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## Effects of pre-pregnancy body mass index and gestational weight gain on neonatal birth weight in women with gestational diabetes mellitus



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ARTICLEINFO	A B S T R A C T
<i>Keywords:</i> Gestational diabetes Body mass index Weight gain Birth weight Macrosomia	Aim: To study the impact of pre-pregnancy body mass index (BMI) and gestational weight gain (GWG) on neonatal birth weight in women with gestational diabetes mellitus (GDM). Methods: This was a prospective cohort study of 622 singleton pregnant women diagnosed with GDM recruited from 1 April 2014 and 30 December 2014 in a university teaching hospital in China. Binary logistic regression was used to analyze the factors influencing macrosomia. Results: Pre-pregnancy BMI categories were: underweight (10.6%), normal (65.6%), overweight (18.0%) and obese (5.8%). Mean GWG was $14.4 \pm 4.8$ kg and birth weight $3353.1 \pm 467.3$ g. The incidence of macrosomia was 7.8% and low birth weight 2.3%. Logistic regression analysis showed that pre-pregnancy BMI was not associated with macrosomia. However, excessive GWG was a risk factor for macrosomia (odds ratio (OR) 2.884, 95% confidence interval (CI) 1.385–6.004, p < 0.01). In addition, high maternal fasting plasma glucose (FPG) (OR 1.933, 95% CI 1.126–3.316) and serum triglyceride (TG) (OR 1.235, 95% CI 1.053–1.449) in the third trimester of pregnancy were risk factors for macrosomia. Conclusions: Patients with GDM can be advised that excessive GWG and uncontrolled hyperglycaemia influence their chances for macrosomia.

#### 1. Introduction

Obesity is one of the most important global health threats and obese women of reproductive age represent a clinically important subpopulation. A recent survey showed that the increasing prevalence of obesity and diabetes in women of reproductive age in developing countries could be associated with a parallel increase in macrosomic births [1]. In order to support optimal pregnancy outcomes, including an appropriate for gestational age birth weight, the American Institute of Medicine (IOM) re-examined guidelines for weight gain during pregnancy and made new recommendations for women according to their weight status, based on the World Health Organization (WHO) body mass index (BMI) categories [2]. In addition, the Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study demonstrated a continuous relationship between maternal glucose levels and the risk of adverse pregnancy outcomes, and issued new diagnostic guidelines for hyperglycemia during pregnancy [3], increasing further the number of women who can be defined as having gestational diabetes mellitus (GDM).

Great concerns were raised in China regarding the control of

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maternal weight gain and plasma glucose after the publication of these two international recommendations. Although it is well established that both pre-pregnancy BMI and gestational weight gain (GWG) are independent determinants of birth weight in women [4], few studies have specifically evaluated their associations in women with GDM. However, because GDM is also a known risk factor for macrosomia, it is difficult to differentiate the specific impacts of pre-pregnancy BMI, GWG and GDM on birth weight [5]. Moreover, associations between maternal glucose and lipid levels and fetal growth have been identified, and these could also be influenced by GDM, maternal BMI and GWG [6, 7]. Therefore, the aims of this study were to evaluate the relationships between pre-pregnancy BMI, GWG, plasma glucose and serum lipids in Chinese women with GDM, and their association with birth weight.

#### 2. Methods

#### 2.1. Research design and study population

A prospective cohort study of pregnant women diagnosed with GDM in the Obstetrics and Gynecology Hospital of Fudan University,

Shanghai, China, was undertaken between 1 April 2014 and 30 December 2014. Women were eligible if they: 1) had registered and attended their first prenatal care session for a live singleton neonate at < 20 weeks' gestation; 2) planned to give birth in the study hospital; 3) were diagnosed with GDM between 24 and 28 weeks' gestation, based on the International Association of Diabetes in Pregnancy Study Groups (IADPSG) guidelines; 4) received care from diabetes nurses after diagnosis of GDM; and 5) were able to give written consent to participate.

The care offered included instructions regarding diet and physical exercise. Patients performed self-monitoring of blood glucose and additional insulin was given based principally on maternal glucose levels. Women were excluded from the study if they had hypertension or pre-GDM through their medical history. Women whose fasting plasma glucose (FPG)  $\geq$  7.0 mmol/L and/or glycated hemoglobin (HbA<sub>1c</sub>)  $\geq$  6.5% at their first prenatal visit would be also regarded as pre-existing diabetes [8] and excluded. The study was approved by the Research Committee of the Obstetrics and Gynecology Hospital Fudan University, and written consent was obtained from all participants.

#### 2.2. Questionnaire data

Maternal sociodemographic characteristics, parity, medical history, lifestyle and dietary habits were collected through interviewer-administered questionnaires at the patients' first GDM clinic care visit by a diabetes nurse. Clinical information was also collected retrospectively by reviewing patients' medical records. All of the data were collected and checked by specifically trained medical staff.

