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Original article

Greater early and mid-pregnancy gestational weight gain are associated with increased risk of gestational diabetes mellitus: A prospective cohort study

Chunrong Zhong [a], Xiating Li [a], Renjuan Chen [a], Xuezhen Zhou [a], Chaoqun Liu [a], Jiangyue Wu [a], Shangzhi Xu [a], Weiye Wang [b], Mei Xiao [c], Guoping Xiong [d], Jing Wang [e], Xuefeng Yang [a], Liping Hao [a], Nianhong Yang [a, *]

[a] *Department of Nutrition and Food Hygiene, Hubei Key Laboratory of Food Nutrition and Safety, MOE Key Laboratory of Environment and Health, School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, China*
[b] *Department of Epidemiology and Biostatistics, School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, China*
[c] *Hubei Maternal and Child Health Hospital, China*
[d] *The Central Hospital of Wuhan, China*
[e] *Jiang'an Maternal and Child Health Hospital, China*

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SUMMARY

Background & aims: Gestational diabetes mellitus is associated with adverse short- and long-term consequences for both the mother and the offspring. To examine the relationship between the rates of gestational weight gain (RGWG) during early and mid-pregnancy and the risk of gestational diabetes mellitus (GDM).
Methods: 2090 singleton pregnant women from the Tongji Maternal and Child Health Cohort (TMCHC) without overt diabetes before pregnancy were analyzed in our study. Gestational weight were measured regularly in every antenatal visit. Gestational diabetes mellitus was assessed with the 75-g, 2-h oral glucose tolerance test at 24–28 weeks of gestation. Multivariable logistic regression was performed to estimate effect of RGWG on GDM.
Results: A total of 8.3% (n = 173) of pregnant women were diagnosed with GDM. Women with elevated rate of gestational weight gain prior to glucose screening test (RGWG-PG) increased the risk of GDM (adjusted *p*-trend = 0.004; odds ratios (OR) 1.64, 95% confidence intervals (CI) 1.01–2.68 and OR 2.30,95% CI 1.44–3.66 for 0.297–0.384 kg/wk and 0.385 kg/wk or more vs. 0.213 kg/wk or less, respectively). Women with greater rate of gestational weight gain in the first trimester (RGWG-F) increased the risk of GDM (adjusted *p*-trend = 0.048; OR 1.83, 95% CI 1.14–2.94 and OR 1.76, 95% CI 1.10–2.83 for 0.086–0.200 kg/wk and 0.201 kg/wk or more vs. −0.025 kg/wk or less, respectively). The rate of gestational weight gain in the second trimester (RGWG-S) was significantly associated with GDM only among women with RGWG-F more than 0.086 kg/wk (adjusted *p*-trend = 0.035; OR 2.04, 95% CI 1.16–3.59 for 0.658 kg/wk or more vs. 0.418 kg/wk or less).
Conclusions: Greater early pregnancy weight gain are associated with increased risk of GDM. Elevated weight gain in mid-pregnancy increased the risk of GDM only among pregnant women with greater weight gain in the first trimester.

1. Introduction

Gestational diabetes mellitus is classified as glucose intolerance of varying degrees of severity with onset or first recognition during pregnancy [1]. Gestational diabetes mellitus is associated with an increased risk of macrosomia, neonatal hypoglycemia, and cesarean

* Corresponding author. Department of Nutrition and Food Hygiene, Hubei Key Laboratory of Food Nutrition and Safety, MOE Key Laboratory of Environment and Health, School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, 13 Hangkong Road, Wuhan, Hubei, 430030, China.
E-mail address: zynh@mails.tjmu.edu.cn (N. Yang).

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delivery [2]. Both the mothers with GDM and their offsprings are at elevated risk of future development of type 2 diabetes mellitus and abnormal metabolic function [3–5].

Previous studies suggested that excessive gestational weight gain (GWG) is associated with adverse maternal and neonatal outcomes [6,7], maternal postpartum weight retention [8] and offspring obesity [9,10]. Excessive GWG may result in maternal fat deposition, which may decrease insulin sensitivity. It is biologically plausible that GWG is positively associated with GDM. However, due to the therapeutic intervention, weight gain of women with GDM in their third trimesters were significantly less than women with normal glucose levels. [11], and reverse causation was found when assessed the relationship between total GWG and the development of GDM [12,13]. Several recent studies have examined the association between GWG prior to GDM screening test and the risk of GDM, but the reported data were not consistent. Several case–control studies found that elevated GWG before the glucose screening test, particularly in early pregnancy was associated with the risk of GDM, but GWG in the second trimester [11,14–17] was not, while other studies found that there was a relationship between GWG in the second trimester and the risk of GDM [18,19]. Furthermore, one cohort study found that higher GWG before GDM screening was only associated with glucose intolerance in pregnancy but not the risk of GDM [20]. Hence, it remains unclear whether greater overall or trimester-specific GWG prior to glucose screening are associated with an elevated risk of GDM.

