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Gestational Weight Gain in Insulin Resistant Pregnancies

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Abstract

Objective—To examine the Institute of Medicine (IOM) guidelines for gestational weight gain (GWG) in insulin-resistant pregnancy.

Study Design—Secondary analysis of a prospective cohort of 435 women with type 2 or gestational diabetes from 2006–2010. The exposure was categorized as GWG less than, within, or greater than the IOM recommendations for body mass index. The maternal outcome was a composite of preeclampsia, eclampsia, 3rd–4th degree laceration, readmission, or wound infection. The neonatal outcome was a composite of preterm delivery, level 3 nursery admission, oxygen requirement >6 hours, shoulder dystocia, 5-minute Apgar 3, umbilical cord arterial pH<7.1, or base excess <–12. Secondary outcomes were cesarean delivery (CD), macrosomia, and small for gestational age (SGA).

Results—Incidence of the maternal outcome did not differ with GWG ($p=0.15$). Women gaining more than recommended had an increased risk of CD (relative risk (RR) 1.31, 95% confidence interval (CI) 1.01–1.69) and the neonatal outcome (RR 1.40, 95% CI 1.01–1.95) compared to women gaining within the IOM recommendations. Women gaining less than recommended had an increased risk of SGA (RR 3.29, 95% CI 1.09–9.91) without a decrease in the risk of the maternal outcome (RR 0.93, 95% CI 0.49–1.78) or CD (RR 0.74–0.40–1.37) compared to women gaining within the IOM recommendations.

Conclusions—Women with insulin resistance should be advised to gain within the current IOM guidelines.

Keywords

gestational diabetes; gestational weight gain; type 2 diabetes

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Introduction

The Institute of Medicine (IOM) recommendations for gestational weight gain in pregnancy released in 2009 do not make specific recommendations for pregnancies complicated by pregestational or gestational diabetes.¹ Obesity and weight gain are tightly linked to the development of and morbidity associated with type 2 diabetes outside of pregnancy;^{2, 3, 4, 5} modest weight loss in diabetic adults can improve insulin sensitivity and outcomes in non-pregnant adults.^{6, 7} Similarly, obesity and weight gain early in pregnancy have also been associated with the development of gestational diabetes,^{8, 9} a temporary insulin-resistant state that may herald development of type 2 diabetes later in life. Given the close associations between weight gain and insulin resistance, many obstetricians are hesitant to recommend weight gain in pregnant women with type 2 and gestational diabetes, for fear of compounding pre-existing insulin resistance and adversely impacting perinatal outcomes.

However, inadequate gestational weight gain may be as harmful as excessive gestational weight gain. Inadequate gestational weight gain has been linked to small-for-gestational infants, preterm birth and infant mortality.^{10, 11, 12} Therefore, although concerns regarding the effects of excessive gestational weight gain are valid, physicians must also be circumspect about recommending no or little weight gain in insulin-resistant pregnancies before understanding the effects.

Although several studies examine the risk of developing gestational diabetes with varying gestational weight gain,^{13, 14, 15} few studies examine the impact of gestational weight gain in pregestational and gestational diabetes on maternal and neonatal outcomes. Therefore, we aimed to estimate the impact of weight gain within, less than, and greater than the IOM recommendations on maternal and neonatal outcomes in pregnancies complicated by type 2 and gestational diabetes mellitus.

Materials & Methods

This is a secondary analysis of a prospective, 4-year cohort of women with gestational diabetes (GDM) and type 2 pregestational diabetes mellitus (DM). Institutional review board approval was obtained from Washington University School of Medicine Human Research Protection Office prior to study initiation.

Women were approached for enrollment at entry to prenatal care (type 2 DM) or upon diagnosis (GDM). Exclusion criteria were type 1 DM, multiple gestation and fetal anomalies diagnosed at the mid-trimester anatomy ultrasound or delivery. Women with unknown prepregnancy body mass index (BMI), unknown gestational weight gain, and incomplete delivery records were excluded from this secondary analysis. Women were considered to have type 2 diabetes if they had been diagnosed with diabetes prior to pregnancy, by review of medical records and patient self-report. Women were screened for gestational diabetes with a 1-hour, 50-gram glucose challenge test. Women were considered screen positive if this test was ≥ 140 mg/dL, and a diagnostic 3-hour 100-gram glucose tolerance test was performed. Two abnormal values according to the National Diabetes Data Group criteria

were required for the diagnosis of GDM.⁸ Timing of testing was determined by the practitioner, but was typically performed between 24–28 weeks of gestation.

