The Relative Contribution of Prepregnancy Overweight and Obesity, Gestational Weight Gain, and IADPSG-Defined Gestational Diabetes Mellitus to Fetal Overgrowth

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OBJECTIVE—The International Association of Diabetes in Pregnancy Study Groups (IADPSG) criteria for diagnosis of gestational diabetes mellitus (GDM) identifies women and infants at risk for adverse outcomes, which are also strongly associated with maternal overweight, obesity, and excess gestational weight gain.

RESEARCH DESIGN AND METHODS—We conducted a retrospective study of 9,835 women who delivered at ≥20 weeks' gestation; had a prenatal, 2-h, 75-g oral glucose tolerance test; and were not treated with diet, exercise, or antidiabetic medications during pregnancy. Women were classified as having GDM based on IADPSG criteria and were categorized into six mutually exclusive prepregnancy BMI/GDM groups: normal weight ± GDM, overweight ± GDM, and obese ± GDM.

RESULTS—Overall, 5,851 (59.5%) women were overweight or obese and 1,892 (19.2%) had GDM. Of those with GDM, 1,443 (76.3%) were overweight or obese. The prevalence of large-for-gestational-age (LGA) infants was significantly higher for overweight and obese women without GDM compared with their normal-weight counterparts. Among women without GDM, 21.6% of LGA infants were attributable to maternal overweight and obesity, and the combination of being overweight or obese and having GDM accounted for 23.3% of LGA infants. Increasing gestational weight gain was associated with a higher prevalence of LGA in all groups.

CONCLUSIONS—Prepregnancy overweight and obesity account for a high proportion of LGA, even in the absence of GDM. Interventions that focus on maternal overweight/obesity and gestational weight gain, regardless of GDM status, have the potential to reach far more women at risk for having an LGA infant.

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Both International Association of Diabetes in Pregnancy Study Groups (IADPSG)–defined gestational diabetes mellitus (GDM) (1,2) and maternal overweight and obesity (2–4) are associated with increased risk for adverse maternal and perinatal outcomes, such as fetal overgrowth, shoulder dystocia and birth injury, pre-eclampsia, and preterm delivery. Although most studies addressing the effects of maternal BMI on adverse outcomes include women with GDM (2–6), a few have reported these associations in overweight or obese women with normal glucose tolerance (7–9). Scant data exist that demonstrate associations between GDM and adverse outcomes in the absence of overweight or obesity (9).

Although it is currently estimated that 10–25% of pregnant women develop GDM by IADPSG criteria (1,2,10), 50–60% of women are overweight or obese at the start of their pregnancies (6,7,11,12). Prepregnancy overweight and obesity are also associated with GDM development, as 65–75% of women with GDM are also overweight or obese (11,13). As such, the relative impact of prepregnancy BMI and maternal glycemia during pregnancy on adverse maternal and perinatal outcomes is difficult to tease apart. Moreover, excess gestational weight gain complicates a large number of pregnancies and is highly correlated with maternal overweight and obesity, as well as the development of GDM (14–16). Despite the fact that studies have reported increases in the risk of adverse outcomes with increasing gestational weight gain (13,15–18), many studies examining the effects of maternal obesity and/or glucose levels have not accounted for this important factor.

The purpose of this study was to examine the effects of prepregnancy overweight and obesity among women with and without IADPSG-defined GDM on clinically important adverse outcomes, focusing primarily on fetal overgrowth, one of the most prevalent adverse conditions associated with maternal and neonatal morbidity. In addition to magnitude of association, we determine the proportion of large-for-gestational-age (LGA) infants attributable to each risk factor and combinations thereof. We also examine the relative contribution of increasing gestational weight gain to the development of LGA.

