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RESEARCH ARTICLE

Combined Effect of Maternal Obesity and Diabetes on Excessive Fetal Growth: Pregnancy Risk Assessment Monitoring System (PRAMS), United States, 2012−2015

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Introduction: Obesity and dysregulation in glucose metabolism are risk factors for excessive fetal growth, but their combined effects are not often examined in a single study.

Methods: Data from the Centers for Disease Control and Prevention's Pregnancy Risk Assessment Monitoring System Phase 7 (2012−2015) were used. Logistic regression was used to investigate the association between maternal prepregnancy BMI and pre-existing diabetes/gestational diabetes on the odds of delivering a large-for-gestational-age infant or an infant with macrosomia.

Results: Complete data for 128,199 singleton births were used. The proportions of large-for-gestational-age infants and infants with macrosomia increased with the degree of obesity ($p<0.001$) and were higher in women with diabetes than in those without ($p<0.001$). Compared with the AOR among normal-weight women, the AOR of delivering large-for-gestational-age infants and infants with macrosomia among women with morbid obesity (BMI$\geq$40) were 2.82 ($p<0.001$) and 2.67 ($p<0.001$), respectively. Compared with the AOR among nondiabetic women, the AOR of delivering a large-for-gestational-age infant was 1.88 ($p<0.001$) among those with pre-existing diabetes and 1.49 ($p<0.001$) among those with gestational diabetes. Except for the underweight group, women with pre-existing diabetes were nearly twice as likely to deliver a large-for-gestational-age infant as those with similar BMI without diabetes. Women with morbid obesity and gestational diabetes were twice as likely to have a large-for-gestational-age infant and an infant with macrosomia as nondiabetic women with normal BMI.

Conclusions: We have shown that when maternal obesity and diabetes, particularly pre-existing diabetes, occur together, the risk of delivering large-for-gestational-age and macrosomia increases significantly. Our findings call for public health attention to address maternal obesity and diabetes to minimize suboptimal fetal growth.

INTRODUCTION

The rise in obesity over the last 3 decades has contributed to many health complications at the individual level, burdening many countries' health systems and economies. The latest data from the Centers for

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Disease Control and Prevention (CDC) shows that >4 in 10 adults aged ≥20 years in the U.S. are obese (42%).[1] Furthermore, it has been predicted that by the year 2030, nearly 1 in 2 adults will have obesity (49%), with severe obesity projected to become the most common BMI category among women (28%).[2] Numerous studies have reported strong associations between maternal obesity and other chronic diseases such as hypertension, cancers, cardiovascular diseases, and diabetes.[3−5] For instance, the risk of developing gestational diabetes is 9 times higher in women who are obese than in normal-weight women of similar age.[6] Obesity, when it occurs together with pre-existing diabetes or gestational diabetes, increases the risk for cesarean section and maternal morbidity.[7−9] In addition, women with gestational diabetes are at a higher risk of recurrence of gestational diabetes and developing Type 2 diabetes later in life.[10,11]

Furthermore, obesity increases the risk of impaired glucose metabolism during pregnancy, causing excessive fetal growth, including large for gestational age (LGA) and macrosomia.[12−14] *LGA* is defined as birthweights greater than the 90th percentile birth weight for their gestational age, race, and fetal sex, and CDC Pregnancy Risk Assessment Monitoring System (PRAMS) classified infants as macrosomic if their birth weight was >4,500 g.[15] *Macrosomia* is commonly defined as birth >4,000 g or 4,500 g.[15,16] LGA and macrosomia increase the risk for infant shoulder dystocia, clavicle fractures, and death.[17−20] Infants with macrosomia are also more likely to become children with overweight/obesity[17,18,21] and to have large babies later in life.[6,17]

Although most studies often focus on the individual relationship, such as obesity and LGA or macrosomia or gestational diabetes and macrosomia,[22,23] data on the combined effect of obesity and diabetes on LGA and macrosomia are limited. Thus, few studies have simultaneously compared the independent and additive impact of obesity and diabetes on the risk of delivering an LGA infant or an infant with macrosomia. Furthermore, most studies often involved fewer participants and focused on gestational diabetes, not pre-existing diabetes. Because pre-existing diabetes and gestational diabetes could have different effects on clinical comorbidities such as chronic hypertension, pre-eclampsia, delivery-related risks, and birth weight,[14,22,24−26] it is important to examine how both conditions contribute to the risk of LGA and macrosomia. This study aimed to evaluate the independent and combined effect of prepregnancy obesity and diabetes on the risk of LGA and macrosomia among singleton live births in the U.S.

