# Diabetes during Pregnancy: Influence of Body Mass Index on Composite Morbidity

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## **Abstract**

## Keywords

- body mass index
- composite maternal morbidity
- composite neonatal morbidity
- ▶ diabetes
- obesity
- pregnancy
- ► MM
- ► NM
- ► BMI

**Objective** This study aims to compare composite maternal and neonatal morbidities (MM, NM) among pregnant women with diabetes mellitus whose body mass index (BMI) at delivery was < 30 (group 1), 30.0 to 39.9 (group 2), and  $\geq$  40 kg/m² (group 3). We hypothesized that increased BMI class at delivery would be associated with worsening maternal and neonatal outcomes.

**Methods** This is a retrospective cohort study. MM was defined as: chorioamnionitis, wound infection, eclampsia, diabetic ketoacidosis, hypoglycemia admission, third/fourth degree laceration, and/or death. NM was defined as umbilical arterial pH < 7.0, 5 minute Apgar < 4, respiratory distress syndrome, mechanical ventilation, neonatal sepsis, still-birth, and/or death. Odds ratios were adjusted for possible confounders.

**Results** MM was noted in 8, 13, and 24% of groups 1, 2, and 3, respectively, and significantly more common in group 2 versus 1 (adjusted odds ratio [aOR]: 1.66) and group 3 versus 1 (aOR: 3.06). NM was noted in 7, 8, and 15% of each BMI group, respectively, and differed significantly between group 3 vs. 2 (aOR: 1.77).

**Conclusions** The increased rate of morbidities between the BMI groups is useful to inform diabetic women and highlights the need for further investigation of diabetes and obesity as comorbidities in pregnancy.

In the United States, preexisting and gestational diabetes mellitus (GDM) complicate approximately 10% of all pregnancies. While all types of diabetes are on the rise, there has been a disproportionate growth of preexisting diabetes in young women of reproductive age. Compared with healthy women, those with GDM have increased risk of primary cesarean delivery, preeclampsia, birth weight > 90%, shoulder dystocia, and traumatic delivery. Similarly, those with preexisting diabetes

(type 1 [DM1], type 2 [DM2]) have an increased risk of perinatal mortality and congenital anomalies over nondiabetics.<sup>4</sup>

Obesity is a well-known risk factor for diabetes. Approximately 24.5% of women aged 20 to 44 are overweight, and an additional 20% are obese which translates to over 20 million women in the United States. 5.6 Approximately 80% of diabetics within the general population are overweight or obese. Obesity has been cited as a poor prognostic indicator

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in pregnant women with diabetes, but this relationship remains incompletely elucidated.<sup>8,9</sup> A recent study showed that GDM diagnosis was positively associated with actual body mass index (BMI) as well as prepregnancy BMI, age, and history of GDM.<sup>10</sup> Increased BMI was also associated with elevated fasting glucose and diminished insulin sensitivity.<sup>10</sup> In short, diabetes and obesity in pregnancy appear to have a synergistic effect in worsening pregnancy outcomes more so than either physiologic condition by itself.<sup>3</sup>

The goal of this study was to evaluate diabetic pregnancies for adverse health outcomes associated with increased BMI in women and neonates of singleton gestations. The hypothesis was that increased BMI class at delivery would be associated with worsening maternal and neonatal outcomes both individually and as a composite.

## **Materials and Methods**

#### **Data Collection**

This study was designed as a retrospective cohort. A database of pregnant diabetic women was constructed via chart review. Women with DM1, DM2, and GDM who delivered between 2011 and 2014 were retrospectively identified from two large teaching hospitals in Houston, TX. The secure online database service Research Electronic Data Capture (REDCap) was used to collect electronic medical record patient data for this study. Institutional review board approval was obtained before beginning data collection. The sample size was determined by the number of charts available to the researchers during this time period. Each patient was given a unique identification number. Maternal demographics, obstetric history, antenatal, delivery, and neonatal complications were documented.