RESEARCH DESIGN AND METHODS

Population and data sources

The Kaiser Permanente Southern California (KPSC) Medical Care Program is a large prepaid group-practice managed

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See accompanying commentary, p. 6.

health care organization with over 3.3 million members in 2010. Members receive their health care in KPSC-owned facilities throughout the seven-county region. This study was approved by the KPSC institutional review board. The study population consisted of women who had their prenatal care and delivery of a live singleton neonate at ≥20 weeks' gestation at KPSC Bellflower Medical Center between 30 October 2005 and 31 December 2010. All pregnant women receiving care at this facility were requested to have a 2-h, 75-g oral glucose tolerance test (OGTT) between 24 and 28 weeks' gestation. According to institution-specific guidelines, women whose test results met at least two thresholds (fasting ≥100, 1-h ≥195, or 2-h ≥160 mg/dL) were initially treated with diet and exercise therapy, with fasting and 1-h postbreakfast plasma glucose concentrations assessed by the hospital laboratory on a weekly basis thereafter (19). Those whose fasting glucose was consistently ≥105 mg/dL or 1-h postprandial glucose was ≥140 mg/dL were treated with insulin or glyburide in addition to diet and exercise (20). After excluding women who received any form of treatment during pregnancy (n = 624), we used OGTT results to identify women with GDM based on IADPSG guidelines (at least one OGTT value: fasting ≥92 mg/dL, 1-h ≥180 mg/dL, or 2-h ≥153 mg/dL) (2). For women with more than one OGTT during pregnancy, outcomes were analyzed based on the test result within or nearest to 24–28 weeks' gestation. For women with more than one birth during the study period, only data from the first pregnancy were analyzed.

Maternal age at delivery, race/ethnicity, and parity were obtained from infant birth certificates. Information on prenatal smoking was obtained from the electronic health record (EHR). Infant sex, gestational age at birth, birth weight, and birth length were obtained from the birth certificate or EHR. Ponderal index was calculated as birth weight/height^3 × 100 (21).

Measures of prepregnancy BMI and gestational weight gain

Maternal prepregnancy weight and height were obtained from the EHR (n = 8,777; 89.3%) or the infant birth certificate, if not available from the EHR (n = 1,058; 10.7%). Among those with data available from the EHR, the identification of measured prepregnancy weight was contingent upon the timing of the clinical visit closest to the last menstrual period. For women with multiple measures, prepregnancy and delivery weight were selected hierarchically, as previously described (11). Prepregnancy BMI was classified as normal weight (BMI <25 kg/m^2), overweight (25≤ BMI <30 kg/m^2), or obese (BMI ≥30 kg/m^2). Women with BMI <18.5 kg/m^2, meeting the criteria for underweight (n = 172, 1.7% of cohort; mean BMI ± SD, 17.6 ± 0.8 kg/m^2), were categorized as normal weight for the purposes of these analyses. Gestational weight gain was calculated as the difference between prepregnancy and delivery weight. The 2009 Institute of Medicine (IOM) guidelines were used to classify excessive gestational weight gain for prepregnancy BMI (normal, >35 pounds; overweight, >25 pounds; obese, >20 pounds) (22).

Obstetrical and neonatal outcomes

LGA infants were defined as sex-, race/ethnicity-, and gestational age–specific birth weight >90th percentile. Consistent with the statistical methods used by the Hyperglycemia and Adverse Pregnancy Outcomes study group (23), percentiles for birth weight were determined by quantile regression stratified by sex and race/ethnicity, with adjustment for gestational age and parity, using data from our study population. Primary cesarean delivery was obtained from infant birth certificates. Preterm delivery was defined as delivery before 37 completed weeks of gestation. Neonatal complications were identified using ICD-9-CM codes and included hyperbilirubinemia (774.0–774.7 within the first week after birth), shoulder dystocia (653.4, 653.5, or 660.4), birth trauma (767.0–767.9), transient tachypnea (770.6), and respiratory distress (769.xx). We identified women with pre-eclampsia/eclampsia (PE/E) by ICD-9-CM codes 642.4–642.6 during pregnancy.

