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Excessive Early Gestational Weight Gain And Risk of Gestational Diabetes Mellitus in Nulliparous Women

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Abstract

Objective—To estimate whether there is an association between excessive early gestational weight gain and the development of gestational diabetes mellitus (GDM) and excessive fetal growth.

Methods—This is a secondary analysis of a randomized controlled trial of vitamins C and E in nulliparous low-risk women. Maternal weight gain from prepregnancy (self-reported) to 15–18 weeks of gestation was measured, and expected gestational weight gain was determined using the Institute of Medicine (IOM) 2009 guidelines for each prepregnancy body mass index (BMI) category. Excessive early gestational weight gain was defined as gestational weight gain greater than the upper range of the IOM guidelines. Rates of GDM, birth weight greater than 4000g, and large for gestational age ([LGA], birth weight 90th percentile or higher) were calculated and compared between women with excessive early gestational weight gain and early nonexcessive gestational weight gain (within or below IOM guidelines).

*For a list of other members of the NICHD MFMU, see the Appendix online at http://links.lww.com/xxx.

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Results—A total of 7,985 women were studied. Excessive early gestational weight gain occurred in 47.5% of women. Ninety-three percent of women with excessive early gestational weight gain had total gestational weight gain greater than IOM guidelines. In contrast, only 55% of women with nonexcessive early gestational weight gain had total gestational weight gain greater than IOM guidelines ($p<0.001$). Rates of GDM, LGA, and birth weight greater than 4000 grams were higher in women with excessive early gestational weight gain.

Conclusions—In our population, excessive early gestational weight gain occurred in 93% of women who had total gestational weight gain greater than the IOM guidelines. In low-risk nulliparous women, excessive early gestational weight gain is associated with the development of GDM and excessive fetal growth.

Background

Gestational weight gain (GWG) occurs due to an increase in maternal body fat and water and consists of 30% maternal fat accumulation. Maternal weight gain varies by trimester but early in pregnancy is disproportionately fat. The second half of pregnancy is characterized by progressive insulin resistance(1, 2), and maternal fat accumulation appears to influence subsequent maternal insulin resistance.(2) The pattern of GWG is higher in the second trimester at a rate of 0.563 kg per week and birthweight is strongly correlated with weight gain during that period.(3)

Abnormal or excessive GWG is a strong predictor of pregnancy and long-term health outcomes for both women and infants. Herring et al in 2009 reported that the higher the GWG, the higher the odds of developing abnormal glucose tolerance in the third trimester of pregnancy (OR 2.14, 95% CI 1.04–4.42).(4) Maternal obesity and postpartum weight retention (PPWR) have also been linked to excessive GWG.(5) In addition to these maternal outcomes, excessive GWG has been associated with large for gestational age (LGA) babies and excessive neonatal and infant weight.(6–8) Margerison et al in 2010 using data from 4,496 births in the National Longitudinal Survey of Youth 1979 described the association between GWG and increased rates of LGA, cesarean delivery and PPWR as well as childhood overweight.(9) In the report, 40% of women with excessive GWG retained greater than 2.5 kg from 12 to 24 months after delivery and 29% of the children had a BMI greater than the 85th percentile. In addition, PPWR is a strong predictor of maternal overweight and obesity a decade or more after the birth.(10, 11)

Previous studies have suggested that excessive early GWG might be associated with an early increase in insulin resistance leading to exhaustion of the pancreatic B cell. This B cell depletion could reduce the capacity to compensate for the increasing insulin resistance of pregnancy, and therefore lead to hyperinsulinemia, maternal hyperglycemia and excessive fetal growth.(2, 4, 12–14)

Identifying excessive GWG early in gestation could allow the opportunity to intervene at an earlier gestational age with behavioral modifications such as nutrition and exercise counseling, potentially decreasing the rate of adverse maternal and neonatal outcomes. Our objective is to estimate the relationship between excessive early GWG and gestational diabetes (GDM) as well as excessive fetal growth.

