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Full Length Research

Impact of maternal weight gain on fetal growth in gestational diabetes

Orli Most[1]* and Oded Langer[2]

[1]Atlantic Maternal Fetal Medicine, 95 Madison Avenue, Morristown, NJ 07960, USA.
[2]St. Luke's –Roosevelt Hospital Center, New York, New York 10019, USA.

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We sought to determine the impact of maternal weight gain on fetal growth in gestational diabetes (GDM) in relation to treatment modality, body mass index (BMI) and glycemic control. 2454 GDMs were evaluated. Obesity was defined as BMI >29; good glycemic control ≤ 100 mg/dl; maternal age < and >30 years; parity ±1; large for gestational age (LGA) >90th percentile and small for gestational age (SGA) <10th percentile. SGA rates were similar in all groups. Obese/overweight diet-treated in glycemic control showed a 4-fold higher rate of LGA compared to insulin treated women. A 36 lb. weight gain in insulin treated patients had a 6-fold higher risk. In poor glycemic control, LGA rates were higher in all BMI/weight gain categories. Logistic regressions for LGA/SGA revealed that level of glycemia, weight gain, parity, obesity and treatment (for LGA only) were significant. Different thresholds used for different maternal BMI categories in addition to the achievement of glycemic control and pharmacological therapy will enhance pregnancy outcome.

Key words: Weight gain in gestational diabetes, pre-pregnancy BMI, glycemic control, treatment modality.

INTRODUCTION

The majority of studies address the issue of the effect of weight gain in non-diabetic patients, especially in overweight and obese women (Potti et al., 2009; Cedergren, 2007; DeVader et al., 2007; Jensen et al., 2005; Edwards et al., 1996; Blomberg, 2011; Artal et al., 2010; Hinkle et al., 2010). The recommendations for weight gain in pregnancy are based on reported guidelines when different weight gain allowances are associated with different BMI categories (Institute of Medicine, 2009). The weight gain recommendations were evaluated in several studies. Bodnar et al. (2010) found that a weight gain of 2.2 to less than 5 kg for obese class III women was associated with approximately 10% large for gestational age (LGA) and small for gestational age (SGA) infants. In another study, Hinkle et al. (2010) concluded that a gestational weight gain below the Institute of Medicine (IOM) guidelines may be associated with lower rates of LGA, SGA and macrosomia. Park et al. (2010) demonstrated decreased risk for LGA and an increased risk for SGA among obese women with weight gain below the IOM recommendations. For women with normal BMI, the suggested weight gain ranges from 11.2 to 15.9 kg (25 to 35 lb.); 6.8 to 11.2 kg (15 to 25 lb.) for overweight and 6.8 kg (15 lb.) for obese women. These guidelines were initially intended to help decrease the risk of fetal growth restriction. However, there are no established guidelines for weight gain for the patient with gestational diabetes (GDM) especially when the reference point is fetal macrosomia.

There are multiple factors that influence growth diversity in GDM. The most significant include targeted levels of glycemic control, obesity, treatment modality (diet and/or insulin), parity and ethnicity (Langer et al., 1994, 2005). Fewer studies address the issue of weight gain in the gestational diabetic woman. The majority of these studies emphasize that the greatest weight gain occurs during the first and second trimesters, that is, generally prior to the diagnosis of the disease (Stevens-Simon et al., 1986; Morisset et al., 2011; Salmenhaara et al., 2010;

*Corresponding author. E-mail: Orli_langer@hotmail.com. Tel: 973-971-7025. Fax: 973-290-8312.

Cheng et al., 2008; Hutcheon et al., 2006; Hedderson et al., 2010). Moreover, the impact of maternal size (BMI), treatment modality and the affect of achieving glycemic control are yet to be established. Therefore, we sought to determine in GDM women, the impact of weight gain on fetal growth diversity (both large and small for gestational age) in relation to treatment modality (diet vs. insulin), maternal pre-gravid BMI and level of glycemic control.

MATERIALS AND METHODS

Subjects and data collection

In a retrospective design, we compared weight gain in pregnancy and its effect on 2454 gestational diabetic women. Eligible women had a singleton pregnancy and were drawn from an inner city population. The study population included patients who had registered for antenatal care in the first trimester and attended prenatal visits before delivery (7±2). Exclusion criteria included women with pre-existing diabetes, those with late registration for prenatal care and multiple gestations. Maternal clinical data were obtained from our computerized diabetic database and included age, parity, ethnicity, pre-pregnancy weight and height, weight at delivery, complications during pregnancy and neonatal outcome data.