Statistical analyses

We categorized women into one of six mutually exclusive prepregnancy BMI/GDM groups: *1*) normal weight, no GDM; *2*) normal weight, GDM; *3*) overweight, no GDM; *4*) overweight, GDM; *5*) obese, no GDM; or *6*) obese, GDM. Maternal demographic, clinical, and anthropometric characteristics, as well as obstetrical and neonatal outcomes, were examined by BMI/GDM group. Associations between categorical variables and BMI/GDM group were assessed using χ^2 tests, with Fisher exact test used for cell variables with cell counts <10. Differences among mean continuous variables by BMI/GDM group were evaluated using ANOVA with a standard Tukey honestly significant difference adjustment for multiple comparisons. Multiple logistic regression models were used to calculate adjusted odds ratios (AORs) and corresponding 95% CIs for association between BMI/GDM group and adverse outcomes. Model 1 for LGA was adjusted for maternal age, race/ethnicity, parity, infant sex, and presence of PE/E; maternal race/ethnicity, parity, and infant sex were included as covariates to control for residual confounding. Model 2 was additionally adjusted for gestational weight gain. AORs from these models were used to calculate the partial population-attributable fraction (PAF) for each group (24,25). In brief, the partial PAF takes into account both the prevalence and the adjusted odds of a given risk factor and is interpreted as the proportion of cases that would be prevented if it were possible to eliminate the risk factor from the population. In order to examine the differential effect of gestational weight gain for each group, we calculated the prevalence of LGA in each of the six BMI/GDM groups per 10 pounds of weight gain. All analyses were performed with SAS version 9.2 (SAS Institute, Cary, NC).

RESULTS—The sample initially included 10,459 women, of whom 2,516 (24.1%) met the IADPSG criteria for GDM. We excluded 624 women who received treatment for hyperglycemia in pregnancy per institutional standards (6.0% of the population; 24.8% of all women with IADPSG-defined GDM). The remaining cohort of 9,835 untreated women had a mean age of 28.9 ± 6.0 years; 74.7% were Hispanic, and 31.7% were overweight and 27.8% obese. Of the 1,892 women (19.3%) with IADPSG-defined GDM, 32.9% were also overweight and 43.3% obese. Overall, overweight and obese women were of greater parity, more likely to be Hispanic or black, and had a higher prevalence of GDM than normal-weight women (Table 1). Moreover, the average BMI within each BMI group tended to be higher for women with GDM compared with their non-GDM counterparts (Table 1).

Although overweight and obese women had, on average, less absolute weight gain during pregnancy than their normal-weight counterparts, they were more likely to exceed the upper limit of

Table 1—*Maternal characteristics by prepregnancy BMI and GDM status*

	Normal weight	Normal weight	Overweight	Overweight	Obese	Obese	
	No GDM	GDM	No GDM	GDM	No GDM	GDM	*P* value*
n	3,535 (35.9)	449 (4.6)	2,493 (25.4)	623 (6.3)	1,915 (19.5)	820 (8.3)	
Mean maternal age ± SD (years)	27.6 ± 6.1†,§,‖,¶,#	30.2 ± 6.1‡,§,¶,#	29.0 ± 5.8‡,†,‖,#	30.9 ± 5.7‡,§,¶	29.1 ± 5.5‡,†,‖,#	31.4 ± 5.3‡,†,§,¶	<0.001
Race/ethnicity (%)							<0.001
Non-Hispanic white	270 (7.6)	32 (7.1)	159 (6.4)	34 (5.5)	105 (5.5)	66 (8.0)	
Black	329 (9.3)	34 (7.6)	246 (9.9)	42 (6.7)	273 (14.3)	79 (9.6)	
Hispanic	2,506 (70.9)	293 (65.3)	1,944 (78.0)	491 (78.8)	1,472 (76.9)	637 (77.7)	
Asian/Pacific Islander	392 (11.1)	85 (18.9)	118 (4.7)	53 (8.5)	42 (2.2)	27 (3.3)	
Other	22 (0.6)	3 (0.7)	17 (0.7)	0 (0)	8 (0.4)	6 (0.7)	
Unknown	16 (0.4)	2 (0.4)	9 (0.4)	3 (0.5)	15 (0.8)	5 (0.6)	
Parity (%)							<0.001
0	1,910 (54.0)	225 (50.1)	1,027 (41.2)	227 (36.4)	703 (36.7)	279 (34)	
≥1	1,580 (44.7)	222 (49.4)	1,430 (57.4)	387 (62.1)	1,178 (61.5)	534 (65.1)	
Unknown	45 (1.3)	2 (0.4)	36 (1.4)	9 (1.4)	34 (1.8)	7 (0.9)	
Mean BMI ± SD (kg/m^2)	22.1 ± 1.9†,§,‖,¶,#	22.7 ± 1.8‡,§,‖,¶,#	27.2 ± 1.4‡,†,¶,#	27.5 ± 1.5‡,†,¶,#	35.0 ± 4.5‡,†,§,‖,#	36.2 ± 5.5‡,†,§,‖,¶	<0.001
Mean weight gain ± SD (pounds)	32.6 ± 11.6§,‖,¶,#	34.3 ± 12.3§,‖,¶,#	29.7 ± 13.8‡,†,¶,#	29.1 ± 14.4‡,†,¶,#	22.1 ± 15.2‡,†,§,‖,#	23.9 ± 15.2‡,†,§,‖,¶	<0.001
Exceeded IOM weight gain limitations (%)	1,279 (36.2)	184 (41.0)	1,528 (61.3)	349 (56.0)	1,004 (52.4)	475 (57.9)	<0.001
Mean gestation at OGTT ± SD (weeks)	26.9 ± 2.8	27.0 ± 3.1	26.7 ± 2.6	26.9 ± 3.3	26.8 ± 2.9	26.6 ± 3.5	0.019
Mean OGTT values ± SD (mg/dL)							
Fasting (h)	79.9 ± 5.5†,§,‖,¶,#	92.1 ± 10.0‡,§,¶,#	81.5 ± 5.5‡,†,‖,¶,#	92.9 ± 7.4‡,§,¶,#	82.6 ± 5.4‡,†,§,‖,#	95.3 ± 8.2‡,†,§,‖,¶	<0.001
1	119.4 ± 26.5†,§,‖,¶,#	158.8 ± 30.9‡,§,¶,#	127.1 ± 25.8‡,†,‖,¶,#	162.9 ± 28.7‡,§,¶	129.8 ± 24.9‡,†,§,‖,#	163.4 ± 28.5‡,†,§,¶	<0.001
2	99.9 ± 20.0†,§,‖,¶,#	129.3 ± 27.1‡,§,¶,#	104.9 ± 19.8‡,†,‖,#	128.6 ± 25.2‡,§,¶,#	105.2 ± 18.2‡,†,‖,#	124.9 ± 23.7‡,†,§,‖,¶	<0.001
Prenatal smoking (%)							0.529
No	3,348 (94.7)	429 (95.5)	2,370 (95.1)	591 (94.9)	1,797 (93.8)	764 (93.2)	
Yes	148 (4.2)	17 (4.1)	94 (3.8)	25 (4.0)	90 (4.7)	46 (5.6)	
Unknown	39 (1.1)	3 (0.7)	29 (1.2)	7 (1.1)	28 (1.5)	10 (1.2)	

