Xie et al. BMC Pregnancy and Childbirth (2025) 25:333
https://doi.org/10.1186/s12884-025-07352-2

BMC Pregnancy and Childbirth

RESEARCH

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Racial/ethnic disparities in the association of maternal diabetes and obesity with risk of preterm birth among 17 million mother-infant pairs in the United States: a population-based cohort study

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Abstract

Background The racial/ethnic disparities in the prevalence of obesity, diabetes, and adverse birth outcomes such as preterm delivery indicate that it is essential to account for the varying risks associated with pregnant women of different races and ethnics during clinical prenatal examinations. However, the racial and ethnic disparities in how pre-pregnancy diabetes in mothers relates to preterm birth as well as the combined association of maternal diabetes and pre-pregnancy obesity with preterm birth remain unclear. In this study, we aimed to 1) examine the racial/ethnic disparities in the association of maternal diabetes including gestational diabetes mellitus (GDM) and pre-pregnancy diabetes with preterm birth 2) and the racial/ethnic disparities in the joint associations of maternal diabetes and pre-pregnancy obesity with preterm birth.

Methods In this population-based cohort study, we included 17,027,792 mothers documented in the National Vital Statistic System in the U.S. from 2016 to 2020. All these data were analyzed in 2021. Maternal pre-pregnancy diabetes was defined as having diabetes diagnosed prior to this pregnancy, and GDM was defined as having newly diagnosed diabetes in this pregnancy. Pre-pregnancy BMI (kg/m^2) was classified as underweight (< 18.5 kg/ m^2), normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), obesity class I (30.0–34.9 kg/m^2), obesity class II (35.0–39.9 kg/ m^2), and obesity class III (≥ 40 kg/m^2). Preterm birth, defined as delivery occurring at less than 37 weeks of gestation, was the main outcome of interest. We further categorized preterm birth into three subtypes: extremely (< 28 weeks), very (28–31 weeks), and moderately (32–36 weeks) preterm birth. Logistic regression models were used for association analyses in this study.

Results Among 17,027,792 mothers (mean age: 29.4 ± 5.4 years), 1,374,286 (8.07%) mothers delivered a preterm infant. Women with pre-pregnancy diabetes had the highest risk of preterm birth followed by women with GDM overall and across all racial/ ethnic groups. However, from pre-pregnancy underweight to obesity III, the magnitude

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of the association between pre-pregnancy diabetes and preterm birth decreased for non-Hispanic Black women (underweight, 4.47 [3.34–5.99], normal weight 4.28 [3.98–4.60], overweight 3.29 [3.11–3.49], obesity I 3.09 [2.93–3.26], obesity II 2.98 [2.82–3.16], obesity III 3.19 [3.04–3.35]), while it showed an increasing trend for non-Hispanic Asians (underweight 1.45 [0.91–2.30], normal weight 2.16 [1.90–2.47], overweight 2.71 [2.47–2.97], obesity I 3.10 [2.82–3.41], obesity II 3.58 [3.13–4.09], obesity III 3.99 [3.34–4.77]). The corresponding OR was (underweight 4.33 [3.21–5.83], normal weight 3.69 [3.47–3.93], overweight 3.26 [3.10–3.42], obesity I 3.33 [3.19–3.49], obesity II 3.47 [3.29–3.65], obesity III 3.89 [3.68–4.11]) among Hispanics and (underweight 5.17 [4.34–6.17], normal weight 5.01 [4.83–5.21], overweight 4.98 [4.80–5.17], obesity I 4.66 [4.48–4.85], obesity II 4.58 [4.38–4.79], obesity III 4.50 [4.31–4.69]) among non-Hispanic White. Comprehensive analysis of the association between diabetes, pre-pregnancy diabetes, obesity, ethnicity, and preterm birth found that compared to white women with normal weight and normal blood glucose levels, any other racial\ ethnic group has an elevated risk of preterm birth, particularly when accompanied by unhealthy weight, GDM, or pre-pregnancy diabetes. Specifically, non-Hispanic Black individuals with normal blood sugar levels (1.69 [1.67–1.70]) have a higher risk of preterm birth than non-Hispanic White individuals with GDM (1.37 [1.35–1.40]). Similarly, Asian pregnant women with class 2 and class 3 obesity (1.72 [1.65–1.78], 1.96 [1.83–2.10]), as well as Hispanic pregnant women with class 2 and class 3 obesity (1.46 [1.44–1.48], 1.64 [1.61–1.67]), also have a higher risk of preterm birth than white women with GDM 1.37 [1.35–1.40].