#### **Analysis**

The inclusion criteria were nonanomalous, singleton gestations with gestational or pregestational diabetes, and documented BMI at delivery who delivered at or after 24 weeks gestational age. Women were stratified into three groups based on BMI at the time of delivery: < 30 (group 1, nonobese), 30.0 to 39.9 (group 2, obese), and  $\geq$  40 kg/m² (group 3, morbidly obese).

Gestational diabetes was diagnosed as a 3-hour glucose tolerance test (100 g oral glucose load) with two out of four abnormal values exceeding 95 mg/dL fasting, 180 mg/dL after 1 hour, 155 mg/dL after 2 hours, or 140 mg/dL after 3 hours. Additionally, women with a 1-hour value of greater than 200 mg/dL after a 50 g oral glucose load were also diagnosed with GDM.

Outcomes were calculated independently as well as collectively as composite maternal morbidity (MM) and composite neonatal morbidity (NM). MM was defined as the presence of any of the following: chorioamnionitis, wound infection (wound separation of either cesarean incision site or perineal lacerations with erythema, purulent drainage, or fascial dehiscence), eclampsia, diabetic ketoacidosis (triad of hyperglycemia, anion gap metabolic acidosis, and ketonemia), admission for hypoglycemia (generally in women on

pharmacologic agents), third or fourth degree laceration, and/or death. NM was defined as an umbilical arterial pH < 7.0, Apgar score < 4 at 5 minutes, respiratory distress syndrome (RDS) defined as the presence of clinical signs of respiratory distress accompanied by radiologic evidence, need for mechanical ventilation, culture-proven neonatal sepsis, seizure, stillbirth, and/or neonatal death. Apgar < 4 was selected as this value has been reported as a predictor of neonatal death and chronic neurologic disability.  $^{12,13}$ 

Odds ratios were calculated to compare outcomes between groups 1 versus 2, groups 1 versus 3, and groups 2 versus 3 and are provided in **Tables 1–4**. Odds ratios were adjusted (aOR) for maternal age, ethnicity, nulliparity, cigarette use, diagnosis of chronic hypertension, and gestational age at delivery and calculated using STATA software Version 13.1 (August 2013, StataCorp). <sup>14</sup> In addition, 95% confidence intervals (CI) were calculated; differences were considered significant if the 95% CI did not cross the integer 1. STROBE guidelines for reporting cohort studies were employed. <sup>15</sup> As all individuals in this study carried a diagnosis of diabetes, gestational diabetics that did not require pharmacologic therapy (A1GDM) were deemed the reference group.

## Results

Of the 1,266 women with DM in the original database, 1,257 (99%) met the inclusion criteria. In the study population, 264 (21%) were in group 1, 696 (55%) in group 2, and 297 (24%) in group 3. Regarding the relevance of BMI stratification, maternal demographic and medical history showed the three BMI groups differed significantly for ethnicity, the presence of chronic hypertension, and type of diabetes ( Tables 1 and 2). African-Americans exhibited three times the odds of being included in the obese and morbidly obese groups; Hispanic representation in the obese group was nearly twice the odds of Hispanics representing the nonobese group, and Asian ethnicity presence in the morbidly obese category was significantly lower than nonobese group (-Table 1). The distribution of smokers and nulliparous mothers did not significantly differ between BMI categories (►Table 1).

The odds ratio of obese patients having chronic hypertension was 2.15, increasing to 4.24 when morbidly obese women were evaluated (**-Table 1**). A similar odds ratio profile was evident when obese and morbidly obese patients were evaluated for the type of diabetes present; obese patients had 2.64 and 2.34 times the odds of having A2GDM and DM2, respectively; and morbidly obese patients had 3.26 and 5.11 times these odds (**-Table 2**).