To address this question, we conducted a large-scale prospective cohort study to examine the association between the rates of weight gain during early and mid-pregnancy and GDM.

2. Materials and methods

2.1. Study population and design

This study was part of the TMCHC study, which is a multicenter, population-based, prospective cohort study designed to examine maternal dietary and lifestyle effects on the outcomes of mother-infant pairs in Wuhan, China. Women receiving their first prenatal care prior to 16 weeks of gestation during September 2013 to May 2016 eligible for the study were invited to join the cohort.

All participants had completed a questionnaire about maternal demographics, parity, last menstrual period, and family history of diabetes, pre-pregnancy smoking and drinking habits, sleep quality during early pregnancy, physical activity in pre-pregnancy and early pregnancy, and pre-gravid weight at enrollment. Meanwhile, each participant's height and weight was accurately measured by our trained staffs. Bodyweight were measured regularly in every following antenatal examinations and the physical activity in the second trimester was questioned. The 75-g, 2-h oral glucose tolerance test was conducted at 24–28 weeks of gestation. The diagnosis of GDM was made according to the criteria of the American Diabetes Association [21] when any of the following plasma glucose values were exceeded: fasting: ≥5.1 mmol/L (92 mg/dl), 1 h: ≥10.0 mmol/L (180 mg/dl), 2 h: ≥8.5 mmol/L (153 mg/dl). 2090 singleton pregnancies without pre-gestational diabetes and with weight measurement at 13 ± 2 and 24 ± 2 weeks of gestation were included in this study. All participants provided written informed consent when recruited to the TMCHC project. This study was approved by the ethics review committee of Tongji Medical College of Huazhong University of Science and Technology in China.

2.2. Gestational weight gain

The trimester-specific rates of gestational weight gain were calculated as follows: RGWG-PG = (the measured weight at 24 ± 2 weeks of gestation - pre-pregnancy weight)/gestational weeks at the measurement; RGWG-F = (the weight at 13 ± 2 weeks of gestation - pre-pregnancy weight)/weeks of gestation; RGWG-S = (measured weight at 24 ± 2 weeks − measured weight at 13 ± 2 weeks)/weeks between the two measurements.

The weight gain at 24 ± 2 weeks of gestation was classified by the cut-offs of Institute of Medicine (IOM) recommendations [7] into three groups: below, within, and above the IOM recommendations. The cut-offs were determined by subtracting 13 weeks from the 24 ± 2 weeks of gestation and multiplied the recommended second-trimester weight gain per week for each pre-pregnancy BMI category,and then adding to the recommended first-trimester weight gain.

2.3. Assessment of covariates

On the basis of self-reported pre-pregnancy weight and height measured at the first visit, pre-pregnancy BMI was calculated using self-reported pre-pregnancy weight (in kilograms) divided by the maternal height (in meters squared) and was categorized as underweight (BMI < 18.5), normal weight (18.8 ≤ BMI < 24.0), overweight (24.0 ≤ BMI < 28.0), or obese (BMI ≥ 28.0) [22]. Owing to the descriptive similarities and small numbers, overweight and obese women were combined in the analysis. A validation study was performed to assess the relationship between self-reported pre-gravid weight and the measured weight within 8 weeks of the last menstrual period, and found that the intraclass correlation coefficient between the two weights was 0.96.

According to the number of completed schooling years, educational level was classified as ≤12, 13–15, and ≥16 years. Maternal sleep quality during early pregnancy was categorized as never, occasionally (1–3 times a month), sometimes (1–2 times a week) and frequently insomnia (more than 3 times a week). Poor sleep quality was regarded to affect those participants who self-reported frequently insomnia. Alcohol consumers were those who drank more than three times a week before pregnancy. Smokers were those who consumed tobacco in pre-pregnancy. Passive smoker were defined as those breathing secondhand smoke for more than 30 min a day before pregnancy. Gestational age was calculated based on the earliest ultrasonography obtained.

2.4. Statistical analysis

Data were expressed as frequency (n) and percentages (%) or means and standard deviations (SD). χ^2 analysis and independent samples T test were used to analyze the relationships between variables. Multivariable logistic regression was used to assess the relationship between the rates of weight gain and GDM, adjusting for the following confounding variables: maternal age, pre-pregnancy BMI, family history of diabetes and poor sleep quality in early pregnancy. Adjusting for ethnicity, education, parity, smoking before pregnancy, drinking habits before pregnancy, and physical activity before pregnancy and during pregnancy did not result in material changes in the magnitudes of the observed associations between RGWG and GDM; therefore, we did not include these variables in the final models. We categorized participants into quartiles on account of the distribution of the rate of weight gain in the women. Women in the first quartile of the distribution of rate of gestational weight gain were used as the reference group. To understand the interactive effects of RGWG-F and RGWG-S to GDM, we divided women into two groups (low group, high group) based on the median of RGWG-F, then stratified analysis was conducted to examine the association between the RGWG-S (classified into four quartiles) and the risk of GDM in groups of RGWG-F. OR and 95% CI