Conclusions In conclusion, while both pre-pregnancy diabetes and GDM were significantly associated with preterm birth, the associations varied by race/ethnicity. The risk of preterm birth for GDM increased with increasing BMI in all race/ethnicity groups. However, the pattern of the joint association of pre-pregnancy diabetes and BMI levels with preterm birth differed by race/ethnicity. Future studies on the underlying mechanisms of the racial/ethnic disparities in the association of diabetes and obesity with preterm birth are needed.

Keywords Race/ethnicity, Preterm birth, Diabetes, Pre-pregnancy obesity

Background

Preterm birth is the leading cause of child mortality worldwide [1]. Globally, preterm birth affects approximately one in 10 live births, with regional prevalence ranged from 13.4% in North Africa to 8.7% in Europe [2]. Therefore, identifying risk factors of preterm birth continues to be significant public health and clinical issues.

Metabolic diseases, like obesity and diabetes, before and during pregnancy have been demonstrated to be associated with the risk of preterm birth [3, 4]. Maternal diabetes often, although not always, occurs in women with pre-pregnancy obesity [5]. Few studies have examined the joint effects of maternal diabetes and pre-pregnancy obesity on preterm birth, but the findings are inconsistent [6–8]. A study conducted among Chinese women indicated that the combination of pre-pregnancy obesity and maternal abnormal glucose metabolism further worsens preterm birth compared with each condition alone [8]. However, a recent Finnish study found that the association between pre-pregnancy diabetes and preterm birth was similar in all body mass index (BMI) strata [7]. Population characteristics, including racial/ethnic differences, may to some extent explain the variance in outcomes.

In fact, there are significant racial/ethnic differences in the prevalence of obesity and diabetes among women of reproductive age, GDM, as well as preterm births [2, 9–11]. Recent studies, including ours, also highlight the need to address racial/ethnic disparities in the relationship between metabolic risk factors and preterm birth [12–15]. Among women with GDM, compared with whites, blacks women was associated with the highest risk of preterm birth followed by Hispanics, and American Indianans, and Asians [15]. Our previous study showed that the association between pre-pregnancy obesity and preterm birth varied according to maternal age and race/ethnicity [14]. However, no studies have yet comprehensively examined the relationship of pre-pregnancy diabetes or gestational diabetes, obesity, race/ethnicity, with preterm birth. Resolving this scientific question contributes to understanding the discrepancies in previous findings and offers a scientific foundation for physicians to provide tailored clinical recommendations and prenatal care to mothers before and during pregnancy.

Therefore, in this study, we took advantage of a large and diverse dataset, the US National Vital Statistics System (NVSS), to comprehensively examine the racial/ethnic disparities in the association of maternal diabetes with preterm birth and the joint association of maternal diabetes and pre-pregnancy obesity with preterm birth.

Methods

Study population

The NVSS, the Federal compilation of this data, is the result of the cooperation between the National Center for Health Statistics (NCHS) and States to provide access to statistical information from birth certificates [16]. NVSS uses two uniform documents (a facility worksheet and a maternal worksheet) to collect natality data which includes information on a wide range of maternal and infant demographic and health characteristics for all births registered in 50 states and the District of Columbia in the U.S. Detailed descriptions and vital statistics are both available on the official website.

In this study, we used birth data from NVSS 2016–2020, because the 2003-revised standard birth certificate of live birth was fully implemented across the country since 2016. Therefore, only data collected after 2016 are based on 100% of births registered to residents of the 50 states and the District of Columbia (D.C.). Meanwhile, to minimize the impact of COVID-19, we have confined our analysis to birth data through the year 2020. We included all adult mothers who had a live singleton birth and available data on pre-pregnancy diabetes, GDM, pre-pregnancy BMI, race/ethnicity, and gestational age. This study was exempt from institutional review board approval, because these records are publicly available and the data are de-identified.

