกิดภาวะความดันโลหิตสูงขณะตั้งครรภ์สูงขึ้น (p น้อยกว่า 0.001) อัตราการผ่าตัดคลอดบุตรสูงขึ้น (p น้อยกว่า 0.001) อัตราของการที่ศีรษะทารกไม่ได้สัดส่วนกับอุ้งเชิงกรานสูงขึ้น (p เท่ากับ 0.001) และ อัตราของการที่ทารกมีน้ำหนักแรกเกิดตั้งแต่ 4,000 กรัมสูงขึ้น (p น้อยกว่า 0.001) อย่างมีนัยสำคัญทางสถิติ*

สรุป*: ในสตรีตั้งครรภ์ที่มีความเสี่ยงต่อการเกิดภาวะเบาหวานขณะตั้งครรภ์ แม้ว่าผลการตรวจคัดกรองภาวะเบาหวานขณะตั้งครรภ์จะเป็นปกติ สตรีตั้งครรภ์ที่น้ำหนักก่อนการตั้งครรภ์เกินมาตรฐานจะมีโอกาสเกิดภาวะความดันโลหิตสูงขณะตั้งครรภ์ การผ่าตัดคลอดบุตร ขนาดศีรษะทารกไม่ได้สัดส่วนกับอุ้งเชิงกราน รวมถึงน้ำหนักทารกแรกเกิดตั้งแต่ 4,000 กรัมขึ้นไป ได้มากกว่าสตรีตั้งครรภ์ที่มีน้ำหนักก่อนการตั้งครรภ์อยู่ในเกณฑ์ปกติ อย่างมีนัยสำคัญทางสถิติ*