All subjects were followed at the Center for Diabetes in Pregnancy, a clinic managed by Maternal-Fetal Medicine specialists at Washington University School of Medicine/Barnes Jewish Hospital, St. Louis, MO. Upon entry to care, women received diabetic education and dietary counseling. Counseling regarding gestational weight gain was at the discretion of the provider. The standard of care at the Center for Diabetes in Pregnancy is to follow fasting and post-prandial blood sugars with a treatment goal of maintaining fasting blood sugar <95 mg/dL and one-hour post-prandial blood sugar <140 mg/dL. These goals are achieved with the use of diet, glyburide or insulin. Indication for treatment escalation is >50% of blood glucose measures at any given time point above goal. Women were classified by gestational weight gain within, less than, or greater than the 2009 IOM recommendations for body mass index (Table 1).¹ For women delivering prior to 37 weeks gestation, appropriate weight gain range was determined from the IOM recommendations for weight gain in the first trimester (0.5–2.0 kg) and weight gain per week. Body mass index was determined from the self-reported pregnancy weight at entry to care, with confirmation at the first prenatal visit weight and height measurement.¹⁶ When a significant difference existed, the measured height and weight were used. Gestational weight gain was determined by subtracting prepregnancy weight from the final measured weight at delivery.

The composite outcome was selected based on outcomes that are related to diabetes, infant weight, and/or gestational weight gain.^{1, 8, 17} A woman was considered to have the maternal composite outcome if she had at least one of the following: preeclampsia, eclampsia, 3rd or 4th degree laceration as documented by the delivery physician, readmission, or wound infection. Preeclampsia was defined as systolic blood pressure \geq 140 mm Hg or diastolic blood pressure \geq 90 mm Hg associated with proteinuria ($>$ 1+ on urine dip or \geq 300 mg/24 hours) and has been demonstrated to be increased in excessive gestational weight gain.^{10, 18} Third degree lacerations were those extended through the rectal sphincter as determined by the delivery physician, and 4th degree lacerations were those extending through the rectal mucosa, as determined by the delivery physician. Maternal lacerations were included as part of the composite as they are associated with fetal macrosomia.¹⁹ Maternal readmission and wound infection were considered as they may be related to diabetic control, which may be impacted by gestational weight gain. Cesarean delivery (CD), primary cesarean delivery, use of any hypoglycemic medications for GDM (i.e. A2 GDM), and use of insulin for GDM were secondary maternal outcomes. Neonates were considered to have the composite outcome if they had at least one of the following: preterm delivery (<37 wks), admission to level 3 nursery, oxygen requirement $>$ 6 hours after birth, shoulder dystocia (diagnosed clinically by the delivering attending physician), 5-minute Apgar \leq 3, umbilical cord arterial pH $<$ 7.1, or base excess $<$ -12. Secondary neonatal outcomes were birth weight, small for gestational age (SGA, defined as birth weight $<$ 10th percentile by the Alexander growth standard)²⁰, and macrosomia (defined as birth weight \geq 4000 g).

The baseline characteristics of subjects gaining within, less than, or greater than the IOM recommendations were compared with descriptive and bivariate statistics using unpaired analysis of variance or analysis of covariance tests for continuous variables and χ^2 or

Fisher's exact tests for categorical variables as appropriate. Normal distribution of continuous variables was testing using the Kolmogorov-Smirnov test. Relative risks of the outcomes of interest were calculated for subjects gaining less than or greater than the IOM recommendations using weight gain within the IOM recommendations as the reference. All analyses were completed using Stata SE, version 11 (College Station, Texas).

Results

Of 435 women enrolled in the study, 339 were included in this analysis (20 excluded for congenital anomalies, 5 excluded for deliveries prior to 24 weeks, 59 excluded for unknown gestational weight gain, 12 for undocumented birth weight). Of the included women, 71 (20.9%) gained within the IOM recommendations for their BMI category and gestational age at delivery, 54 (15.9%) gained less than the IOM recommendations, and 214 (63.1%) gained more than the IOM recommendations. Women in each gestational weight gain category were similar with respect to maternal age, race, insurance status, smoking, chronic hypertension, prior cesarean, body mass index, type of diabetes (gestational versus type 2 diabetes), and measures of glycemic control (Table 2). Women gaining within the IOM recommendations were less likely than those gaining outside of the IOM recommendations to have been on a hypoglycemic agent prior to pregnancy.