METHODS

Study Population

We used data obtained from CDC's PRAMS, a survey designed to evaluate the maternal health of U.S. women and infants. Specifically, we used PRAMS Phase 7 (2012−2015) data with analysis restricted to singleton live births. Related questions from PRAMS Phase 7 are available from the CDC website,[27] and detailed methodology for PRAMS study design is reported elsewhere.[28,29] Using standardized data collection methodology across states, PRAMS data collection is conducted by state, territorial, tribal, or local health departments in partnership with CDC's Division of Reproductive Health. Birth certificate records are used in each participating jurisdiction to select a representative sample of all women who delivered a live-born infant. Annual state sample sizes range from approximately 1,000 to 3,000 women. Each participating state collects state-specific, population-based data on maternal attitudes and experiences before, during, and shortly after pregnancy. The PRAMS methodology and protocol are reviewed and approved by CDC IRB.[29] The primary outcome of this study was the risk of delivering an LGA infant or an infant with macrosomia given maternal BMI and diabetes status.

Measures

We examined CDC PRAMS data explicitly focusing on maternal sociodemographic and health information before and during pregnancy and after delivery. Specifically, maternal prepregnancy BMI, pre-existing diabetes, gestational diabetes, and birthweight of the infants were examined. Infants with birthweights greater than the 90th percentile were classified as LGA. Birthweight >4,000 g was classified as macrosomic.

The analysis included the mother's age (<25, 25−29, 30−34, 35−39, and 40+ years), parity (0,1, or 2+), newborn sex, race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, other [Asian, American Indian/Alaska Native, Pacific Islander, or multiple]), mother's education (<12, 12, or >12 years), marital status (married or not married), initiation of prenatal care (first trimester, after the first trimester [late], or not at all), and the number of prenatal care visits and gestational weight gain in the most recent pregnancy. Subjects were characterized by maternal prepregnancy BMI, divided into underweight (BMI<18.5 kg/m^2), normal (BMI=18.5−24.9 kg/m^2), overweight (BMI=25.0−29.9 kg/m^2), and obese (obese Class I, BMI=30.0−34.9 kg/m^2; obese Class II, BMI=35.0−39.9 kg/m^2; and obese Class III, BMI≥40 kg/m^2).[30,31] *Pre-existing diabetes* was defined as diabetes

reported before the recent pregnancy, whereas gestational diabetes occurred only during the pregnancy.

Statistical Analysis

Descriptive characteristics for infants and mothers are presented as frequencies (unweighted) and weighted percentages (% [SE]) for categorical variables and (mean [SE]) for continuous variables. A chi-square test of independence was performed to determine whether there was a significant association between maternal or infant characteristics with BMI status or birth outcomes (LGA versus non-LGA and macrosomic versus nonmacrosomic infants). Weighted logistic regression models were fitted to examine the relationships between maternal BMI and diabetes and the odds of delivering an LGA infant or an infant with macrosomia. The results were expressed as ORs and AORs with corresponding 95% CIs. The weighted logistic regressions adjusted for maternal age, race/ethnicity, mother's education, marital status, parity, prenatal care (initiation and the number of prenatal care visits), health insurance, gestational weight gain, and newborn sex. Interaction terms between diabetes status and LGA (and macrosomia) were included in the respective models. Statistical analyses were performed with Stata (Version 14; Stata Corp., College Station, TX) with sample weights and design variables to account for the complex sample design. Statistical comparisons were evaluated at a 2-sided significance level, and $\alpha=0.05$ was considered statistically significant.

RESULTS

The total data consisted of 147,747 subjects, where 6,689 subjects had missing records for BMI. Among the 141,058 participants with BMI records, we selected subjects with nonmissing records for diabetes status, LGA, macrosomia, and singleton live births data for the analysis ($n=128,199$, i.e., weighted $n=6,690,013$). The mean (SD) for BMI for underweight, normal weight, overweight, and obese (Classes I, II, and III) were 17.5 (0.9), 22.0 (1.7), 27.2 (1.4), 32.2 (1.4), 37.2 (1.4), and 44.9 (4.8), respectively. The proportion of participants in underweight, normal weight, overweight, and obese (Classes I, II, and III) categories were respectively 4.0%, 49.1%, 24.4%, 12.4%, 6.0%, and 4.1%. The proportions of women that reported pre-existing and gestational diabetes were 2.2% and 5.5%, respectively (data not shown). Demographic data and clinical information for the study population are presented in Table 1. BMI was strongly associated with women's age ($p<0.001$), race/ethnicity ($p<0.001$), education ($p<0.001$), marital status ($p<0.001$), parity ($p<0.001$), and prenatal care (number

of prenatal care visits [$p<0.001$]), health insurance at delivery ($p<0.001$), and gestational weight gain ($p<0.001$). Diabetes status (both pre-existing and gestational diabetes) was also associated with BMI ($p<0.001$) (Table 1).