Intrapartum outcomes were also distinct between BMI groupings. Compared with the nonobese group, the morbidly obese group had higher odds of preterm delivery starting at 28 weeks (**Table 3**). Also, the obese group demonstrated a trend to higher odds of delivery between 32 to 36.6 and 37.0 to 38.6 weeks of gestation. Although the indication for cesarean delivery did not differ significantly between groups, the difference of overall cesarean delivery rates was significant between groups 1 (34%), 2 (47%), and 3 (62%). Shoulder

**Table 1** Maternal demographics

	BMI < 30 (N = 264)	BMI 30.0-39.9 (N = 696)	OR (95% CI) Group 1 vs. 2	BMI ≥ 40.0 (N = 297)	OR (95% CI) Group 1 vs. 3		
Maternal age (y)							
< 20	4 (2%)	23 (3%)	2.22 (0.76, 6.51)	8 (3%)	1.68 (0.50, 5.68)		
20-34 <sup>a</sup>	168 (64%)	435 (63%)	Ref	200 (67%)	Ref		
≥ 35	92 (35%)	238 (34%)	0.99 (0.74, 1.35)	89 (30%)	0.81 (0.57, 1.17)		
Ethnicity							
Caucasian <sup>a</sup>	27 (10)	40 (6)	Ref	21 (7)	Ref		
African-American	24 (9)	97 (14)	3.73 (1.41, 5.29)	64 (22)	3.42 (1.62, 7.17)		
Hispanic	184 (70)	515 (75)	1.89 (1.12, 3.17)	193 (66)	1.35 (0.74, 2.47)		
Asian	16 (6)	13 (2)	0.54 (0.23, 1.32)	1 (0.34)	0.08 (0.01, 0.66)		
Other	13 (5)	25 (4)	1.29 (0.56, 2.97)	14 (5)	1.38 (0.54, 3.57)		
Nulliparous	58 (22)	150 (22)	0.98 (0.70, 1.37)	51 (17)	0.73 (0.48, 1.12)		
Smoker	11 (4)	30 (4)	1.03 (0.51, 2.08)	21 (7)	1.74 (0.82, 3.69)		
cHTN	18 (7)	95 (14)	2.15 (1.27, 3.64)	71 (24)	4.24 (2.45, 7.34)		

Abbreviations: BMI, body mass index; cHTN, chronic hypertension; CI, confidence interval; OR, odds ratio.

Note: Data presented as mean  $\pm$  standard deviation or % (N).

dystocia distribution among the BMI groups was not of significance (**>Table 3**).

Evaluation of NM showed that neonates of mothers with elevated BMIs had higher odds of increased birthweight, developing RDS, and being admitted to the NICU ( $\neg$  Table 4). Overall, birth weight was different among all groups. The odds of birthing a macrosomic newborn (birth weight  $\geq$  4,000 g) were significantly different: 3% for group 1; 10% for group 2; and 18% for group 3. RDS was significantly more common in neonates of morbidly obese and obese mothers than in neonates of nonobese mothers ( $\neg$  Table 4).

Differences in morbidity were assessed between BMI groups for neonates and mothers alike. Overall, NM was noted in 9% of neonates and differed between the obese and morbidly obese groups (**~Table 4**). MM was noted in 15% of diabetic women and was significantly more common in obese and morbidly obese women. Similarly, MM continued

to rise with increasing obesity class (**-Table 3**). Postpartum hemorrhage was more common in obese and morbidly obese women than nonobese women (aOR: 1.70, 0.99–2.94; aOR: 3.21, 1.79–5.76). Overall, the stillbirth and neonatal death rate did not differ between the groups.

### **Discussion**

In this study, adverse outcomes were amplified when BMIs exceeded 30 kg/m². Importantly, the obese and morbidly obese groups were more likely to be DM2 or A2GDM than A1GDM. Compared with Caucasian women, African-American and Hispanic ethnicities were more likely to have a BMI > 30, while Asians were less likely. The effects of elevated blood glucose and BMI on the vascular system were evident in the increased odds of exhibiting hypertension and preeclampsia.