Screening and diagnosis for GDM

All subjects were screened for GDM with a one-hour 50-gm glucose challenge test at 24 to 28 weeks of gestation. When the screening results were >130 mg/dl, the subjects underwent a 100-gm oral glucose tolerance test (OGTT) after a 3-day normal diet containing at least 300 gm of carbohydrates followed by a fast of at least 10 hours prior to the test. Gestational diabetes was defined as 2 or more abnormal values on the oral glucose tolerance test based on the Carpenter and Coustan Criteria (Carpenter et al., 1982).

Maternal assessment and treatment

A registered nutritionist instructed each patient in the standard isocaloric diet consisting of three meals and four snacks daily (40% carbohydrate diet) based on 25 kcal/kg of desirable body weight for obese and overweight patients and 35 kcal/kg for normal weight subjects. Patients were placed on diet therapy for a two week period and if fasting plasma glucose levels exceeded 95 mg/dl or postprandial values ≥120 mg/dl, they were assigned to insulin therapy (ACOG Practice Bulletin, 2001).

All participants were instructed in the use of memory-based self-monitoring blood glucose by a diabetic nurse educator. They were advised to test 7/daily (pre-meal, 2-h postprandial and at bedtime). The targeted glycemic level was defined as mean blood glucose in the range of 90 to 105 mg/dl, fasting blood glucose 60 to 90 mg/dl, and 2-h postprandial <120 mg/dl. Targeted level of glycemic control was equated with blood glucose levels ≤105 mg/dl. Maternal/fetal medicine staff and diabetic educators evaluated blood glucose levels of participants on a weekly basis at the diabetic clinics.

Study outcome measurements

Patient pre-pregnancy body mass index (BMI) was calculated based on measurement of height and patient disclosure of pre-pregnancy weight at first obstetrical examination. Pre-pregnancy weight categories were normal (BMI 18.5 to 24.9), overweight (BMI 25.0 to 29.9) and obese (BMI ≥30). Patients were weighed at initial prenatal visit and at every subsequent visit with final weight determination upon delivery. Pregnancy weight gain was defined as weight at delivery minus pre-pregnancy weight. The "corrected maternal weight gain" was calculated using maternal body weight at delivery minus pre-pregnancy weight + neonatal birth weight + 500 [constant for placental weight]. Pregnancy weight gain was stratified into 5-pound increments. The weight gain recommendations of the American College of Obstetrics and Gynecology (ACOG Practice Bulletin, 2001) and the IOM (Institute of Medicine, 2009) were used for comparison: a weight gain of 25 to 35 pounds for normal BMI, 15 to 25 pounds for overweight women and 11 to 20 pounds for all obese categories. Gestational age was determined by a history of last menstrual period and early vaginal examination. When possible, a sonogram was performed at <20 weeks gestation to confirm gestational age.

Neonatal anthropometric measurements included birth weight, length on a measuring board and head circumference with a measuring tape. Neonatal growth diversity was defined by large for gestational age (>90th percentile) or small for gestational age (<10th percentile] for our study population. Finally, previous fetal macrosomia was defined as birth weight ≥4000 g.

Statistical analysis

For purpose of analysis, weight gain was stratified into 5-lb increments to identify change in rate of growth diversity (SGA, LGA) in each weight category. Calculation of the odds ratio between categories was performed using the Mantel-Haensel test. Baseline maternal characteristics, that is, gestational age at delivery, neonatal birth weight, weight gain in pregnancy, etc., were compared across weight gain groups using either an unpaired Student's t-test for continuous variables or the chi-square test for categorical data.

When performing a multiple logistic regression analysis, the dependent variable was LGA and the independent variables included treatment modality (diet vs. insulin), established levels of glycemic control (< or > mean blood glucose of 105 mg/dl), previous macrosomia (yes/no), parity (primigravid vs. multigravid), weight gain in pregnancy, obesity (pre-pregnancy BMI categories), ethnicity and GDM disease severity (fasting plasma ≥ 95 mg/dl).

RESULTS

Participant characteristics

The average maternal age of GDM participants was 29±6. Twenty percent were nulliparous with an ethnic mix of 75% Hispanic, 16% non-Hispanic White, 2% Asian and 7% African-American. Of the 2454 women, 26% were normal weight, 35% overweight and 39% obese. Forty-seven percent of subjects were treated with diet alone with the remainder treated with insulin. Patient demographics were comparable for both treatment groups. The overall total weight gain was 24 lbs; the bulk of weight gained prior to the diagnosis of GDM was 18 lbs. with minimum weight gain from diagnosis to delivery. The mean weight gain in the diet treated group was 22.5±17 lb., whereas in the insulin treated group 24.6±19 lb. (p=0.003). Mean blood glucose was 104±16 mg/dl for the diet and 110±17 mg/dl for the insulin treated women. Gestational age at diagnosis and delivery was comparable for treatment groups, 28±5 and 39±4 weeks,

respectively. The weight gain from conception to GDM diagnosis (pre-pregnancy maternal weight minus weight at diagnosis) was 18±16 lb. with weak correlation (r=0.09, p=0.0000) to fetal birth weight and birth percentile. The maternal weight gain during the disease period (maternal weight at delivery minus weight at diagnosis) was 6.33±5 (r=0.12, p=0.0000). The "corrected net weight gain" in pregnancy was 12 pounds and overall weight gain in pregnancy 24±16 lb.