Table 2 shows the frequencies of LGA or macrosomia in newborn infants by maternal and infant characteristics. First, we looked at the single effect of the degree of obesity and diabetes status on LGA or macrosomic infant delivery. The proportions of newborns classified as LGA and macrosomic are 10.0% and 8.9%, respectively. If the cut off for classifying macrosomia were changed from 4,000 g to 4,500 g, the proportion of infants with macrosomia would be much smaller at 1.2% (Appendix Table 1, available online, for details). Both LGA and macrosomia have a statistically significant relationship ($p<0.001$) with maternal age, BMI, parity, and the total number of prenatal care visits. The proportion of women delivering an LGA infant and an infant with macrosomia increased with the degree of obesity ($p<0.001$). The weighted prevalence of LGA and macrosomia by BMI class and diabetes status are presented in Table 3. The prevalence of newborns classified as LGA increased from 3.6% (underweight), 7.5% (normal weight), 13.6 % (obese Class I), to 16.9% (obese Class III). The prevalence of newborns classified as macrosomic increased from 3.1% (underweight), 7.3% (normal weight), 11.3% (obese Class I), to 13.5% in obese Class III. Women with pre-existing diabetes are at an elevated risk for delivering LGA (19.9% vs 9.3%, $p<0.001$) and macrosomic (12.6% vs 8.6%, $p<0.001$) infants compared with women without diabetes. Similarly, women with gestational diabetes showed higher risks for LGA (17.6% vs 9.3%, $p<0.001$) and macrosomia (12.2% vs 8.6%, $p<0.001$) than women without diabetes. Thus, an increase in BMI and the presence of either pre-existing or gestational diabetes results in a significantly increased risk for LGA and macrosomia.

Next, we calculated the odds of delivering an LGA infant or an infant with macrosomia by the degree of obesity and diabetes status, adjusting for demographic and prenatal care factors influencing birthweight (Table 4). Overall, the odds (AOR) of delivering an LGA infant or an infant with macrosomia increased with the degree of obesity. Compared with that of normal-weight mothers, the odds of LGA increased from 1.56 (overweight, $p<0.001$) to 2.82 (obese Class III, $p<0.001$). The odds of delivering an infant with macrosomia increased with obesity, from 1.49 (overweight, $p<0.001$) to 2.67 (obese Class III, $p<0.001$). The odds of delivering an LGA infant were higher in women with pre-existing diabetes than in those with gestational diabetes (AOR=1.03, $p=0.014$). Compared with women without diabetes, those with pre-existing

Table 1. BMI Status Across Maternal Characteristics Among Singleton Pregnancies From CDC PRAMS, U.S., 2012–2015