Exposure measures

Maternal pre-pregnancy diabetes was defined as having diabetes diagnosed prior to this pregnancy, and GDM was defined as having newly diagnosed diabetes in this pregnancy. Pre-pregnancy BMI (kg/m^2) was calculated as pre-pregnancy weight in kilograms divided by the square of height in meters and classified as underweight (< 18.5 kg/ m^2), normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), obesity class I (30.0–34.9 kg/ m^2), obesity class II (35.0–39.9 kg/m^2), and obesity class III (≥ 40 kg/m^2) [17].

Outcome measures

Gestational age was calculated based on the obstetric estimate of gestation at delivery (OE), which was defined as "the best obstetric estimate of the infant's gestation in completed weeks based on the birth attendant's final estimate of gestation" [18]. Preterm birth, defined as delivery occurring at less than 37 weeks of gestation, was the main outcome of interest. We further categorized preterm birth into three subtypes: extremely (< 28 weeks), very (28–31 weeks), and moderately (32–36 weeks) preterm birth [19].

Covariates

Information about maternal age, race/ethnicity, educational level, smoking before and during pregnancy, and marital status was collected directly from mothers via the mother's worksheet. Information about parity, prenatal care, history of preterm birth, and infant sex was extracted from prenatal care records provided on facility worksheet.

The following covariates were included in the analyses: maternal age (20–24.9, 25–29.9, 30–34.9, 35–39.9, and ≥ 40 years), race/ethnicity (Hispanic, non-Hispanic black, non- Hispanic white, non-Hispanic Asian, and other), parity (1, 2, 3, and ≥ 4), maternal education levels (lower than high school, high school, and higher than high school), smoking status during pregnancy (yes vs. no), previous history of preterm birth (yes vs. no vs. nulliparous), marital status (yes vs. no), infant sex (boy vs. girl), and timing of initiation of prenatal care (No prenatal care, 1st-3rd month, 4th-6th month, and ≥ 7th month). We included these covariates as they are known confounders that influence both diabetes during pregnancy and preterm birth [20, 21].

Statistical analysis

Participants were categorized into 3 groups: non-diabetes, pre-pregnancy diabetes, and GDM. Comparisons in descriptive statistics across groups were tested by Chi-Square analysis or Fisher exact test, where appropriate. Logistic regression models were used to investigated the association and joint association of maternal diabetes and pre-pregnancy obesity with preterm birth, further to explore the racial/ethnic disparities.

Maternal age, race/ethnicity were adjusted in model 1. Maternal age, race/ethnicity, parity, education levels, smoking during pregnancy, previous history of preterm birth, marital status, infant sex, timing of initiation of prenatal care and BMI categories were adjusted in model 2. In model 3, gestational weight gain was adjusted based on model 2 due to that it is associated with preterm birth and pre-pregnancy obesity. In model 4, eclampsia/preeclampsia, gestational hypertension, and pre-pregnancy hypertension were adjusted based on model 2. Model 2 is the main model. Race/ethnicity and pre-pregnancy BMI category were removed from models, respectively, when they serve as stratification variables. Interaction analysis was used to investigated racial/ethnic difference on the association between maternal diabetes and preterm birth and then the stratified association by race/ethnicity. All statistical analyses were performed with SAS software (version 9.4; SAS Institute, Cary, NC). Two-sided test was employed, with statistical significance defined as $P < 0.05$.

Results

Among the 17,027,792 adult mothers (mean age: 29.4 ± 5.4 years) who delivered a live singleton birth, 165,137 (0.97%) mothers had pre-pregnancy diabetes and 1,173,669 (6.89%) had GDM. Compared with mothers without diabetes, those with pre-pregnancy diabetes or GDM were more likely to be older, overweight or obese, smokers, have lower education levels, and had preterm birth history. Detailed statistical description of the study population is shown in Table 1.

The prevalence of preterm birth in this analysis was 8.07% ($n = 1,374,286$) overall, and 25.83% ($n = 42,658$) among women with pre-pregnancy diabetes, 11.39% ($n = 133,689$) among women with GDM, and 7.64% ($n = 1,197,939$) among those without diabetes. The prevalence of preterm birth according to population characteristics is shown in Appendix Table 1.