Materials and Methods

This study is a secondary analysis of the NICHD Maternal–Fetal Medicine Units Network randomized clinical trial of vitamin C and vitamin E to prevent complications of pregnancy hypertension in nulliparous low-risk women. The study was conducted at 16 clinical centers between 2003 and 2008. Full details of the study design and primary results have been

previously described.(15) In brief, nulliparous women between 9 and 16 weeks gestation were randomized to receive vitamin C (1,000 mg) and vitamin E (400 IU) versus placebo to estimate if antioxidant supplementation early in pregnancy prevented preeclampsia in a low-risk population.

For this analysis, women were included if their height and self-reported pre-pregnancy weight were recorded, and weight measurements were available between 15–18 weeks of gestation (to assess early weight gain) and within the 2 weeks prior to delivery (to assess total weight gain). Women were excluded from this secondary analysis if they delivered prior to 20 weeks, died prior to delivery, had an elective or spontaneous abortion, or their infant was found to have a major congenital malformation. Excessive early GWG was defined as GWG greater than the upper range of IOM 2009 guidelines for each pre-pregnancy body mass index (BMI) category (underweight, normal weight, overweight, and obese).(3) Specifically, the cutoff for excessive early GWG was determined by adding a first trimester weight gain of 4.4 pounds plus second trimester weight gain per week of 1.3 pounds for underweight, 1.0 pounds for normal weight, 0.7 pounds for overweight, and 0.6 pounds for obese women.(3)

Outcomes included gestational diabetes, birthweight greater than 4,000 grams and large for gestational age (LGA). LGA was defined as a birth weight at or above the 90th percentile using customized growth centiles.(16) Rates were calculated and compared between women with excessive early GWG and early GWG within or below IOM guidelines. Categorical variables were compared using the chi-square test and continuous variables using the Wilcoxon rank-sum test. Multivariable logistic regression was used to assess the relationship between excessive early GWG and study outcomes, adjusting for the following variables selected a priori: maternal age, race, smoking and treatment group (vitamins versus placebo). Odds ratios and 95% confidence intervals were reported. A p value < 0.05 was considered statistically significant. Analyses were performed using SAS software (Cary, NC). This study was approved by the institutional review boards at the University of Texas Health Science Center at Houston and Children's Memorial Hermann Hospital.

Results

Of the 10,154 women who were randomized in the original trial, outcome data were available on 9,969 women. Of these, 1,984 were excluded, the majority for missing weight measurements at either pre-pregnancy, 15–18 weeks' gestation or within 2 weeks of delivery. . The demographic and clinical characteristics of the 7,985 women are summarized in Table 1. The patient population had a high proportion of African Americans (23.9%) and Hispanics (29.8%), and 38% of the patients had governmental insurance.

Overall, 47.5% of women enrolled in the study had excessive early GWG. Forty-five percent of women with an underweight pre-pregnancy BMI had excessive early GWG as well as 46% of normal weight, 54% of overweight and 45% of obese women. Weight gain from pre-pregnancy to 15–18 weeks was higher in women with excessive early GWG compared with women with early non-excessive GWG (median lbs [25^{th}–75^{th} percentile], 12 [9–17] vs 2 [−2–5], $p<0.001$). The relationship between excessive early GWG and total GWG according to IOM guidelines is shown in Table 2. Ninety-three percent of women with excessive early GWG had total GWG greater than IOM guidelines and 55% of women with early non-excessive GWG had total GWG greater than IOM guidelines ($p < 0.001$). Total weight gain was higher in women with excessive early GWG compared with women with early non-excessive GWG (median lbs [25^{th}–75^{th} percentile], 43 [35–52] vs 29 [21–36], $p<0.001$). The sensitivity and specificity of excessive early GWG as a predictor of total

weight gain greater than IOM guidelines are 60% (95% CI 59–61%) and 87% (95% CI 85–88%).