#### 2.3. Measures of pre-pregnancy BMI and GWG

Pre-pregnancy BMI was calculated from self-reported pre-pregnancy weight and height measured at the first prenatal visit. Women were placed into four groups according to their BMI (Chinese categories): underweight (BMI <  $18.5 \text{ kg/m}^2$ ), normal weight (BMI  $18.5-23.9 \text{ kg/m}^2$ ), overweight (BMI  $24.0-27.9 \text{ kg/m}^2$ ) or obese (BMI  $\ge 28.0 \text{ kg/m}^2$ ) [9]. GWG was defined as the difference between the maternal weight recorded for each woman at the delivery unit and their pre-pregnancy weight. Women with a GWG within the IOM-recommended range were categorized as having adequate GWG, while women with a GWG below this were categorized as having excessive GWG. A previous study showed that maternal body weight status and GWG categorized in this way was slightly more effective for the assessment of predicted probabilities and observed responses than the WHO BMI categories [5].

#### 2.4. Maternal glucose and lipid measurements

Maternal blood samples were scheduled to be taken at the women' first antenatal visit between 11 and 16 weeks of gestation, and between 34 and 40 weeks of gestation as routine antenatal examinations. Fasting plasma glucose and serum lipids (TGs and cholesterol) were measured in the morning following an overnight fast.

#### 2.5. Obstetric and neonatal outcomes

Details of birth outcomes were obtained from birth certificates or medical records. Large for gestational age (LGA) was defined as birth weight greater than the 90th percentile for gestational age based on Chinese national birth weight data [10]. Fetal macrosomia was defined as a birth weight of  $\geq$  4000 g, irrespective of gestational age. Low birth weight was defined as < 2500 g and gestational week was calculated from the first day of the woman's last menstrual period (LMP). Term was calculated from the date of the LMP or ultrasound term was used when no LMP date was available. Birth weight was measured with calibrated electronic scales immediately after birth.

#### 2.6. Statistical analysis

Women were placed into one of four mutually exclusive pre-pregnancy BMI groups: 1) low weight, 2) normal weight, 3) overweight and 4) obese. Maternal demographics, anthropometric characteristics, clinical, obstetrical and neonatal outcomes, were assessed according to BMI group. Associations between categorical variables and BMI group were evaluated using the chi-square test. Differences among continuous variables were assessed using the ANOVA F test or Kruskal-Wallis test (in the case on nonnormal distribution), according to BMI group. Post hoc testing was performed using the Bonferroni multiple comparison procedure to correct significance levels for detecting which groups differed statistically. A binary logistic regression that was adjusted for potential confounders was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs), to identify risk factors associated with macrosomia. Maternal age, parity, gestational age, insulin administration and infants' sex were regarded as potential confounding factors and were included as covariates in the adjusted analyses. The reference categories were normal pre-pregnancy BMI, in accordance with the Chinese cut-offs, or GWG within the guidelines, as defined above. In our study, the low incidence rate of small for gestational age births (SGA) made it impossible to identify risk factors for SGA using a binary logistic regression. Therefore, to explore the association between GWG and SGA, we also placed women into three groups based on their GWG and used the chi-square test to analyze these. Statistical significance was established with p < 0.05. Data were analyzed using the SPSS software package (version 18.0; SPSS Inc., Chicago, IL, USA).

#### 3. Results

#### 3.1. Description of the study population

Six hundred and twenty-two women were originally included in the study. Twelve women were excluded because of incomplete data and nine who had not given birth in the study hospital were excluded, leaving a total of 601 women and their offspring. The general characteristics of the study population based on maternal pre-pregnancy BMI are shown in (Table 1). Maternal age was 30.5  $\pm$  3.4 years and 504 (83.9%) were nulliparous. The median (interquartile range) BMI was 21.7 (19.7-23.9) kg/m<sup>2</sup>. Of the 601 eligible women, 64 (10.6%) were underweight, 394 (65.6%) were of normal weight, 108 (18.0%) were overweight and 35 (5.8%) were obese, based on their pre-pregnancy BMI (Chinese categories). GWG was 14.4  $\pm$  4.8 kg in the whole and  $14.5 \pm 4.4$ ,  $15.0 \pm 4.5$ ,  $12.9 \pm 5.8$ population and  $12.4 \pm 4.0 \text{ kg}$  for underweight, normal-weight, overweight and obese pregnant women, respectively (Chinese BMI categories). Compared with the IOM recommendations for total weight gain, only 44.4% of women with GDM had a GWG that was within the recommended range. The incidences of macrosomia and low birth weight were 7.8% and 2.3%, respectively.

## 3.2. Pre-pregnancy BMI, GWG and their associations with neonatal birth weight

By chi-square test, both pre-pregnancy BMI and GWG had statistically significant effects on the chances of delivering a macrosomic infant, but neither maternal pre-pregnancy BMI nor GWG were significantly associated with delivery of low birth weight infants (Tables 2 and 3). Logistic regression analysis showed, after controlling for potential confounding factors, that pre-pregnancy BMI was not significantly associated with macrosomia. In contrast, excessive GWG was a risk factor for macrosomia (odds ratio (OR) 2.884, 95% confidence interval (CI) 1.385–6.004, p < 0.01). In addition, maternal fasting plasma glucose (FPG) (OR 1.933, 95% CI 1.126–3.316) and maternal serum triglyceride (TG) levels (OR 1.235, 95% CI 1.053–1.449) in the third trimester of pregnancy were risk factors for macrosomia (Table 4).

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