Data are *n* (%) unless otherwise indicated. *P values based on χ^2 test, with Fisher exact test used for variables with any cell count <10, or ANOVA adjusted with Tukey honestly significant difference for continuous variables, $P < 0.05$. ‡Significantly different than normal weight, no GDM. †Significantly different than normal weight, GDM. §Significantly different than overweight, no GDM. ‖Significantly different than overweight, GDM. ¶Significantly different than obese, no GDM. #Significantly different than obese, GDM.

weight gain for their BMI recommended by the IOM (22) (Table 1). Mean prepregnancy BMI and absolute gestational weight gain, as well as the proportion of women exceeding weight gain limits set by the IOM, were significantly higher for obese women with GDM compared with their non-GDM counterparts (Table 1). Among women who did not develop GDM, those who were overweight had significantly higher mean fasting, 1-h, and 2-h OGTT glucose levels than normal-weight women; those who were obese had significantly higher fasting and 1-h levels than overweight women (Table 1). Among women who developed GDM, those who were overweight did not have significantly higher OGTT glucose values than normal-weight women. However, obese women with GDM had significantly higher mean fasting and 1-h glucose than normal-weight women, and significantly higher mean fasting glucose than overweight women with GDM (Table 1).

The prevalence of most adverse obstetrical and neonatal outcomes tended to increase with increasing BMI among women with and without GDM (Supplementary Table 1). Among women without GDM, the proportion of LGA infants born to overweight women was significantly higher than the proportion born to those of normal weight ($P < 0.001$) (Fig. 1). Likewise, the prevalence of LGA was higher in infants born to obese women without GDM than to their overweight ($P = 0.050$) or normal-weight ($P < 0.001$) counterparts (Fig. 1). A similar trend in increasing prevalence of LGA by increasing prepregnancy BMI was observed for women with GDM, with obese GDM women having a significantly higher proportion of LGA infants than either overweight ($P = 0.005$) or normal-weight ($P < 0.001$) women with GDM (Fig. 1). A similar relationship between increasing prepregnancy BMI and increasing mean ponderal index, for women with and without GDM, was also observed (Supplementary Fig. 1).