Table 3 shows the relationship between excessive early GWG and study outcomes for all women combined and then separately by pre-pregnancy BMI category. The prevalence of GDM in women with excessive early GWG was 4%. The sensitivity of excessive early GWG to predict GDM was 59% (95% CI 53–65%), and the specificity was 53% (95% CI 52–54%).

The prevalence of LGA babies in women with excessive early GWG was 12%. Excessive early GWG had a sensitivity of 54% (95% CI 51–58%) and specificity of 53% (95% CI 52–54%) to predict LGA babies.

After adjusting for maternal age, smoking, race and treatment group (vitamins versus placebo), the odds of developing GDM were 43% higher in the excessive early GWG group [Adjusted OR 1.4 (95% CI 1.1–1.9)], the odds of delivering a LGA baby were 40% higher [Adjusted OR 1.4 (95% CI 1.2–1.6)] and the odds of having a baby with birthweight greater than 4,000 grams were 51% higher [Adjusted OR 1.5 (95% CI 1.3–1.8)]. In overweight women, excessive early GWG was not associated with a significant increase in the odds of developing GDM [Adjusted OR 1.6 (95% CI 1.0–2.6), p = 0.06]; however, it was associated with a significant increase in the odds of delivering a LGA baby [Adjusted OR 1.4 (95% CI 1.1–1.9), p = 0.02]. Obese women did not demonstrate a difference between excessive early GWG and early non-excessive GWG with regard to rates of GDM, birthweight greater than 4,000 grams, or delivery of an LGA baby.

Table 4 shows the obstetrical outcomes in the different study groups. Labor was induced in 39% of the patients with excessive early GWG compared with 34% of women without excessive early GWG (OR 1.2, 95% CI 1.1–1.3). The most common primary indications for labor induction were post term induction (25%), preeclampsia/hypertension (25%), elective induction (14%), premature rupture of membranes (13%), oligohydramnios (9%) and abnormal fetal testing (5%). Women with excessive early GWG also had an increased risk of cesarean delivery compared with women that did not have excessive early GWG (28% vs 22%, OR 1.3, 95% CI 1.2–1.5). Mean birthweight also was higher in women with excessive early GWG compared with women that did not have excessive early GWG ($p<0.001$).

Discussion

In 2009, the U.S. Institute of Medicine (IOM) published revised guidelines for gestational weight gain. The goal of these guidelines is to optimize both maternal and child outcomes, and to decrease the rates of both maternal postpartum and childhood obesity.(17) These guidelines do not specifically address the timing of excessive weight gain during the pregnancy (early vs. late).

In this study, 48% of the women enrolled had excessive early GWG and 73% had a total weight gain greater than the 2009 IOM recommendations. We found that 93% of women with excessive early GWG ultimately had total weight gain during the pregnancy that was greater than the 2009 IOM recommendations.

Excessive early GWG was found to have a sensitivity of 60% and specificity of 87% for total pregnancy weight gain greater than 2009 IOM guidelines. Early prediction of excess GWG could allow targeting of these women with behavioral and lifestyle modifications potentially leading to a decrease in total GWG.

The prevalence of GDM in our population was 4%, and excessive early GWG had a sensitivity of 59% and specificity of 53% for development of GDM. After adjusting for maternal age, smoking, race and treatment group (vitamins versus placebo), the rates of GDM [OR 1.4 (95% CI 1.1–1.9)], LGA [OR 1.4 (95% CI 1.2–1.6)] and birth weight greater than 4,000 grams [OR 1.5 (95% CI 1.3–1.8)] were higher in women with excessive early GWG compared with women with early non-excessive GWG. The strongest impact of excessive early GWG was observed in women with a normal pre-pregnancy BMI. We speculate that normal weight women with excessive early GWG have a higher increase in the risk of developing GDM, LGA babies and birthweight greater than 4,000 grams when compared with overweight or obese women because those patients with a higher pre-pregnancy BMI already have metabolic derangements and are therefore less impacted by excessive weight gain.