The composite maternal outcome was not significantly different across gestational weight gain groups (Table 3). The incidence of cesarean delivery and primary cesarean delivery increased as gestational weight gain increased ($p<0.01$ and $p=0.02$, respectively). When compared to women gaining within the IOM recommendations, women gaining less than the IOM recommendations did not have an increased risk of cesarean delivery (40.7% versus 49.3%, relative risk (RR) 0.83, 95% confidence interval (CI) 0.55–1.23); however, women gaining more than the IOM recommendations were at increased risk of cesarean delivery compared to those gaining within the recommendations (64.5% versus 49.3%, RR 1.31, 95% CI 1.01–1.69). In women with gestational diabetes, the need for hypoglycemic medications of any kind and the need for insulin were not different between gestational weight gain categories.

The composite neonatal outcome was not increased in women gaining less than recommended compared to women gaining within the recommended amount (43.4% versus 37.7%, RR 1.15, 95% CI 0.75–1.77) (Table 4). Women gaining more than recommended were at an increased risk of the composite neonatal outcome compared to women who gained within the recommendations (52.8% versus 37.7%, RR 1.40, 95% CI 1.01–1.95). Birth weight was significantly impacted by gestational weight gain category ($p<0.01$). Women gaining less than recommended were at significantly increased risk of SGA compared to those gaining within recommendations (18.5% versus 5.6%, RR 3.29, 95% CI 1.09–9.91), although gaining more than the recommendations was not protective (5.6% versus 5.6%, RR 1.00, 95% CI 0.33–2.99). The incidence of macrosomia decreased as gestational weight gain increased (3.7% versus 14.1% versus 22.0%, $p<0.01$), although the relative risk of macrosomia in women gaining more than the IOM recommendations compared to those gaining within the IOM recommendations did not reach statistical significance (i.e. the confidence interval crossed 1).

Discussion

Gestational weight gain above the IOM recommendations for BMI category resulted in an increased risk of the neonatal but not maternal composite adverse outcomes. Gestational weight gain above the IOM recommendations was also associated with an increased risk of cesarean delivery. Weight gain less than the IOM recommendations was associated with an increased risk of SGA, but did not result in a decreased risk of cesarean delivery, A2 diabetes, or the maternal or neonatal composite adverse outcomes. These findings suggest that the current IOM recommendations for gestational weight gain apply to diabetic pregnancies, particularly in high-risk pregnancy populations.

In this study, women with type 2 diabetes and with gestational diabetes were considered together for several reasons. First, as both disease processes are closely linked to obesity, these diseases are frequently treated in a similar fashion. More importantly, peripheral insulin resistance is the root cause of both diseases.^{21, 22, 23} In fact, studies have demonstrated findings of insulin resistance (elevated C-peptide, decreased glucose uptake in response to insulin) even in the first trimester of pregnancy in women subsequently diagnosed with gestational diabetes, suggesting that although GDM is not diagnosed until the third trimester, metabolic derangements begin in the first trimester.^{22, 24} For these reasons, we felt that analyzing subjects with GDM and type 2 diabetes together was appropriate, as gestational weight gain will impact pregnancies impacted by these diseases in the same pathologic fashion.

Cheng et al examined the effect of gestational weight gain using a retrospective data base of approximately 30,000 women whose pregnancies were complicated by gestational diabetes.²⁵ Similar to our study, they found an increases in cesarean delivery and macrosomia with weight gain above the IOM guidelines and increases in small for gestational age with weight gain below the IOM guidelines. This study also reported an increase in the risk of preterm delivery with gestational weight gain below the IOM guidelines; however, gestational weight gain is dependent on the length of pregnancy, and it is unclear from this study if gestational weight gain was adjusted for the length of gestation. As this study was published in 2008, it examined the IOM recommendations from 1990. These recommendations vary from the 2009 guidelines in that BMI categories were defined slightly differently, an important point as pregnancy outcomes, gestational weight gain, and prepregnancy BMI are closely linked. Also, the 1990 IOM recommendations did not define an upper limit of weight gain for obese women; therefore, in this analysis it is hard to know what cut off was used for defining gestational weight gain above the recommendations in obese women.