Pre-pregnancy diabetes and GDM were significantly associated with preterm birth, with the adjusted ORs (95%CI) of 3.40 (3.36–3.44) and 1.45 (1.44–1.46), respectively. Pre-pregnancy diabetes and GDM were associated with increased risk of all preterm birth subtypes (Appendix Table 2). The interaction between diabetes and race/ethnicity was significant (P values for interaction < 0.0001). Therefore, we further conducted stratified analyses by race/ethnicity and found that women with pre-pregnancy diabetes and GDM had higher risk of preterm birth among all racial/ethnic groups with different magnitudes. Compared with non-diabetic women, the OR (95% CI) of preterm birth was 3.02 (2.95–3.09) for pre-pregnancy diabetes and 1.48 (1.46–1.50) for GDM among Hispanics, 4.01 (3.94–4.09) and 1.44 (1.43–1.45) among non-Hispanic whites, 3.16 (3.08–3.24) and 1.45 (1.42–1.47) among non-Hispanic blacks, 2.22 (2.11–2.34) and 1.38 (1.35–1.40) among non-Hispanic Asians, respectively (Table 2).

The joint association of maternal diabetes and race/ethnicity with preterm birth is shown in Appendix Fig. 1 and Appendix Table 3. In the Joint analysis, individuals with pre-pregnancy diabetes had the highest risk of preterm delivery, while the risk was higher in non-Hispanic Blacks than non-Hispanic Whites, followed by Hispanics and then Asians. The association of GDM with preterm birth was also highest in non-Hispanic Blacks, but there were no significant differences among other racial\ethnic groups. Among those without diabetes, non-Hispanic Blacks had a higher risk than Hispanics, followed by Asians and then non-Hispanic Whites. Notably, the risk for non-Hispanic Blacks without diabetes was also higher than that for non-Hispanic Whites with GDM.

The joint association of pre-pregnancy obesity and race/ethnicity with preterm birth were shown in Appendix Fig. 2 and Appendix Table 4. In the Joint analysis, women with pre-pregnancy obesity had the highest risk of preterm birth, while the risk was higher in non-Hispanic Blacks than Asians, followed by Hispanic and then Whites.

We further examined the joint association of maternal diabetes and severity of pre-pregnancy obesity with preterm birth overall and stratified by race/ethnicity (p for interaction < 0.0001) (Fig. 1 and Appendix Table 5). In the overall population, women with pre-pregnancy diabetes regardless of severity of pre-pregnancy obesity had the highest risk of preterm delivery followed by women with GDM. This pattern was consistent across different racial/ethnic groups. Moreover, compared with non-diabetic women with normal weight, the ORs (95%CI) of preterm birth for GDM increased with the severity of pre-pregnancy obesity, which was 1.60 (1.52–1.68) for underweight, 1.37 (1.35–1.39) for normal weight, 1.50 (1.48–1.51) for overweight, 1.70 (1.68–1.72) for obesity I, 1.87 (1.84–1.89) for obesity II, and 2.12 (2.09–2.15) for obesity III. This trend was consistent across all racial/ethnic groups.

Compared with non-diabetic women with normal weight, the ORs (95% CI) of having preterm birth was 4.32 (3.82- 4.88), 4.36 (4.24–4.48), 3.91 (3.82–4.01), 3.78 (3.69–3.87), 3.80 (3.70–3.91), and 3.99 (3.89–4.10) for pre-pregnancy diabetic women with underweight, normal weight, overweight, obesity I, obesity II, and obesity III, respectively. However, the pattern for pre-pregnancy diabetes varied by race/ethnicity. For example, as severity of pre-pregnancy obesity increases, the association between pre-pregnancy diabetes and preterm birth raised among non-Hispanic Asians, but decreased among non-Hispanic Blacks (Fig. 1 and Appendix Table 5).

Upon comprehensive consideration of the relationships between diabetes, pre-pregnancy diabetes, obesity, ethnicity, and preterm birth, it was found that compared to white women with normal weight and normal blood glucose levels, any other racial\ethnic group has an elevated risk of preterm birth, particularly when accompanied by unhealthy weight, GDM, or pre-pregnancy diabetes. Overall, regardless of body weight, pregnant women with pre-pregnancy diabetes have a significantly higher risk of preterm birth than those with GDM or normal blood sugar levels. However, significant differences in risk exist among various ethnic groups. Specifically, non-Hispanic Black individuals with normal blood sugar levels have a higher risk of preterm birth than non-Hispanic White individuals with GDM. Similarly, Asian pregnant women with obesity, as well as Hispanic pregnant women with class 2 and class 3 obesity, also have a higher risk of preterm birth than white women with GDM (Appendix Table 6).