**Table 2** Maternal diabetes stratification

	BMI < 30 (N = 264)	BMI 30.0-39.9 (N = 696)	OR (95% CI) Group 1 vs. 2	BMI ≥ 40.0 (N = 297)	OR (95% CI) Group 1 vs. 3		
Maternal diabetes							
A1 Gestational DM <sup>a</sup>	161 (61)	285 (41)	Ref	90 (30)	Ref		
A2 Gestational DM	56 (21)	234 (34)	2.64 (1.66, 3.35)	102 (34)	3.26 (2.15, 4.94)		
Type 2	35 (13)	145 (21)	2.34 (1.54, 3.55)	100 (34)	5.11 (3.22, 8.12)		
Type 1	12 (5)	30 (4)	1.41 (0.70, 2.83)	5 (2)	0.75 (0.25, 2.18)		

Abbreviations: BMI, body mass index; CI, confidence interval; DM, diabetes mellitus; OR, odds ratio. Note: Data presented as mean  $\pm$  standard deviation or % (N).

<sup>&</sup>lt;sup>a</sup>Denotes reference group.

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**Table 3** Intrapartum outcomes and composite maternal morbidity

	BMI < 30 (N = 264)	BMI 30.0-39.9 (N = 696)	aOR (95% CI) Group 1 vs. 2	BMI ≥ 40.0 (N = 297)	aOR (95% CI) Group 1 vs. 3		
Maternal morbidity <sup>a</sup>	22 (8)	93 (13)	1.66 (1.01, 2.74)	71 (24)	3.06 (1.78, 5.27)		
Chorioamnionitis	3 (1)	22 (3)	2.84 (0.84, 9.57)	4 (1)	1.18 (0.26, 5.36)		
Hypoglycemia	51 (20)	134 (20)	1.08 (0.74, 1.58)	72 (25)	1.26 (0.82, 1.97)		
PPROM	8 (3)	30 (4)	1.43 (0.65, 3.18)	2 (0.68)	0.22 (0.46, 1.03)		
Antenatal corticosteroids	15 (6)	47 (7)	1.19 (0.66, 2.17)	28 (9)	1.71 (0.89, 3.24)		
Gestational age (wk) <sup>b</sup>	Gestational age (wk) <sup>b</sup>						
24.0-27.6	3 (1) 9 (1)		1.43 (0.38, 5.44)	4 (1)	2.46 (0.52, 11.56)		
28.0-31.6	3 (1)	8 (1)	1.27 (0.33, 4.94)	8 (3)	4.92 (1.23, 19.62)		
32.0-36.6	40 (15)	131 (19)	1.56 (0.99, 2.45)	62 (21)	2.86 (1.64, 4.99)		
37.0-38.6	136 (52)	385 (55)	1.35 (0.96, 1.90)	180 (61)	2.44 (1.56, 3.83)		
39.0-40.6°	72 (27)	151 (22)	Ref	39 (13)	Ref		
≥ 41	10 (4)	12 (2)	0.57 (0.24, 1.39)	4 (1)	0.74 (0.22, 2.51)		
Shoulder dystocia	1 (0.38)	10 (2)	3.87 (0.49, 30.4)	8 (3)	7.3 (0.91, 58.77)		
Route of delivery	Route of delivery						
Vaginal <sup>c</sup>	168 (64)	361 (52)	Ref	109 (37)	Ref		
Operative vaginal	5 (2)	9 (1)	0.83 (0.28, 2.54)	3 (1)	0.92 (0.22, 3.94)		
Cesarean	91 (34)	323 (47)	1.65 (1.22, 2.22)	184 (62)	3.12 (2.20, 4.41)		
Indication for cesarean	Indication for cesarean						
CP disproportion	2 (2)	11 (3)	1.82 (0.38, 8.78)	8 (4)	2.52 (0.42, 15.2)		
Labor dystocia	10 (11)	40 (12)	0.94 (0.42, 2.09)	19 (10)	1.29 (0.51, 3.28)		
Failed induction	1 (1)	16 (5)	3.95 (0.50, 31.6)	14 (8)	6.35 (0.72, 56.01)		
Fetal distress	11 (12)	52 (16)	1.22 (0.58, 2.54)	20 (11)	0.66 (0.27, 1.60)		
Abnormal presentation	9 (10)	33 (10)	1.06 (0.48, 2.34)	14 (8)	1.08 (0.42, 2.83)		
Previous section	41 (45)	129 (40)	0.96 (0.54, 1.73)	84 (46)	0.99 (0.53, 1.88)		
Abruption/previa	3 (3)	3 (1)	0.31 (0.05, 1.78)	1 (1)	1.48 (0.41, 5.40)		
Preeclampsia/HTN	4 (4)	18 (6)	1.48 (0.41, 5.40)	(9)	2.00 (0.49, 8.23)		
Other	1 (11)	19 (6)	0.48 (0.19, 1.21)	7 (4)	0.33 (0.11, 1.05)		