Characteristics	Underweight (n=5,670)	Normal (n=61,466)	Overweight (n=31,164)	Obese Class I (n= 16,398)	Obese Class II (n=7,762)	Obese Class III (n= 5,741)	p-Value	Unweighted count
Total, %	4.0 (0.1)	49.1 (0.2)	24.4 (0.2)	12.4 (0.3)	6.0 (0.2)	4.1 (0.1)		128,199
Maternal age, years, %							<0.001	
<25	5.9 (0.2)	49.8 (.5)	22.9 (0.4)	12.0 (0.3)	5.9 (0.2)	3.5 (0.2)		36,791
25–29	4.2 (0.2)	48.5 (0.4)	24.3 (0.3)	12.7 (0.3)	5.9 (0.2)	4.5 (0.2)		36,950
30–34	2.9 (0.1)	50.6 (0.4)	24.9 (0.4)	11.8 (0.3)	5.7 (0.2)	4.1 (0.2)		34,782
35–39	2.8 (0.2)	47.0 (0.6)	26.0 (0.5)	13.5 (0.3)	6.5 (0.3)	4.3 (0.2)		15,950
≥40	1.2 (0.2)	45.1 (1.3)	27.7 (1.2)	14.7 (0.9)	7.2 (0.6)	3.9 (0.4)		3,724
Maternal education, %							<0.001	
<12 years	6.0 (0.3)	44.1 (0.7)	26.2 (0.6)	13.9 (0.5)	5.9 (0.3)	3.9 (0.3)		17,099
12 years	4.7 (0.2)	43.9 (0.5)	24.0 (0.4)	14.7 (0.3)	7.3 (0.3)	5.4 (0.2)		31,842
>12 years	3.4 (0.1)	52.1 (0.3)	24.2 (0.2)	11.3 (0.2)	5.5 (0.1)	3.7 (0.1)		77,857
Marital status, %							<0.001	
Married	3.5 (0.1)	51.9 (0.3)	24.4 (0.2)	11.4 (0.2)	5.3 (0.1)	3.5 (0.1)		75,743
Other[a]	4.9 (0.2)	44.6 (0.4)	24.3 (0.3)	14.0 (0.3)	7.0 (0.2)	5.2 (0.2)		51,948
Parity, %							<0.001	
0	4.7 (0.1)	53.8 (0.3)	21.9 (0.3)	10.7 (0.2)	5.1 (0.1)	3.7 (0.1)		52,884
1	3.8 (0.1)	48.6 (0.4)	25.5 (0.3)	12.5 (0.3)	5.5 (0.2)	4.1 (0.2)		39,506
≥2	3.3 (0.2)	42.4 (0.4)	26.9 (0.4)	14.9 (0.3)	7.8 (0.3)	4.8 (0.2)		34,962
Infertility treatment, %							0.017	
No	4.0 (0.1)	49.0 (0.2)	24.5 (0.2)	12.4 (0.2)	5.9 (0.1)	4.1 (0.1)		104,888
Yes	3.0 (0.5)	51.8 (1.7)	21.3 (1.4)	11.2 (1.0)	7.5 (1.0)	5.2 (0.8)		1,713
First PNC visit, %							<0.001	
First trimester	3.7 (0.1)	49.4 (0.2)	24.5 (0.2)	12.3 (0.2)	6.0 (0.1)	4.1 (0.1)		106,592
After the first trimester	5.3 (0.3)	47.1 (0.7)	24.3 (0.6)	13.2 (0.5)	6.0 (0.4)	4.1 (0.3)		18,016
No PNC visits	8.2 (2.5)	49.3 (2.9)	22.2 (2.1)	10.0 (1.7)	4.1 (0.9)	6.1 (1.3)		1,065
Number of PNC visits, %							<0.001	
≤8	5.3 (0.3)	48.2 (0.6)	24.3 (0.5)	12.0 (0.4)	6.2 (0.3)	3.9 (0.2)		26,569
9–11	4.1 (0.2)	50.8 (0.4)	23.7 (0.3)	12.2 (0.3)	5.5 (0.2)	3.6 (0.2)		39,090
≥12	3.5 (0.1)	48.4 (0.3)	24.8 (0.3)	12.7 (0.2)	6.2 (0.2)	4.5 (0.1)		57,962
Payment at delivery, Medicaid, %							<0.001	
No	3.7 (0.1)	50.9 (0.3)	24.3 (0.2)	11.9 (0.2)	5.5 (0.1)	3.6 (0.1)		95,380
Yes	5.0 (0.2)	42.7 (0.5)	24.6 (0.4)	14.2 (0.3)	7.6 (0.3)	5.9 (0.2)		32,600
Gestational weight gain (mean, SE), LB[b]	30.2 (0.3)	32.3 (0.1)	31.0 (0.1)	27.1 (0.2)	23.7 (0.3)	20.1 (0.4)	<0.001	123,278
Diabetes status, %							<0.001	
Nondiabetic	4.1 (0.1)	50.6 (0.2)	24.3 (0.2)	11.8 (0.1)	5.5 (0.1)	3.7 (0.1)		117,472
PD	3.3 (0.5)	36.7 (1.4)	24.0 (1.3)	17.8 (1.1)	9.2 (0.8)	9.0 (0.9)		3,094
GDM	2.3 (0.3)	29.0 (0.8)	25.6 (0.8)	21.2 (0.8)	12.1 (0.6)	9.7 (0.6)		7,633