Neonatal growth diversity

Overall, birth weight for the study population was 3269 ± 360 g. The rate of SGA infants was 7% (mean birth weight 2336±546 g) and the LGA infant rate 16% (mean birth weight of 4093±310 g). There was no significant difference among SGA infants in all weight gain categories that ranged from 4 to 10% (p=0.18). In contrast, there was a 2-fold increased rate of LGA infants when weight gain was ≥ 26 lbs., odds ratio (O.R.) 1.78, 95% confidence interval [C.I.] 1.48 to 2.15 (Figure 1).

The association among pre-pregnancy BMI, weight gain categories, and rates of LGA/SGA

Women with normal BMI had a 3-fold higher increased rate of LGA with a weight gain threshold of ≥35 pounds (7 vs. 21%; p=0.0000) O.R. 3.13, 95% C.I. 2.2 to 4.5; overweight women, a weight gain threshold of ≥15 pounds (8 vs. 19%, p=0.0002), O.R. 2.52, 95% C.I. 1.5 to 4.2; and obese women with weight gain threshold of ≥15 pound (15 vs. 25%, p=0.0000) O.R. 1.95, 95% C.I. 1.5 to 2.5.

In women with normal pre-pregnancy BMI, the rate of SGA for a weight gain threshold of ≤10 pound was 2-fold higher (17 vs. 8%) O.R. 2.57, 95% C.I. 1.5 to 4.6, and the risk for overweight women was 11 vs. 4%, O.R. 2.77, 95% C.I. 1.5 to 4.2. Obese women had a similar rate of SGA in all weight gain categories (5 to 9%).

The association among pre-pregnancy BMI, weight gain and treatment modalities

Diet therapy was associated with a 2 to 3-fold increased rate of LGA for obese and overweight in comparison to normal pre-pregnancy BMI women even within minimal weight gain categories (<5, 6 to 10, 11 to 15, 16 to 20 lb.). In contrast, women with normal BMI with a threshold weight gain ≥ 35 pounds (7 vs. 22%, p=0.0000) had O.R. 1.95, 95% C.I. 1.5 to 2.5 (Figure 2). For insulin-treated patients with normal pre-pregnancy BMI, the rate of LGA was similar in all weight gain categories. Only at a threshold weight gain of ≥40 pounds was there a significant increase in LGA rate (8 vs. 21%, p=0.0001) with an O.R. 3.5, 95% C.I. 2.2 to 5.7. In overweight women with a weight gain threshold ≥30 pounds, the LGA rate was 8 vs. 21%, p=0.0001 (O.R. 3.3, 95% C.I. 2.0 to 5.5). In obese patients, a weight gain threshold ≥26 pounds resulted in rates of 13 vs. 27%, p=0.0003 (O.R. 2.4, 95% C.I. 1.8 to 3.3) (Figure 3).

A comparison between treatment modalities (diet or insulin), glycemic control and overweight/obese patients

Diet treated patients who achieved established levels of glycemic control at a weight gain up to 20 lbs. had significantly higher rates of LGA when compared to insulin treated women (O.R. 4.08, 95% C.I. 2.8 to 5.9). For insulin treated patients, a threshold of 36 lbs. was associated with LGA (O.R. 5.94, 95% C.I. 3.7 to 9.5).

When levels of glycemic control remained unmet, the rate of LGA was higher in all pre-pregnancy BMI and weight gain categories regardless of treatment modality (diet vs. insulin). For diet treated patients, the rate of LGA was 21% in patients with poor glycemic control and 15% in those with good glycemic control (O.R. 1.61, 95% C.I. 1.2 to 2.2, p=0.0009). For insulin treated patients in poor glycemic control, the rate of LGA was 19% and for those in good control, 10% (O.R. 1.93, 95% C.I. 1.5 to 2.5, p=0.0000).

The incidence of SGA in all weight gain categories in both treatment modality groups who attained targeted levels of glycemic control was similar (5 to 10%) regardless of pre-pregnancy BMI. Significantly higher rates of SGA were observed in normal and overweight women who gained <10 pounds and who had been treated with insulin (10%) vs. diet (5%).

To evaluate the net effect of different factors that may contribute to the occurrence of LGA, a multiple regression analysis was performed. Modifiable (level of glycemic control, weight gain in pregnancy and treatment modality) and "unmodifiable" variables during pregnancy (parity, maternal age and obesity) were included in the analysis.