Abbreviations: aOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; CP, cephalopelvic; HTN, hypertension. Note: Data presented as mean  $\pm$  standard deviation or % (N).

The above medical issues present in the mother became apparent during the peripartum period and manifested as an increased likelihood of delivering prematurely as BMI increased. This finding was increased even further when the BMI exceeded the morbidly obese threshold. These premature deliveries may explain why a lack of elevated odds was present in regard to shoulder dystocia; neonates were delivered before full physiologic development and body weight distribution may have differed from that of their term counterparts. The 263 g difference between babies from nonobese and morbidly obese mothers is equivalent to the weight of three apples. This additional weight may be

potentially dangerous to both mother and child. Increased rates of cesarean delivery among obese and morbidly obese mothers may also contribute to the lack of difference in shoulder dystocia events.

NM differed among BMI groups and was most profound in regard to NICU admission and RDS development. Not surprisingly, if women with elevated BMIs have a tendency to deliver earlier, it is reasonable to deduce the pulmonary development of the neonate was not sufficient enough to provide independent respiratory faculties. As such, the premature neonates were at higher odds of developing RDS and being admitted to the NICU for a higher level of care.

<sup>&</sup>lt;sup>a</sup>Maternal morbidity, composite maternal morbidity.

<sup>&</sup>lt;sup>b</sup>aOR were not corrected for gestational age at delivery when determining odds of delivery at each gestational age. aOR otherwise adjusted for maternal age, ethnicity, nulliparity, cigarette smoking, marital status, chronic HTN, and gestational age at delivery.

<sup>&</sup>lt;sup>c</sup>Denotes reference group.

**Table 4** Neonatal morbidity

	BMI < 30 (N = 264)	BMI 30.0-39.9 (N = 696)	aOR (95% CI) Group 1 vs. 2	$\begin{array}{c} BMI \geq 40.0 \\ (N=297) \end{array}$	aOR (95% CI) Group 1 vs. 3	aOR (95% CI) Group 2 vs. 3
Composite neonatal morbidity	18 (7)	55 (7.9)	1.04 (0.59, 1.84)	45 (15)	1.82 (0.99, 3.35)	2.06 (1.44, 2.96)
RDS	11 (4)	39 (6)	1.28 (0.64, 2.60)	31 (11)	2.24 (1.06, 4.71)	1.78 (1.06, 2.99)
NICU admission	45 (17)	155 (23)	1.39 (0.95, 2.04)	88 (31)	1.74 (1.13, 2.70)	1.30 (0.94, 1.81)
Stillbirth	2 (0.76)	3 (0.43)	0.47 (0.07, 2.93)	3 (1)	0.62 (0.08, 4.92)	1.43 (0.23, 8.88)
Neonatal death	3 (1)	6 (0.9)	0.62 (0.14, 2.71)	5 (2)	0.83 (0.17, 4.15)	1.91 (0.48, 7.63)
Macrosomic (≥ 4 kg)	8 (3)	70 (10)	4.27 (1.91, 9.53)	53 (18)	7.37 (1.38, 3.14)	2.07 (1.37, 3.12)
Birth weight	3,076.6 ± 600.8	3,294.6 ± 666.6	192.5 (99.8, 285.3) <sup>a</sup>	3,339.6 ± 797.3	330.8 (206.8, 454.7) <sup>a</sup>	157.1 (59.4, 254.7)

Abbreviations: aOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; NICU, neonatal intensive care unit; RDS, respiratory distress syndrome;

Note: aOR for maternal age, ethnicity, nulliparity, cigarette smoking, marital status, chronic hypertension, and gestational age at delivery. AGA, appropriate for gestational age (birth weight between 10 and 89% for gestational age).

ap value < 0.01.