The adjusted odds of having an LGA infant increased with increasing BMI among women who did not develop GDM. After controlling for all demographic and clinical confounders, including total gestational weight gain, overweight women without GDM were 1.65 times as likely (95% CI 1.36–2.01), and obese women without GDM were 2.63 times as likely (2.13–3.24), to have an LGA infant as their normal-weight counterparts (Table 2). These increases in adjusted odds of having an LGA infant due to overweight and obesity are concomitant with substantial population-attributable risk. Among women without GDM, prepregnancy overweight and obesity each accounted for 8.8 and 12.8% of LGA infants, respectively (Table 2). Thus, among women who did not develop GDM, ~21.6% of LGA was attributable to maternal overweight and obesity combined.

In the absence of overweight or obesity, GDM was associated with higher odds of having an LGA infant. After accounting for demographic and clinical confounders, as well as total gestational weight gain, normal-weight women with GDM were 1.96 times as likely (95% CI 1.43–2.68) to have an LGA infant as their non-GDM counterparts (Table 2). Thus, among normal-weight women, those who developed GDM were nearly twice as likely to have an LGA infant as those who did not. However, due to the somewhat small

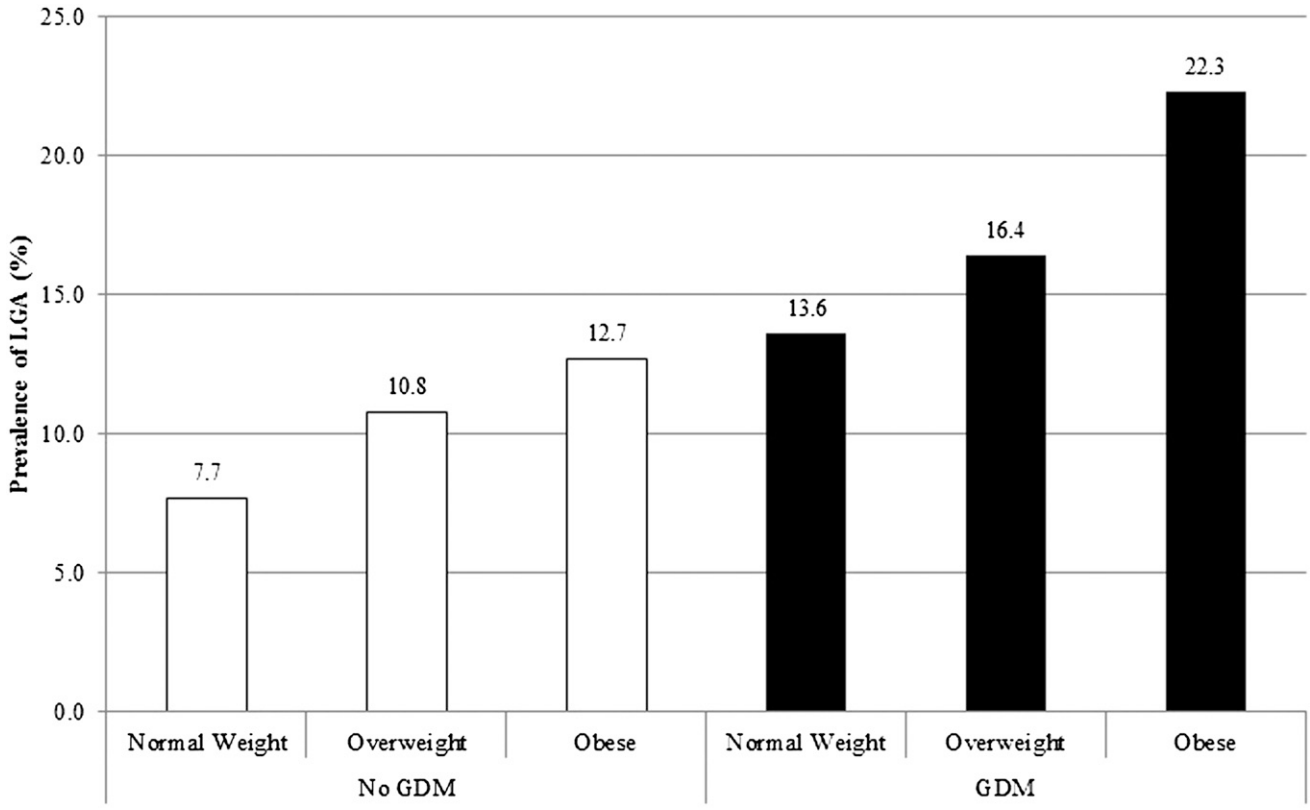

Figure 1—*Prevalence of LGA infants for each prepregnancy BMI/GDM group. White bars, no GDM; black bars, GDM.*