Note: All reported percentages (SE) are weighted and design corrected. Each row is a category for participants' characteristics. The second to the seventh columns are the proportions for each BMI level in the category for the row. The eighth column gives *p*-values for chi-square (the design-based test values were used) between BMI levels and other characteristics. The last column shows the number of subjects in the category for each row.
[a]Asian, American Indian/Alaska Native, Pacific Islander, or multiple.
[b]The *p*-value for gestational weight gain was based on adjusted Wald test.
CDC, Centers for Disease Control and Prevention; GDM, gestational diabetes mellitus; lb, pound; PD, pre-existing diabetes; PNC, prenatal care; PRAMS, Pregnancy Risk Assessment Monitoring System.

diabetes had increased odds of delivering large infants (LGA: AOR=1.88, *p*<0.001; macrosomic: AOR=1.47, *p*=0.018). Likewise, compared with women without diabetes, women with gestational diabetes had increased odds of delivering large infants (LGA: AOR=1.49, *p*<0.001). Other independent predictors for delivering an LGA infant included maternal age (*p*<0.001), maternal

ethnicity/race (*p*=0.001), parity (*p*<0.001), gestational weight gain (*p*<0.001), and male sex of the infant. Independent predictors for delivering an infant with macrosomia were maternal ethnicity/race (*p*=0.001), parity (*p*<0.001), gestational weight gain (*p*<0.001), and male sex of the infant (*p*<0.001). The interaction of obesity and diabetes on the odds of LGA or macrosomia was

Table 2. LGA and Macrosomia in Newborn Infants by Maternal and Infant Characteristics Among Singleton Pregnancies From CDC PRAMS, 2012−2015

Characteristics	LGA (>90th percentile)			Macrosomia (birthweight >4,000 g)		
	No (n=115,696)	**Yes (n=12,503)**	*p*-Value	**No (n=117,184)**	**Yes (n=11,015)**	*p*-Value
%	90.0 (0.1)	10.0 (0.1)		91.1 (0.1)	8.9 (010)	
Maternal age, %			<0.001			<0.001
<25	92.9 (0.3)	7.1 (0.3)		93.6 (0.2)	6.4 (0.2)	
25−29	90.4 (0.2)	9.6 (0.2)		91.3 (0.2)	8.7 (0.2)	
30−34	88.4 (0.3)	11.6 (0.2)		89.4 (0.2)	10.6 (0.2)	
35−39	87.5 (0.4)	12.5 (0.4)		89.4 (0.4)	10.6 (0.4)	
≥40	87.1 (0.8)	12.9 (0.8)		90.4 (0.7)	9.6 (0.7)	
Maternal education, %			<0.001			<0.001
<12	91.4 (0.4)	8.6 (0.4)		93.2 (0.4)	6.8 (0.4)	
12	91.1 (0.3)	8.9 (0.3)		92.4 (0.3)	7.6 (0.3)	
≥12	89.4 (0.2)	10.6 (0.2)		90.3 (0.2)	9.7 (0.2)	
Marital status, %						
Married	89.2 (0.2)	10.8 (0.2)	<0.001	90.0 (0.2)	10.0 (0.2)	<0.001
Other	91.3 (0.2)	8.7 (0.2)		93.0 (0.2)	7.0 (0.2)	
Parity, %			<0.001			<0.001
0	92.8 (0.2)	7.2 (0.2)		92.7 (0.2)	7.3 (0.2)	
1	88.8 (0.2)	11.2 (0.2)		90.6 (0.2)	9.4 (0.2)	
≥2	87.3 (0.3)	12.7 (0.3)		89.3 (0.3)	10.7 (0.3)	
Infertility treatment, %			0.679			0.298
No	90.1 (0.1)	9.9 (0.1)		91.2 (0.1)	8.8 (0.1)	
Yes	89.6 (1.1)	10.4 (1.1)		90.1 (1.0)	9.9 (1.0)	
First PNC visit, %			0.012			0.008
First trimester	89.8 (0.1)	10.2 (0.1)		90.9 (0.1)	9.1 (0.1)	
After the first trimester	91.1 (0.4)	8.9 (0.4)		92.1 (0.4)	7.9 (0.4)	
No PNC visits	90.4 (1.5)	9.6 (1.5)		93.1 (1.4)	6.9 (1.4)	
Number of PNC visits, %			<0.001			<0.001
≤8	91.3 (0.3)	8.7 (0.3)		93.5 (0.3)	6.5 (0.3)	
9−11	90.7 (0.2)	9.3 (0.2)		92.3 (0.2)	7.7 (0.2)	
≥12	89.1 (0.2)	10.9 (0.2)		89.5 (0.2)	10.5 (0.2)	
Payment at delivery, Medicaid, %			0.002			<0.001
No	89.8 (0.2)	10.2 (0.2)		90.6 (0.1)	9.4 (0.1)	
Yes	90.8 (0.3)	9.2 (0.3)		93.0 (0.2)	7.0 (0.2)	
Sex, %			0.180			<0.001
Male	90.2 (0.2)	9.8 (0.2)		89.0 (0.2)	11.0 (0.2)	
Female	89.8 (0.2)	10.2 (0.2)		93.4 (0.2)	6.6 (0.2)	