Maternal age, ethnicity and gestational age at treatment initiation did not contribute to the rate of LGA. Analysis when the dependent variable was SGA revealed that previous SGA, parity, mean blood glucose, obesity and maternal weight gain are all independent contributing factors (Table 1).

Finally, when the rates of growth diversity (LGA and SGA) in the study were compared to the ACOG and IOM threshold weight gain recommendations, we found higher rates of LGA than the expected rate of 10%. For women with a normal BMI, weight gain >35 lbs. was associated with a two-fold increased risk of LGA. Overweight patients with a weight gain $\geq$14 lbs. and obese women had a higher rate of LGA in all weight gain categories (Table 2).

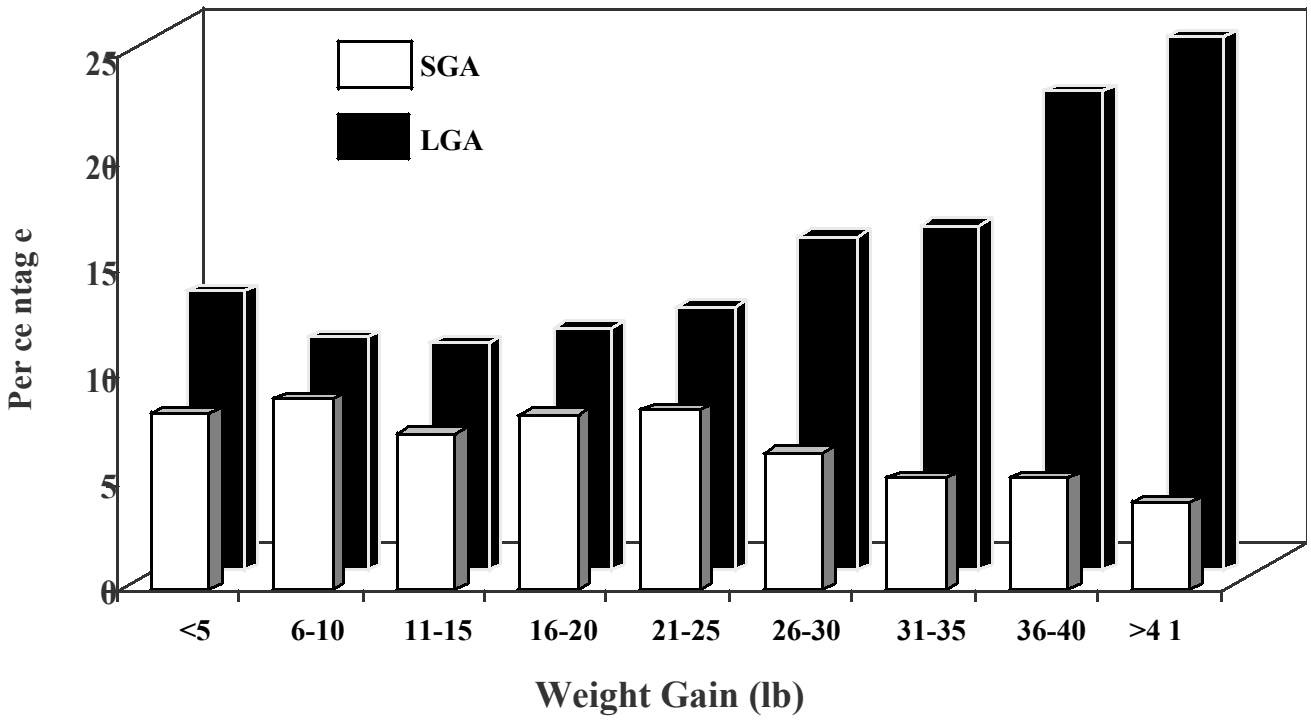

Figure 1. GDM: SGA and LGA categories by weight gain categories.