Table 2—*AORs and partial PAF for LGA infants*

	AOR	95% CI	Partial PAF (%)	95% CI (%)
Model 1*				
Normal weight, no GDM	Reference	—	—	—
Normal weight, GDM	2.10	1.54–2.86	3.1	2.1–4.2
Overweight, no GDM	1.54	1.27–1.87	8.0	5.0–10.9
Overweight, GDM	2.56	1.97–3.33	5.9	4.4–7.3
Obese, no GDM	1.85	1.52–2.27	9.6	7.3–11.8
Obese, GDM	4.08	3.27–5.09	14.9	12.7–17.0
Model 2‡				
Normal weight, no GDM	Reference	—	—	—
Normal weight, GDM	1.96	1.43–2.68	2.9	1.7–4.1
Overweight, no GDM	1.65	1.36–2.01	8.8	5.9–11.6
Overweight, GDM	2.77	2.12–3.63	6.2	4.8–7.7
Obese, no GDM	2.63	2.13–3.24	12.8	12.1–13.6
Obese, GDM	5.47	4.34–6.90	17.1	14.8–19.4

*Odds for LGA were adjusted for maternal age, race/ethnicity, parity, infant sex, and presence of PE/E. ‡Odds for LGA were adjusted for maternal age, race/ethnicity, parity, infant sex, presence of PE/E, and weight gain during pregnancy.

proportion of normal-weight women who develop GDM, only 2.9% of LGA was attributable to GDM among these women.

Women who were overweight or obese prior to pregnancy and developed GDM had substantially higher odds of having an LGA infant than overweight or obese women without GDM, compared with normal-weight, non-GDM women. Overweight women with GDM were 2.77 times as likely (95% CI 2.12–3.63), and obese women with GDM were 5.47 times as likely (4.34–6.90), to have an LGA infant as normal-weight women without GDM (Table 2). Among women with GDM, 6.2% of LGA cases were attributable to prepregnancy overweight and 17.1% to obesity. Thus, the combination of being overweight or obese prior to pregnancy and having GDM accounted for ~23.3% of LGA infants (Table 2).

To determine the extent to which gestational weight gain may differentially contribute to LGA prevalence among the six groups, we examined the proportion of LGA infants born to women in each of the six prepregnancy BMI/GDM groups per 10 pounds of weight gain (Fig. 2). Within each group, there was a monotonic increasing trend for higher prevalence of LGA with increasing gestational weight gain. The prevalence of LGA was highest for obese women with GDM compared with the other groups of women, at all levels of weight gain (Fig. 2). Although the prevalence of LGA was similar for overweight and normal-weight women with GDM at levels of gestational weight gain <40 pounds, a significantly higher proportion of LGA infants were born to overweight GDM women who gained ≥40 pounds of weight during pregnancy compared with normal-weight women with GDM who gained the same amount (36.8 vs. 22.0%; $P = 0.013$). Among women without GDM, there were no significant differences in the proportion of