All reported percentages are weighted and design corrected. Each row is a category for a characteristic. The second and third columns are the proportions for LGA category for the row. The fifth and sixth columns are the proportions for macrosomia. The fourth and seventh columns give *p*-values for chi-square (the design-based *p*-values were used) between LGA and macrosomia levels and other characteristics, respectively. *LGA* is defined as >90th percentile birthweight for gestational age, race, and fetal sex.
CDC, Centers for Disease Control and Prevention; LGA, large for gestational age; PNC, prenatal care; PRAMS, Pregnancy Risk Assessment Monitoring System.

significant only for the morbidly obese category (LGA: OR=2.15, *p*=0.001; macrosomia: OR=2.06, *p*=0.008).

DISCUSSION

In this large population-based study of pregnancy and prepregnancy health surveillance data, we evaluated the combined effect of maternal obesity and diabetes (pre-existing or gestational diabetes) on the risk of having an LGA infant or an infant with macrosomia. We found that the proportion of women with pre-existing and gestational diabetes increased with the degree of obesity. Maternal obesity and pre-existing and gestational diabetes were strong predictors of delivering an LGA infant or an infant with macrosomia. Obesity and diabetes had an

Table 3. Weighted Prevalence (%) of LGA and Macrosomia by BMI and Diabetes Status Among Singleton Pregnancies From CDC PRAMS, 2012−2015

Characteristics	LGA (>90th percentile), mean (SE)	Macrosomia (birthweight >4,000 g), mean (SE)	Unweighted count *n*
BMI			
Underweight (<18.5)	3.7 (0.4)	3.2 (0.4)	5,670
Normal weight (18.5−24.9)	7.5 (0.2)	7.3 (0.2)	61,466
Overweight (25.0−29.9)	11.6 (0.3)	10.1 (0.3)	31,164
Class 1 obesity (30.0−34.9)	13.6 (0.4)	11.3 (0.4)	16,396
Class 2 obesity (35.0−39.9)	15.7 (0.8)	12.1 (0.7)	7,762
Class 3 obesity (≥40.0)	16.9 (0.8)	13.5 (0.8)	5,741
Diabetes status			
Nondiabetic	9.3 (0.1)	8.6 (0.1)	117,472
PD	19.9 (1.3)	12.6 (0.9)	3,094
GDM	17.6 (0.1)	12.2 (0.6)	7,633

Note: Values are weighted percentages (95% CI) and took into account the design effect.
CDC, Centers for Disease Control and Prevention; GDM, gestational diabetes mellitus; LGA, large for gestational age; PD, pre-existing diabetes; PRAMS, Pregnancy Risk Assessment Monitoring System.

additive effect on the odds of delivering LGA infants or infants with macrosomia.

In a recent study using U.S. natality data covering the period 1971−2017, the incidence of macrosomia varied considerably depending on the cut off birthweight used to classify birthweight.[32] The authors reported 8.14% (Grade 1 macrosomia: birthweight=4,000−4,499 g), 1.32% (Grade 2 macrosomia: birthweight=4,500−4,999 g), and 0.16% (Grade 3 macrosomia≥5,000 g). These estimates are consistent with the findings from our study. Therefore, the estimated proportion of macrosomia in the population could vary considerably on the basis of the cut off (e.g., >4,000 g vs 4,500 g) used to define the infant weight status. Although previous studies have shown that maternal obesity and gestational diabetes were associated with an increased risk of having an LGA infant or an infant with macrosomia,[26,33−40] data on the combined effect are limited. This study provided evidence of the combined effects of maternal obesity and pre-existing and gestational diabetes on the odds of having an LGA infant and an infant with macrosomia. Furthermore, although previous studies often focus on either pre-existing diabetes or gestational diabetes, we simultaneously compared LGA and macrosomia across different BMI categories, including the degree of adiposity by diabetes types, providing stronger evidence than what is reported in most studies. Our results showed that the risk for both LGA and macrosomia increased with the degree of adiposity (obesity grade). The risk of LGA and macrosomia were higher for mothers with pre-existing and gestational diabetes than for those without diabetes. Our results show that the risk of having an LGA infant and an infant with