We found 40% greater odds of delivering a LGA baby [Adjusted OR 1.4 (95% CI 1.1–1.9), p = 0.02] for overweight women with excessive early GWG. Various prior studies have demonstrated an association between increase in weight gain up to 20 weeks gestation and increased birthweight. Muscati et al in 1996 found that for each 1 kg increase in weight gain up to gestational week 20, birthweight increased by 22 grams.(13) Brown et al found that weight gain during the first trimester was associated with a 31 gram increase in birthweight per kg of maternal gestational weight gain.(14) Another study found that for each kilogram gained by the mother in the first trimester there was a statistically significant increase in fetal birth weight of 18 grams.(18)

Hedderson et al in 2010 reported similar findings to our study. In a nested case control study of 345 women with GDM they found an 82% increase in the odds of developing GDM (OR 1.82, 95% CI 1.24–2.70) if the rate of weight gain in the first trimester was between 0.27 and 1.9 kg/week(2).

Our study differs from Herring et al in 2009 that found in a prospective cohort of 1,960 women, a non-significant association between a high rate of weight gain < 13 weeks gestation but low mid-pregnancy weight gain and the risk of developing GDM (OR 1.70, 95% CI 0.98 – 2.94). Similar results were observed in the group that had a high rate of weight gain < 13 weeks gestation and high mid-pregnancy weight gain (OR 1.19, 95% CI 0.64–2.21).(4) We did not take into account the rate of weight gain after 18 weeks gestation.

This design is not without limitations and among them is that 20% of the women were excluded from the analysis for missing weight measurements at either pre-pregnancy, 15 to 18 weeks' gestation or within 2 weeks of delivery. The baseline demographic characteristics were different between the women included and the women excluded from the analysis. Also, the use of self-reported pre-pregnancy weight to determine GWG could result in under or overestimating the associations found in this study(19). In addition, the gestational age cutoff of 15 to 18 weeks gestation was selected because it coincided with the study visit, but this cutoff could potentially exclude women who had excessive GWG after this period and before the end of the second trimester of pregnancy. Strengths of our study include the use of prospectively collected data in 7,985 nulliparous women who enrolled in the original multicenter randomized clinical trial at < 17 weeks gestation and the biologic plausibility of a stronger association between GWG during the first trimester and the risk of GDM(20). In addition, patient enrollment from 16 different geographical locations makes our findings more generalizable to different populations.

A benefit of early identification of excess gestational weight gain would be the opportunity for intervention early in pregnancy. Lifestyle modification and education trials have been conducted during pregnancy with the aim of affecting gestational weight gain and pregnancy

outcome. Pregnancy has been proposed to be the ideal time to introduce lifestyle modification strategies, given high maternal motivation to improving her infant's health. (21–23) Streuling et al performed a meta-analysis of 12 trials using physical activity in pregnancy as the intervention arm, and found a mean difference of GWG of −0.61 (95% CI: −1.17, −0.06) between the physical activity group and the control group. (24)

In conclusion, excessive early GWG is associated with adverse pregnancy outcomes including GDM, cesarean delivery and LGA. In particular, the largest effect of excessive early GWG was found in women with a normal pre pregnancy BMI. Further study is needed to determine the efficacy of targeted interventions including behavioral modifications in this group to maintain GWG within the IOM guidelines and ideally decrease GDM and LGA.