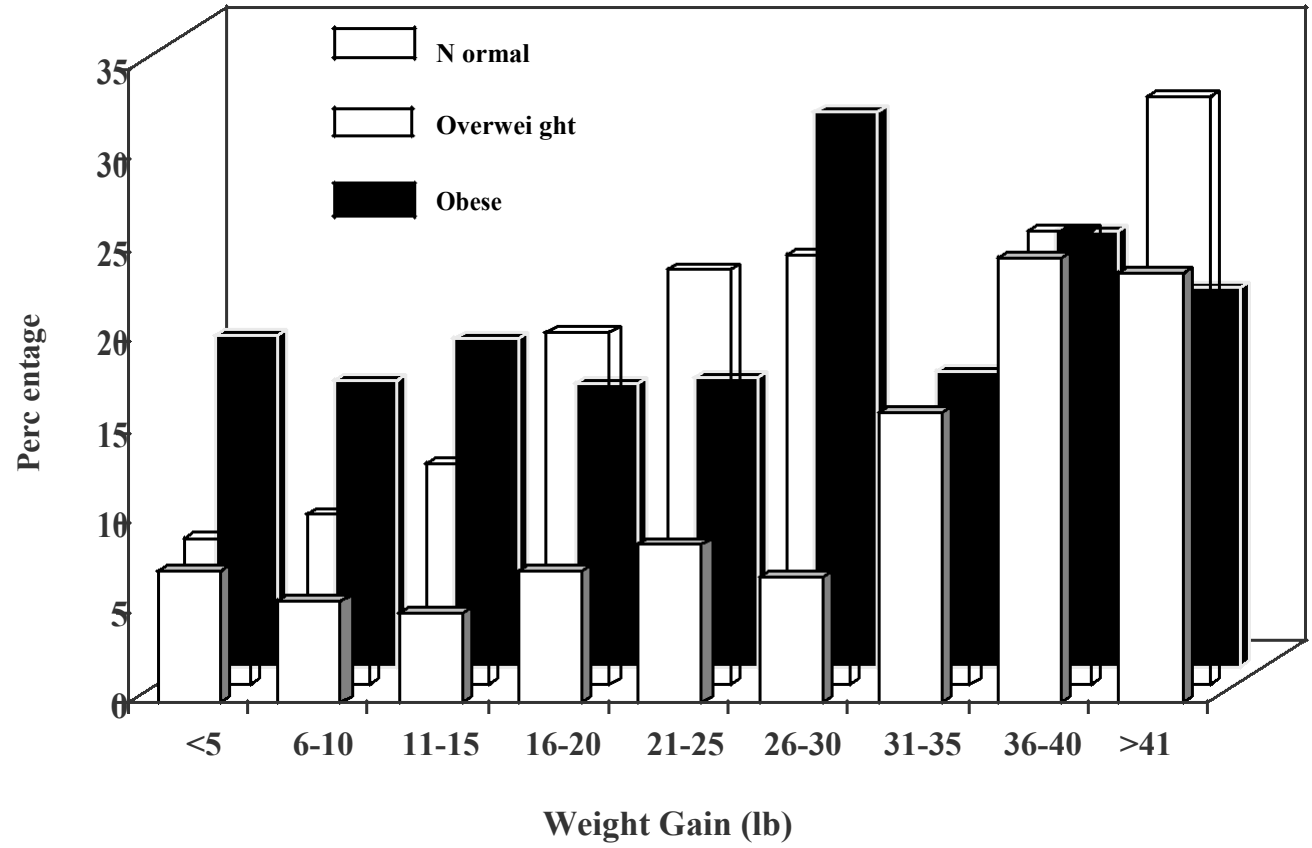

Figure 2. LGA rate by maternal size group (BMI) diet treated.