macrosomia was remarkably higher in women with morbid obesity (BMI=40+) with either pre-existing or gestational diabetes. Overall, the result showed that morbid obesity poses a higher risk for LGA and macrosomia than pre-existing or gestational diabetes alone. Because obesity is directly associated with a dysregulation in glucose metabolism (and exacerbated during pregnancy), this may explain why women with morbid obesity with diabetes were more likely to have LGA infants and infants with macrosomia than those with either condition alone (i.e., women with obesity without diabetes or normal weight women with diabetes).

Mechanistically, women with diabetes are more likely to have large babies because of the abnormally higher glucose concentration available to the fetus. In gestational diabetes, there is poor maternal glucose utilization, leading to more glucose crossing the placenta into the fetal circulation.[41] Fetal hyperinsulinemia occurs to correct the high glucose concentration by stimulating excessive fetal anabolism and growth.[26,42] It appears that the effects of maternal gestational diabetes continue to have a negative impact beyond infancy. For instance, it has been shown that infants born to mothers with gestational diabetes are at an increased risk of becoming obese at a younger age (adolescent) and are more likely to develop Type II diabetes in later life—creating a vicious cycle of diabetes.[43] Thus, maternal diabetes during pregnancy can lead to transgenerational transmission of diabetes risk.[26] A classic example of intergeneration transmission of birthweight has been illustrated by a strong correlation between birthweights of grandmothers and their granddaughters on the basis of large hospital

Table 4. Association Between BMI and Diabetes Status With LGA and Macrosomia Among Singleton Pregnancies From CDC PRAMS, 2012−2015

	LGA		Macrosomia (birthweight >4,000 g)	
Characteristics	**OR (95% CI)**	**AOR (95% CI)[a]**	**OR (95% CI)**	**AOR (95% CI)[a]**
BMI				
Underweight (<18.5)	0.47 (0.37, 0.61)***	0.54 (0.42, 0.70)***	0.41 (0.32, 0.53)**	0.53(0.41,0.68)**
Normal weight (18.5−24.9)	ref	ref	ref	ref
Overweight (25.0−29.9)	1.61 (1.50, 1.73)***	1.56 (1.44, 1.70)***	1.42 (1.32, 1.53)***	1.49 (1.37, 1.62)***
Class 1 obesity (30.0−34.9)	1.94 (1.79, 2.12)***	2.01 (1.82, 2.22)***	1.62 (1.48, 1.77)***	1.88 (1.69, 2.08)***
Class 2 obesity (35.0−39.9)	2.29 (2.03, 2.58)***	2.61 (2.24, 3.05)***	1.75 (1.52, 2.01)***	2.28 (1.91, 2.72)***
Class 3 obesity (≥40.0)	2.51 (2.21, 2.85)***	2.82 (2.42, 3.29)***	1.99 (1.73, 2.29)***	2.67 (2.27, 3.14)***
Diabetes status				
Nondiabetic	ref	ref	ref	ref
PD	2.43 (2.07, 2.86)***	1.88 (1.41, 2.50)***	1.54 (1.30, 1.82)***	1.47 (1.07, 2.01)*
GDM	2.09 (1.88, 2.32)***	1.49 (1.20, 1.86)***	1.49 (1.32, 1.68)***	1.10 (0.85, 1.41)
BMI and diabetes interaction				
Normal weight nondiabetic	—	ref		ref
Underweight # PD	—	0.69 (0.17, 2.86)	—	1.27 (0.34, 4.67)
Underweight # GDM	—	1.89 (0.55, 6.45)	—	0.94 (0.16, 5.43)
Overweight # PG	—	1.15 (0.64, 2.05)	—	0.79 (0.48, 1.29)
Overweight # GDM	—	0.94 (0.69, 1.28)	—	0.99 (0.69, 1.42)
Class 1 obesity # PD	—	1.51 (0.96, 2.38)	—	1.14 (0.68, 1.92)
Class 1 obesity # GDM	—	1.13 (0.82, 1.55)	—	1.30 (0.90, 1.87)
Class 2 obesity # PD	—	1.36 (0.78, 2.37)	—	1.14 (0.59, 2.23)
Class 2 obesity # GDM	—	1.21 (0.83, 1.77)	—	1.18 (0.76, 1.84)
Class 3 obesity # PG	—	1.41 (0.80, 2.48)	—	1.40 (0.75, 2.61)
Class 3 obesity # GDM	—	2.15 (1.36, 3.40)**	—	2.06 (1.21, 3.54)**