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Table 1

Clinical Characteristics of the Study Population

Characteristic	Excessive Early Gestational Weight Gain (n=3,796)	Nonexcessive Early Gestational Weight Gain (n=4,189)	*P*
Maternal age (years)	24.2 ± 5.3	23.1 ± 5.0	<0.001
Race			<0.001
Caucasian	1,797 (47.3)	1,749 (41.8)	
African American	929 (24.5)	983 (23.5)	
Hispanic	997 (26.3)	1,379 (32.9)	
Other	73 (1.9)	78 (1.9)	
Smoker	690 (18.2)	519 (12.4)	<0.001
Treatment group			0.045
Vitamins	1,963 (51.7)	2,072 (49.5)	
Placebo	1,833 (48.3)	2,117 (50.5)	
Gestational age at enrollment (weeks)	13.3 ± 2.1	13.5 ± 2.1	<0.001
Prepregnancy BMI			<0.001
Underweight (Lower than 18.5)	169 (4.5)	206 (4.9)	
Normal weight (18.5–24.9)	1,997 (52.6)	2,367 (56.5)	
Overweight (25.0–29.9)	1,008 (26.6)	857 (20.5)	
Obese (30 or higher)	622 (16.4)	759 (18.1)	
Private insurance	1,538 (40.5)	1,519 (36.3)	<0.001
Previous pregnancy before 20 weeks	951 (25.1)	858 (20.5)	<0.001

Data are n(%) or mean ± standard deviation.

BMI; body mass index.

Table 2

Relationship Between Excessive Early Gestational Weight Gain and Total Gestational Weight Gain According to Institute of Medicine Guidelines*

	Total Gestational Weight GainAbove IOM	Total Gestational Weight Gain Within IOM	Total Gestational Weight GainBelow IOM	Total
Excessive early gestational weight gain	3,512 (92.5)	242 (6.4)	42 (1.1)	3,796
Nonexcessive early gestational weight gain	2,319 (55.4)	1,146 (27.4)	724 (17.3)	4,189
Total	5,831	1,388	766	7,985

Data re n(%).

IOM, Institute of Medicine.

* p<0.001.

Table 3

Perinatal Outcomes for Nulliparous Women With and Without Excessive Early Gestational Weight Gain by Prepregnancy Body Mass Index Category

Outcome	Prepregnancy BMI Category	Excessive Early Gestational Weight Gain n=3,796	Nonexcessive Early Gestational Weight Gain n=4,189	Adjusted Odds Ratio (95% CI)
GDM	All women	153 (4.0)	106 (2.5)	1.4 (1.1–1.9)
	Underweight *	2 (1.2)	1 (0.5)	-
	Normal weight	51 (2.6)	34 (1.4)	1.7 (1.1–2.7)
	Overweight	53 (5.3)	26 (3.0)	1.6 (1.0–2.6)
	Obese	47 (7.6)	45 (5.9)	1.3 (0.8–1.9)
Birthweight greater than 4,000 grams	All women	317 (8.4)	236 (5.6)	1.5 (1.3–1.8)
	Underweight *	4 (2.4)	1 (0.5)	-
	Normal weight	151 (7.6)	110 (4.7)	1.7 (1.3–2.1)
	Overweight	106 (10.5)	68 (8.0)	1.3 (0.9–1.8)
	Obese	56 (9.0)	57 (7.5)	1.2 (0.8–1.8)
LGA	All women	455 (12.1)	381 (9.1)	1.4 (1.2–1.6)
	Underweight	16 (9.5)	12 (5.9)	1.8 (0.8–3.9)
	Normal weight	244 (12.3)	221 (9.4)	1.4 (1.2–1.7)
	Overweight	144 (14.4)	91 (10.7)	1.4 (1.1–1.9)
	Obese	51 (8.3)	57 (7.6)	1.1 (0.7–1.6)

Data are n(%).

BMI, body mass index; GDM, gestational diabetes; LGA, large for gestational age.

* Insufficient numbers to calculate adjusted odds ratio.

Table 4

Obstetric Outcomes of the Study Population*

Obstetrical Outcomes	Excessive Early Gestational Weight Gain (n=3,796)	Nonexcessive Early Gestational Weight Gain (n=4,189)	*P*
Labor induction	1,481 (39.1)	1,433 (34.2)	<0.001
Cesarean delivery	1,053 (27.7)	938 (22.4)	<0.001
Birthweight (grams)	3,330 [3,012–3,657]	3,250 [2,930–3565]	<0.001

Data are n(%) or median [25th–75th percentile].