From the same data base as Cheng, Yee et al examined the effect of gestational weight gain on pregnancy outcomes in approximately 2,000 women whose pregnancy was complicated by type 2 diabetes.²⁶ Using the 2009 IOM guidelines, they also found an increase in the risk of cesarean delivery and macrosomia with gestational weight gain above the IOM guidelines. Weight gain below the guidelines resulted in an increase in the risk of SGA without the benefit of decreased risk of cesarean or decreased risk of NICU admission. However, this study did not examine maternal outcomes.

The prospective data collection is one of the main strengths of this study. As the goal of the parent study focuses on glycemic control and neonatal outcomes, specific attention was given to this information in the data collection process. We had detailed neonatal data available such as umbilical arterial cord gas measures, allowing us to examine these important infant outcomes. Another strength of our study is that all patients were managed at a single institution. Because all patients were managed at our center, all patients in this study had similar dietary counseling and diabetic education, and all patients were managed according to the same blood sugar goals. This minimizes the bias in our secondary outcomes of A2 diabetes and the initiation of insulin in women with GDM. Finally, we had a high number of adverse events occurring in this population. As a result, assuming a Type 1 error of 0.05, we had at least 80% power to detect a 2-fold increase in the composite maternal and neonatal adverse outcomes in the less than and more than IOM recommendations groups compared to the within IOM recommendations group, although our power to detect differences in the individual components of the composite outcome was limited.

One potential limitation of this study is the preponderance of obese women in this study (>60% of the study population). This is likely due to a combination of the patient population at our institution and the disease processes being studied, as obesity is a risk factor for both type 2 and gestational diabetes. Consequently, our study findings may be generalizable mainly to an obese population. Also, due to the less than IOM recommendations group being small (n=55), we were unable to perform adjusted analyses or stratify by BMI, type of diabetes, or treatment strategy. The groups were similar with respect to baseline characteristics with the exception of small differences in pre-pregnancy BMI category. However, prepregnancy BMI was considered in the definition of the exposure (gestational weight gain within or outside of the IOM recommendations), thereby limiting this as a potential confounding factor. Additionally, the type of diabetes (type 2 versus GDM), treatment regimen, and glycemic control were similar between groups.

Another potential limitation of this study is that we did not collect data on diet and physical activity. Although the interplay of these factors determines gestational weight gain, but the quality of diet, micronutrient intake and physical activity may also play important roles in determining infant and maternal outcomes which cannot be assessed by solely examining gestational weight gain. Finally, we considered gestational weight gain for the entire pregnancy and did not examine weight gain by trimester, which may play a differential role in both maternal and infant outcomes. However, as patients are typically are counseled regarding weight gain for the entire pregnancy, rather than per trimester, we feel this type of analysis makes our study more accessible to clinicians and patients. While some feel that weight gain early in pregnancy contribute to the development of GDM, the presence of metabolic derangements early in pregnancy^{21, 24} would suggest that early weight gain plays minimal if any role.

In spite of these limitations, we feel that clinically useful conclusions can be made. Gestational weight gain above the IOM recommendations was associated with increased risk of macrosomia, cesarean delivery, and adverse neonatal outcomes. Gestational weight gain below the IOM recommendations was associated with an increased risk of small for gestational age without a reduction in the risk of maternal adverse outcomes or cesarean

delivery. Therefore, until further evidence becomes available, we continue to lack evidence that women with type 2 and gestational diabetes should be advised to gain anything other than within the current Institute of Medicine guidelines based on their prepregnancy BMI category.

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Table 1

IOM Recommendations for Gestational Weight Gain

	Total Range for Pregnancy	Range per Week
Underweight (<18.5 kg/m ²)	28–40 lb (12.5–18 kg)	1–1.3 lb (0.44–0.58 kg)
Normal Weight (18.5–24.9 kg/m ²)	25–35 lb (11.5–16 kg)	0.8–1 lb (0.35–0.50 kg)
Overweight (25.0–29.9 kg/m ²)	15–25 lb (7–11.5 kg)	0.5–0.7 lb (0.23–0.33 kg)
Obese (>30.0 kg/m ²)	11–20 lb (5–9 kg)	0.4–0.6 lb (0.17–0.27 kg)