Note: Boldface indicates statistical significance (*$p<0.05$, **$p<0.01$, and ***$p<0.001$).
[a]Logistic regression adjusted for maternal age (<25, 25−29, 30−34, 35−39, and ≥40 years), race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, other [Asian, American Indian/Alaska Native, Pacific Islander, or multiple]), mother's education (<12, 12, or ≥12 years), marital status (married or not married), parity (0, 1, or ≥2), initiation of prenatal care (first trimester, after first trimester [late], or not at all), health insurance, number of prenatal care visits, gestational weight gain, and newborn sex.
CDC, Centers for Disease Control and Prevention; GDM, gestational diabetes mellitus; LGA, large for gestational age; PD, pre-existing diabetes; PRAMS, Pregnancy Risk Assessment Monitoring System.

records from Aberdeen Maternity and Neonatal Data-bank in the United Kingdom.[44]

These findings show the importance of maternal weight before pregnancy on fetal outcomes and suggest that both obesity and diabetes before and during pregnancy should be of public health interest to increase the chance of optimal birth weight. The results of this work have significance in terms of providing education to women with obesity or diabetes who are planning to become pregnant. Many women are unaware of diabetes status in the preconception phase,[45] and many pregnancies are unplanned/unintended,[46] and because obesity develops over the years and it is difficult to lose weight, it is important to start targeting young women with messages about the importance of a healthy lifestyle and nutrition targeted to maintaining a healthy weight, particularly in underserved populations where the prevalence of both obesity and diabetes tend to be high but

access to health care is poor. Currently, obstetrician-gynecologists provide educational materials to patients with prepregnancy BMI in the overweight/obese ranges. Those with pre-existing diabetes are immediately identified as likely requiring additional clinical management. However, women with the highest risk of adverse pregnancy outcomes are patients with reduced ability to access antenatal care services because of a constellation of mitigating factors.[47] If women are provided increased access to health care and screening for diabetes in adolescents and young women, it would improve their ability to appropriately manage conditions such as diabetes and obesity in pregnancy and help to improve birth outcomes, including birthweights. With increased health-care access to adolescent and young women in underserved populations, they would seek specialist care early as they prepare to conceive and the best prenatal care to optimize fetal growth. Furthermore, as maternal

age for first-time pregnancy continues to rise in the U.S.,[48,49] early counseling, including diabetes education for women planning to conceive, will be important for early detection of pre-existing diabetes and gestational diabetes to optimize maternal diet and care to improve birth outcomes, including birthweight.

Blood glucose management during pregnancy improves pregnancy outcomes in patients with gestational diabetes, but the extent to which the length (time since diagnosis) of pre-existing diabetes contributes to excessive fetal growth is unknown. Studies, particularly among underserved populations, are needed to evaluate the effect of the duration of pre-existing diabetes on excessive fetal growth. Given that most fetal growth occurs during the third trimester, it will be interesting to study the effect of strict maternal blood glucose regulation on excessive fetal growth stratified by maternal age, BMI, and race, which are all associated with fetal birth weight.

Limitations

Data for BMI were based on self-reported weight and height. LGA and macrosomia were based on actual birthweight from birth certificate data. Although there may be some concerns about self-reported weight and height, previous studies comparing self-reported with measured height accuracy suggest that measurements were comparable and provide a reliable proxy measure across sex and race/ethnicity.[50−53]

CONCLUSIONS

In conclusion, this study showed that the risk of both LGA and macrosomia increases with maternal prepregnancy BMI irrespective of maternal diabetes status. Pre-existing diabetes poses a higher risk of delivering large babies than gestational diabetes. Women who are morbidly obese (BMI of $\geq$40 kg/m^2) with diabetes are particularly at severe risk for delivering LGA infants and infants with macrosomia.

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CREDIT AUTHOR STATEMENT

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.focus.2023. 100071.

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