Interestingly, evaluation for hypoglycemia among neonates did not show a difference between BMI groups. A potential cause of this is the increased stress response seen in neonates that are large for gestational age as well as perhaps a prolonged or more complicated delivery. Although the NM did not differ significantly among those with or without obesity, it did increase significantly between morbidly obese over obese pregnancies. MM and obstetric complications including preterm birth and macrosomia were distinctive based on BMI category.

Our results correlate with similar investigations in the literature. In 2015, a register-based study out of Finland showed that women with a BMI of 30 or more had increased risk of severe birth-related complications. The pathophysiology of diabetes and obesity in concert is becoming increasingly understood. As found by Bozkurt et al in 2015, an increased level of fasting glucose and decreased insulin sensitivity early in pregnancy is associated with increased BMI. This supports the notion that elevated BMI is a major contributing factor to earlier, and likely more severe, onset of GDM in pregnancy.

Similarly, Catalano et al. showed a significant difference in birth weight for obese versus nonobese GDM mothers. An important distinction was their use of BMI  $> 33 \text{ kg/m}^2$  as the obesity cutoff. It should be noted that most studies to date have used varying criteria to characterize and stratify obesity in pregnancy. It has been defined as prepregnancy weight (self-reported as well as clinically noted), BMI at first prenatal visit, BMI at the time of oral glucose tolerance test, and BMI at delivery.  $^{3,18}$ 

A clear limitation of this study was the lack of prepregnancy data. In many ways, this is comparable to the lack of medical history available upon initial prenatal visits, which are often well into the second semester. Many pregnancy-related studies, including HAPO, recognize this limitation and utilize weight at oral glucose tolerance test. <sup>19</sup> In addition, it may be helpful to determine BMI "equivalents" at each week of gestation to more accurately define obesity.

The retrospective nature of this analysis should also be considered when evaluating the results. Some of the adverse neonatal outcomes were not uniformly defined before the neonate's care and were left to the discretion of the treating physician. A sample size was not calculated before this analysis, and therefore certain associations may not be present due to lack of statistical power. All patients were treated at tertiary care facilities, and thus the results may not be universally applicable. Although adjusted, there is always a risk of residual confounding within our analysis.

Strengths of this study include the fact that the data came from two large teaching institutions in which diagnostic criteria and management of patients with DM are consistent with The American Congress of Obstetricians and Gynecologists guidelines. In addition, there was a large sample size of over 1,200 pregnancies. Finally, a small team of four core researchers was used for data entry and parameters were set before collection, minimizing variation (and human error) in interpretation. The use of a standardized, web-based data collection tool (REDCap) also limits the errors common in data collection.

In summary, maternal obesity was overwhelming present in three out of four women with DM at delivery. From a preventive medicine standpoint, the increased prevalence of MM and NM in the higher BMI groups is useful to inform women with DM to initiate lifestyle and medical modifications to mitigate maternal and neonatal morbidities. According to the Centers for Disease Control and Prevention, the United States has a neonatal death rate of 5.8 per 1,000 live births as of 2014, yet this study showed a neonatal mortality rate of 12 per 1,000 live births.<sup>20</sup> A higher neonatal death rate among obese diabetics underscores the impact obesity has on diabetic women and their offspring throughout the gestational cycle and perinatal period. Morbidity and mortality that is fundamentally related to preventable causes further establishes the need to both decrease preconception obesity and increase the effectiveness of therapeutic measures.

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