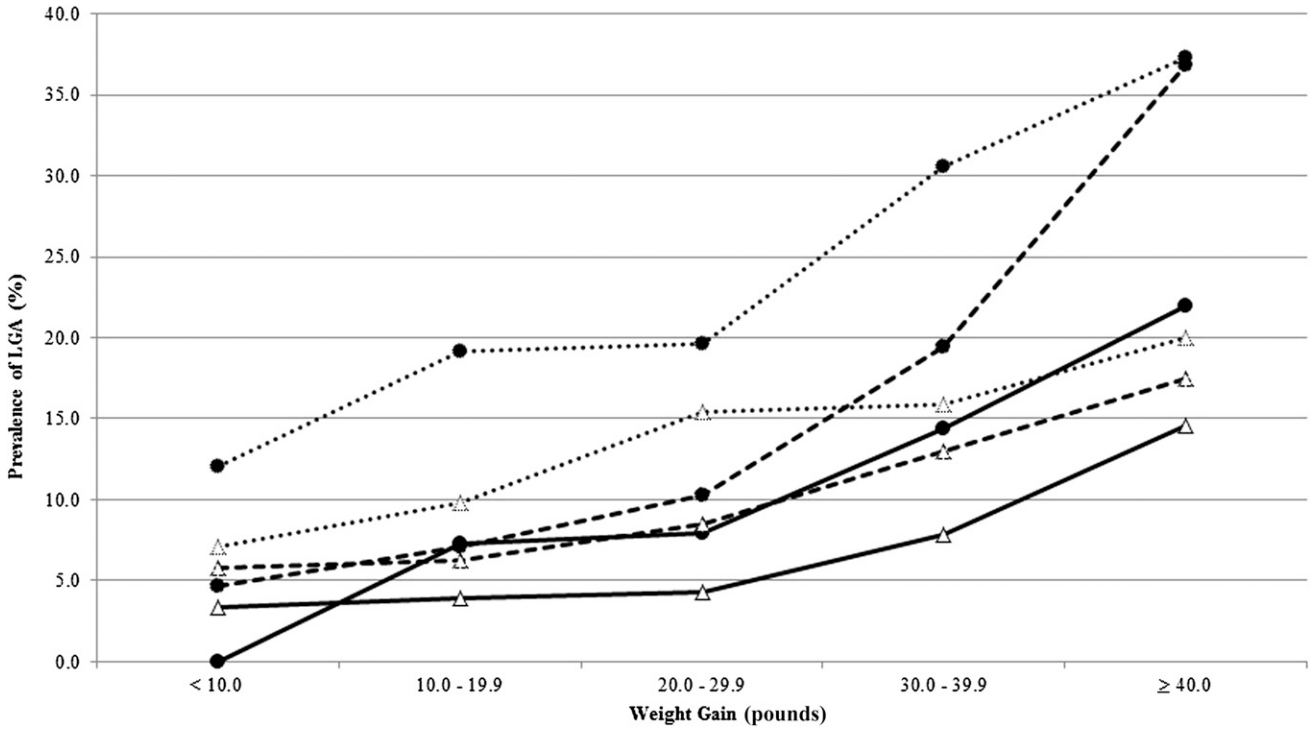

Figure 2—*Prevalence of LGA infants among each prepregnancy BMI/GDM group, per 10 pounds of gestational weight gain. White triangles, no GDM; black circles, GDM; solid lines, normal weight; dashed lines, overweight; dotted lines, obese.*

LGA infants born to overweight versus normal-weight women, at any level of weight gain. Because overweight and obese women who developed GDM delivered, on average, a few days earlier than women without GDM, we also examined the proportion of LGA with respect to the rate of weight gain (average pounds per week). The trends in average weight gain per week of gestation among the six BMI/GDM groups were similar to those of absolute weight gain shown in Fig. 2 (data not shown).

CONCLUSIONS—In an unselected, untreated obstetric population in which ~60% of women were overweight or obese and 19% had GDM by IADPSG criteria, ~75% of women who developed GDM were overweight or obese at the start of their pregnancies. Among women who did and did not develop GDM, there was an increasing trend in fasting and 1-h glucose levels for normal weight, overweight, and obese women, respectively. Overweight or obese women were also more likely to exceed the upper limit of IOM-recommended gestational weight gain for BMI, regardless of GDM status.

The prevalence of LGA increased with increasing prepregnancy BMI among women with and without GDM, with similar trends observed for ponderal index. After accounting for demographic and clinical confounders as well as gestational weight gain, maternal overweight and obesity increase risk for fetal overgrowth in the presence or absence of GDM, and the effects appear to be additive. Relative to normal-weight women without GDM, overweight and obese women with GDM had substantially higher adjusted odds of having an LGA infant than overweight or obese non-GDM women. Consistent with these findings, Catalano et al. (9) recently reported higher adjusted odds of LGA for obese versus nonobese women, among women with and without GDM. Our stratification of overweight and obese groups of women also allowed us to detect increased risk of LGA for overweight compared with normal-weight women.