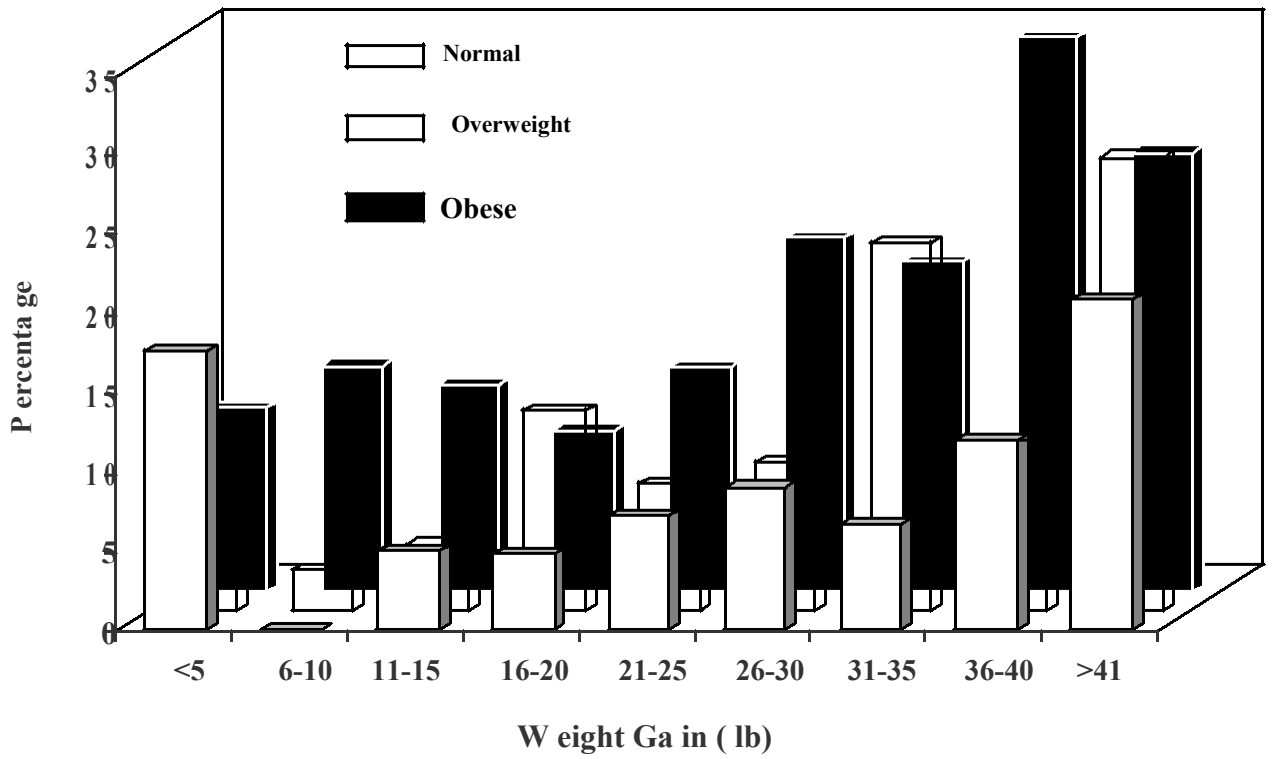

Figure 3. LGA rate by maternal size group (BMI) insulin treated.

Table 1. Multiple logistic regression summary for the impact of independent variable on LGA/SGA.

Independent variable	D.V=LGA		D.V=SGA	
	OR	95% CI	OR	95% CI
Previous macrosomia	2.63	1.99-3.47	---	----
Previous SGA	---	----	2.03	1.09-3.80
Parity	2.18	1.62-2.93	1.86	1.42-2.41
Mean blood glucose	2.08	1.62-2.93	1.64	1.20-2.24
Treatment modality	1.71	1.36-2.16	1.02	0.65-1.59
Obesity	1.49	1.13-1.95	1.46	1.11-1.90
Weight gain	1.02	1.02-1.03	1.02	1.01-1.03
Gestational age for treatment initiation	1.19	0.99-1.41	1.01	0.98-1.02
Maternal age	1.01	0.99-1.03	1.07	0.83-1.37
Race/ethnicity	1.10	0.91-1.33	0.80	0.69-2.24
GDM severity	1.05	0.66-1.67	1.01	0.98-1.02

D.V. = dependent variable, LGA = large for gestational age, SGA = small for gestational age, OR = odds ratio, CI = confidence interval.

DISCUSSION

Overall, our study demonstrated a significant increase in LGA rates for different weight gain categories as defined by the IOM for obese and overweight compared to normal weight subjects. The LGA/SGA rates were further modified by level of glycemic control and treatment modality. The key findings of the study revealed: 1) 75% of the overall weight gain occurred prior to the GDM diagnosis; 2) stratification of GDM subjects by pre-pregnancy BMI categories identified thresholds that may limit excess LGA rates, for normal BMI ≤35 lbs., overweight ≤15 lbs. and obese ≤10 lbs. and for prevention of SGA in normal and overweight women ≥10 lbs.; 3) for obese subjects, there was no effect on the amount of weight gain category on the rate of SGA; 4) in

Table 2. Rate of growth diversity in relation to weight gain recommendations.

Weight gain	Normal* (25-35 lb.)		Over weight* (15-25 lb.)		Obese* (<15 lb.)	
	SGA (%)	LGA (%)	SGA (%)	LGA (%)	SGA (%)	LGA (%)
<10	17.3	7.1	10.9	7.7	6.21	14.6
11-14	7.8	4.7	4.1	9.3	6.4	16.6
15-25	10.6	6.9	5.5	14.7	9.1	12.8
26-35	6.9	9.7	3.3	16.2	6.6	22.4
>36	4.9	21	3.3	26.1	4.8	27.7

*p=0.0000.

insulin treated non-obese patients, the rate of LGA increased only after a weight gain of ≥40 lbs. and for overweight and obese women, a weight gain ≥30 lbs.; 5) for insulin treated patients in good control, only those with a weight gain ≥36 lbs. demonstrated a significant increase in LGA; 6) with the inclusion of glycemic control, diet treated subjects had significantly higher rates of LGA regardless of BMI and weight gain categories; 7) no association was found between SGA infants and level of glycemia, pre-pregnancy BMI category and treatment modality.