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Table 2

Maternal Characteristics

	Less than Recommended (n=54)	Within Recommended (n=71)	Greater than Recommended (n=214)	p
Age (yrs)	30.1 ± 4.9	29.4 ± 5.9	28.5 ± 5.8	0.14
<u>Race</u>				
White (n, %)	15 (27.8%)	13 (18.3%)	50 (23.4%)	
Black (n, %)	34 (63.0%)	49 (69.0%)	149 (69.6%)	
Hispanic	5 (9.3%)	5 (7.0%)	13 (6.1%)	0.08
Public Insurance (n, %)	48 (88.9%)	66 (93.0%)	192 (89.7%)	0.68
Smoking (n, %)	10 (18.5%)	10 (14.1%)	44 (20.7%)	0.23
Chronic Hypertension (n, %)	5 (9.3%)	9 (12.7%)	26 (12.2%)	0.81
Prior Cesarean	15 (28.8%)	21 (29.6%)	80 (37.4%)	0.27
Gestational Diabetes (n, %)	22 (40.7%)	32 (45.1%)	83 (38.8%)	0.65
Hypoglycemic Agent Prior to Pregnancy	12 (22.2%)	2 (2.8%)	21 (9.8%)	<0.01
BMI (kg/m ²)	39.1 (26.8–43.6)	34.0 (28.5–40.3)	33.1 (28.4–40.3)	0.32
<u>BMI Category</u>				
Underweight	2 (3.7%)	0	0	
Normal Weight	8 (14.8%)	9 (12.7%)	23 (10.8%)	
Over Weight	7 (13.0%)	14 (19.7%)	48 (22.4%)	
Obese	37 (68.5%)	48 (67.6%)	143 (66.8%)	0.04
<u>Glycemic Control</u>				
First Trimester Mean Glucose	94 (87–114)	97 (87–107)	96 (85–114)	0.26
Second Trimester Mean Glucose	92 (82–110)	88 (79–103)	92 (83–105)	0.79
Third Trimester Mean Glucose	86 (81–95)	88 (78–101)	88 (81–99)	0.53
Third Trimester Hemoglobin A1c Value	6.1 (5.8–6.8)	6.1 (5.8–6.6)	6.5 (6–7.1)	0.92

Data presented as n (%) or median (interquartile range), as appropriate

Table 3

Maternal Outcome by Gestational Weight Gain Category, Adjusted for BMI

	Gain Less than IOM Recommendations (n=54)	RR (95% CI)	Within IOM Recommendations* (n=71)	Gain More than IOM Recommendations (n=214)	RR (95% CI)	p [†]
Composite Maternal Outcome (n, %)	12 (22.2%)	0.93 (0.49–1.78)	17 (23.9%)	71 (33.2%)	1.39 (0.88–2.19)	0.15
All Cesarean (n, %)	22 (40.7%)	0.83 (0.55–1.23)	35 (49.3%)	138 (64.5%)	1.31 (1.01–1.69)	<0.01
Primary Cesarean (n, %)	11 (28.2%)	0.74 (0.40–1.37)	19 (38.00%)	69 (51.5%)	1.36 (0.92–2.00)	0.02
Gestational Diabetes Only	n=22		n=32	n=83		
Gestational Diabetes, A2	17 (77.3%)	1.17 (0.84–1.65)	21 (65.6%)	64 (77.1%)	1.17 (0.89–1.54)	0.43
Gestational Diabetes, Required Insulin	7 (31.8%)	1.27 (0.54–3.0)	8 (25.0%)	31 (37.4%)	1.49 (0.77–2.90)	0.45

* Reference

† Refers to chi-squared test performed across all 3 gestational weight gain categories

Table 4

Neonatal Outcomes by Gestational Weight Gain Category, Adjusted for BMI

	Gain Less than IOM Recommendations (n=55)	RR (95% CI)	Within IOM Recommendations* (n=71)	Gain More than IOM Recommendations (n=215)	RR (95% CI)	p [†]
Composite Neonatal Outcome (n, %)	23 (43.4%)	1.15 (0.75–1.77)	26 (37.7%)	112 (52.8%)	1.4 (1.01–1.95)	0.07
Birth Weight (g, mean ± s.d.)	3028 ± 745	-	3320 ± 705	3404 ± 866	-	0.01
SGA (n, %)	10 (18.5%)	3.29 (1.09–9.91)	4 (5.6%)	12 (5.6%)	1 (0.33–2.99)	0.02
Macrosomia (n, %)	2 (3.7%)	0.26 (0.06–1.15)	10 (14.1%)	47 (22.0%)	1.56 (0.83–2.92)	<0.01

* Reference

† Refers to chi-squared test performed across all 3 gestational weight gain categories

-Unable to calculate due to no occurrences in reference group