Because of the large proportion of women that began their pregnancies overweight or obese, we found that 21.6% of LGA infants were attributable to maternal overweight and obesity among non-GDM women. Likewise, overweight and obesity jointly accounted for 23.3% of LGA infants born to women that developed GDM. Yet, among women of normal prepregnancy weight, only 2.9% of LGA was attributable to GDM. Ricart et al. (26) also examined the relative contribution of prepregnancy BMI and hyperglycemia in pregnancy, defined by National Diabetes Data Group (NDDG) criteria, to the development of adverse maternal and perinatal outcomes in a cohort of 9,270 Spanish women. As we did in the current study, these investigators found that overweight and obese women, both with and without GDM, had significantly higher odds of having a large infant than those of normal weight. Additionally, they reported that 16.4% of macrosomia and 13.4% of LGA infants were attributable to overweight and obesity in non-NDDG GDM women, whereas NDDG GDM among normal-weight women only accounted for 2.1% of macrosomia and <1% of LGA (26). Although women with NDDG-defined GDM in the Ricart et al. study were treated for hyperglycemia during pregnancy, which may have reduced their odds of having an LGA infant, the trends observed were similar to ours. Taken together, these findings suggest that although overweight and obesity in the absence of GDM may have a substantial impact on the development of adverse maternal and perinatal outcomes such as LGA, GDM in the absence of overweight or obesity does not account for the preponderance of these cases.

We also observed an increasing proportion of LGA with incremental increases in gestational weight gain among all groups of women. Consistent with the present report, previous studies adjusting for BMI (27) or examining data within BMI categories (28–31) have reported a positive association between gestational weight gain and LGA, as well as other adverse outcomes (27–31). Additionally, the effect of high gestational weight gain among overweight women, specifically, varied by GDM status. Among women without GDM, the proportion of LGA infants born to overweight compared with normal-weight women was similar at high levels of gestational weight gain, but among those who developed GDM in pregnancy, the proportion born to overweight women was substantially and significantly higher than the proportion born to those of normal weight when weight gain exceeded 40 pounds.

There are several limitations to the current study. Although mean ponderal index was significantly higher for infants classified as LGA, specific measures of fetal or neonatal fat mass were not available in the EHR, which precluded us from determining which of the infants classified as LGA were constitutionally large, had excessive body fat, or both. Additionally, the exclusion of women with more severe hyperglycemia, who were subsequently treated and excluded from these analyses, may have resulted in slight attenuation of the PAFs for overweight and obese GDM women. The modest number of normal-weight women with GDM limited our power to detect significant differences among the groups for outcomes with very low prevalence. Lack of information on several maternal behaviors and family history of diabetes also prevented us from controlling for additional confounders, which may have affected some outcomes.

Despite these limitations, our study has several strengths. We were able to retrospectively apply the recent IADPSG criteria to OGTT results from earlier years so that we could base our case definition on laboratory test results and not rely on ICD-9-CM codes for the identification of women with GDM. Moreover, the use of EHRs in a population with early initiation of prenatal care and sonographic confirmation of dates likely enhanced the accuracy of dating and of assessment of gestational weight gain. Finally, women whose 2-h, 75-g OGTT results met or exceeded the IADPSG criteria for GDM diagnosis but fell below our institutional criteria for treating hyperglycemia in pregnancy received only standard care during pregnancy. This enabled estimation of the associations between maternal glycemia and pregnancy outcomes not confounded by treatment.

In summary, our data suggest that prepregnancy overweight and obesity substantially contribute to the prevalence of LGA, as well as other adverse outcomes, in women who never develop IADPSG-defined GDM. Additionally, the effects of GDM and maternal BMI appear to be additive, but GDM in the absence of overweight or obesity accounts for only a small proportion of LGA cases. Maternal overweight and obesity is far more prevalent than GDM and can be identified before pregnancy, among women who may be planning for pregnancy, or at the first prenatal visit for those with unplanned pregnancies. Interventions that effectively help overweight or obese women lose weight before pregnancy and/or control weight gain during pregnancy, regardless of GDM status, have the potential to reach far more women at risk for having an LGA infant and other adverse outcomes.

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M.H.B. researched the data, wrote the manuscript, and contributed to discussion. D.A.S., A.H.X., and J.M.L. reviewed and edited the manuscript and contributed to discussion. M.H.B. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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