Weight gain in pregnancy has continually been a focus for the well-being of the pregnant woman and especially her fetus. The weight gain guidelines were revised to minimize mortality and morbidity risks for low birth weight infants (Potti et al., 2010). Some of the factors in non-diabetic pregnancies that were evaluated for the association between weight gain and pregnancy outcome include gestational duration, maternal birth weight, maternal height, pre-pregnancy weight, total gestational weight increase and previous birth of a macrosomic infant (Wikstrom et al, 1991; Shapiro et al., 2000). Likewise, Deruelle et al. (2004) described that excessive weight gain in pregnancy is associated with fetal macrosomia. Ogunyemi et al. (1998) found that the highest birth weight was associated with women who had excessive weight gain in pregnancy. The work of Luke et al. (1996) addressed the question of when gestational weight gain ceases to benefit birth weight and triggers maternal postpartum obesity.

In diabetic patients, among several risk factors, the inability to maintain established levels of glycemic control throughout pregnancy is considered one of the main contributors for the development of LGA/macrosomia in addition to maternal obesity and excessive weight gain (Langer et al., 1994; Sunehag et al., 1991; Cameron et al., 1998). To date, no criteria for weight gain in pregnancy compromised by diabetes has been established especially when the reference point is accelerated fetal growth (LGA/fetal macrosomia). The majority of the studies that address the effects of GDM and weight gain in pregnancy outcome are based on relatively small sample sizes. Jensen et al. (2005) in 481 women with GDM (World Health Organization criteria) investigated the effect of weight gain in pregnancy on obese glucose tolerant women. The study did not address the impact of treatment modality and level of glycemic control throughout pregnancy on overweight and normal weight women. They concluded that weight gain in obese women is associated with increasing pregnancy complications; and, gaining up to 10 kg is beneficial for the overall pregnancy. Catalano et al. (1993) studied maternal weight gain in GDM women and its relation to neonatal birth weight. They found that weight gain in these subjects was lower than in non-diabetic controls. They concluded that the lower weight gain was associated with higher pre-pregnancy maternal weight (BMI). In addition, they found no correlation between neonatal birth weight and maternal weight gain. Again, no reference was made to treatment modalities and glycemic control in the GDM subjects. Bronisz et al. (2005) in 867 GDM patients found that maternal height, BMI, weight gain in pregnancy, triglycerides and glycemic control reflected by HbA1c have a greater impact on neonatal birth weight than social-demographic factors in pregnancy complicated by GDM. There is a paucity of studies on the effect of treatment modalities and glycemic profile using self-monitoring blood glucose.

Hutcheon et al. (2006) in a retrospective analysis of 90 women with at least 2 GDM pregnancies evaluated the impact of blood glucose, obesity and maternal weight gain on sibling differences. They concluded that controlling maternal weight gain may reduce offspring birth weight in women with GDM. In addition, there was no association between fasting blood glucose and weight gain; postprandial glucose was significantly associated with birth weight. Ray et al. (2001) prospectively studied the effects of weight gain and obesity in 428 GDM and 146 pre-gestational diabetic subjects. They demonstrated that maternal obesity and to a lesser degree excessive weight gain were independent risk factors for adverse maternal and neonatal outcomes. In addition, they found an association between LGA even with a weight gain >5 kg. However, the effect of glycemic control was not measured. Lepercq et al. (2002) studied 69 GDM and 61 type 1 diabetic women and concluded that corrected weight gain is a more accurate estimate of true accretion of maternal weight. They suggested that care providers take

this index into account with weight gain recommendations. Although they found no difference between insulin and diet treated patients relative to fetal weight, they did not report the impact of different BMI categories and level of glycemia on the pregnancy outcome.

In our study, we found that from a total weight gain (24 lbs.) in our pregnant diabetic population, the bulk of weight gain occurred prior to the GDM diagnosis (18 lbs.) with minimum weight gain from diagnosis to delivery. This finding is consistent with previous reported studies of weight gain patterns in GDM patients (Morisset et al., 2011; Hedderson et al., 2010). Since the caloric recommendations for GDM women constitute a weight reduction regimen in comparison to their pre-pregnancy eating habits, adherence to the diet recommendations and achievement of targeted levels of glycemic control mitigates maternal weight gain and growth diversity of the fetus.

There is an ongoing debate regarding the impact of different maternal factors (glycemic control, obesity, and weight gain) on birth weight (Lauszus et al., 1999; Saldana et al., 2006). Since pre-pregnancy weight data is often missing, weight gain in pregnancy is in many studies calculated using the weight at the first and last antenatal visits. Weight gain calculated from these two reference points are not an accurate reflection of total pregnancy weight gain. In addition, there is great disparity between health centers as to the gestational week at first visit. Moreover, the use of maternal weight at last antenatal visit as a second endpoint is not an accurate measure since these visits may refer to different gestational weeks for different patients.

A frequently asked question is the accuracy of patient-reported pre-pregnancy weight. Lederman et al. (2004) reported that pre-pregnancy weight reported by mothers is a satisfactory substitute for clinical record data and that the weight differed significantly only in underweight women who over-reported by 2.4 lbs. However, underweight women are highly uncommon in the GDM population. Different studies evaluated weight gain in pregnancy during different periods of gestation. They observed that self-reported pre-pregnancy weight approximates the true value (Morisset et al., 2011; Yu et al., 1992; Rothman et al., 1998; Harris et al., 1998). Stevens-Simon et al. (1986) found that pre-pregnancy estimates in adolescents are accurate enough to be used during pregnancy. They showed a correlation of 0.98 between the stated and the actual prepregnancy weight. Saldana et al. (2006) studied weight gain only until diagnosis of GDM (near the end of the second trimester). Lepercq et al. (2002) studied the concept of “corrected maternal weight gain” that omits fetal, placental and amniotic fluid weights from the “pre-pregnancy weight.” In a report by Schieve et al. (1999) of over 266,000 women, the mean maternal and net weight gains even when adjusted for week of gestation all decreased with increasing BMI. Moreover, overweight and obese women had mean weight gains greater than the Institute of Medicine guidelines.

The weight gain pattern in GDM patients differs from those of non-GDM subjects with the majority of weight gain occurring prior to diagnosis (between 26 and 28 weeks in the majority of cases). Therefore, we analyzed different time periods in relation to maternal weight gain:

1) total pre-pregnancy weight (reported pre-pregnancy weight and weight at delivery); 2) pre-pregnancy weight to diagnosis of GDM (representing the pre-treatment period); 3) weight gain from diagnosis to delivery (treatment period); and, 4) “corrected maternal weight gain.” All these weight determinations showed weak corre-lations to neonatal birth weight. However, a significant increase in the rate of LGA was found for different threshold weight categories in obese and overweight compared to normal weight subjects when this LGA rate was modified by level of glycemic control.

We previously demonstrated that obese patients treated with diet alone who achieved targeted levels of glycemic control had higher rates of LGA and adverse pregnancy outcome in comparison to patients treated with insulin (Langer et al., 2005). The current study confirmed our previous findings. Obese and overweight GDM women treated with diet had 2 to 3 fold higher rates of LGA compared to normal weight subjects. For normal weight insulin treated patients, the rate of LGA increased only after a weight gain threshold ≥ 40 lbs. and for overweight and obese women, a threshold ≥ 30 lbs. was associated with a 2 to 3 fold higher rate of LGA. When glycemic control was included in the analysis, diet-treated women had significantly higher rates of LGA regardless of weight gain category in comparison to insulin treated who achieved targeted levels of control. For insulin patients in good control, only those above a threshold ≥ 36 lbs. showed a significant increase in LGA. No association was found between SGA infants and level of glycemia, pre-pregnancy BMI category and treatment modality.

The strength of our study is the large sample size as well as the unique adjustment that was made for obesity, glycemic control and weight gain in the gestational diabetic pregnancy. Furthermore, although the study design was retrospective, the data was collected prospectively to our computerized database. This factor improved the validity of the information in comparison to the results of studies using birth certificates and/or chart review. We used logistic regression analysis to adjust for known and suspected confounders. This approach helped us to identify the net contribution of factors such as treatment modality and level of glycemic control. However, there may be other confounding variables that may explain the association observed for pregnancy outcome.

Like all observational studies, our study has its limitations. We recognize that despite the multiple studies that supported the validity of self-reported pre-pregnancy

weight, women may still overestimate or underestimate their true weight for various reasons. However, a much wider discrepancy occurs when weight at diagnosis is used for calculating BMI. We also recognize that the rate of fetal growth diversity (LGA and SGA) is dependent upon the accuracy of gestational age determination that is routinely estimated by the clinician (ultrasound and last menstrual period errors). Finally, we acknowledge that our results in this study, like the majority of studies in diabetes in pregnancy, show only statistical associations and do not imply causality.

To study causality on the impact of weight in pregnancy and growth diversity, the absolute answers may be obtained only by conducting a prospective, randomized controlled trial in GDM patients (considering BMI categories, level of glycemia measured by appropriate protocol, treatment modalities, etc.). This may be an unattainable endeavor.

Our data suggest that minimal maternal weight gain might normalize birth weight. We found that well controlled insulin treated GDM patients will result in lower rates of LGA. In addition, our data suggests that different weight gain thresholds should be used for different BMI categories and that pharmacological therapy and obtaining desired levels of glycemic control will result in improved pregnancy outcome for GDM patients. To address the challenge of growth diversity, we need to direct our patient care and research efforts to the variables that are modifiable, that is, glucose control, treatment modality, and proper weight gain allowance rather than to those “unmodifiable” factors such as parity, maternal age, and obesity during pregnancy.

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