Discussion

In this large population-based cohort study, our study revealed that, overall, women with pre-pregnancy diabetes had the highest risk of preterm birth, followed by

Table 1 Population characteristics according to maternal diabetes before and during pregnancy: the National Vital Statistics System 2016–2020 ($N = 17{,}027{,}792$)

Variable	N	Pre-pregnancy diabetes n (%)	Gestational diabetes n (%)	Non diabetes n (%)
Total	17,027,792	165,137 (0.97)	1,173,669 (6.89)	15,688,986 (92.14)
Age, years				
20–24.9	3,496,929	20,991 (12.71)	129,383 (11.02)	3,346,555 (21.33)
25–29.9	5,192,848	40,312 (24.41)	292,918 (24.96)	4,859,618 (30.97)
30–34.9	5,135,061	51,484 (31.18)	396,666 (33.80)	4,686,911 (29.87)
35–39.9	2,619,094	39,212 (23.75)	273,969 (23.34)	2,305,913 (14.70)
≥ 40	583,860	13,138 (7.96)	80,733 (6.88)	489,989 (3.12)
Race/ethnicity				
Hispanic	3,937,173	44,539 (26.97)	301,636 (25.70)	3,590,998 (22.89)
non-Hispanic White	8,918,712	68,884 (41.71)	541,842 (46.17)	8,307,986 (52.95)
non-Hispanic Black	2,366,577	31,611 (19.14)	134,035 (11.42)	2,200,931 (14.03)
non-Hispanic Asian	1,134,797	11,301 (6.84)	144,328 (12.30)	979,168 (6.24)
Other	670,533	8,802 (5.33)	51,828 (4.42)	609,903 (3.89)
Education levels, n (%)				
Lower than high school	1,836,524	25,111 (15.21)	144,346 (12.30)	1,667,067 (10.63)
High school	4,210,412	45,864 (27.77)	276,173 (23.53)	3,888,375 (24.78)
Higher than high school	10,694,830	92,455 (55.99)	737,854 (62.87)	9,947,732 (63.41)
Missing	202,815	1,707 (1.03)	15,296 (1.30)	185,812 (1.18)
Marital status, n (%)				
Married	9,621,316	89,137 (53.98)	703,437 (59.93)	8,828,742 (56.27)
Unmarried	5,767,047	63,173 (38.25)	351,008 (29.91)	5,352,866 (34.12)
Missing	1,639,429	12,827 (7.77)	119,224 (10.16)	1,507,378 (9.61)
Smoking during pregnancy, n (%)				
Yes	1,079,240	12,786 (7.74)	68,444 (5.83)	998,010 (6.36)
No	15,850,216	150,715 (91.27)	1,099,873 (93.71)	14,599,628 (93.05)
Missing	98,706	1,636 (0.99)	5,352 (0.46)	91,718 (0.58)
Parity, n (%)				
1	6,177,812	54,513 (33.01)	388,232 (33.08)	5,735,067 (36.55)
2	5,583,867	50,808 (30.77)	372,284 (31.72)	5,160,775 (32.89)
3	3,007,721	31,063 (18.81)	221,870 (18.90)	2,754,788 (17.56)
≥ 4	2,222,748	28,452 (17.23)	189,607 (16.16)	2,004,689 (12.78)
Missing	35,644	301 (0.18)	1,676 (0.14)	33,667 (0.21)
Timing of initiation of prenatal care, n (%)				
No prenatal care	252,627	1,834 (1.11)	6,808 (0.58)	243,985 (1.56)
1st to 3rd month	13,093,383	129,443 (78.39)	929,095 (79.16)	12,034,845 (76.71)
4th to 6th month	2,633,303	24,652 (14.93)	174,869 (14.90)	2,433,782 (15.51)
7th to final month	712,696	5,961 (3.61)	44,335 (3.78)	662,400 (4.22)
Missing	336,204	3,247 (1.97)	18,562 (1.58)	314,395 (2.00)
Pre-pregnancy BMI category				
Underweight	513,776	1,415 (0.86)	17,134 (1.46)	495,227 (3.16)
Normal weight	6,943,656	27,538 (16.68)	266,815 (22.73)	6,649,303 (42.38)
Overweight	4,659,844	37,382 (22.64)	318,409 (27.13)	4,304,053 (27.43)
Obesity I	2,667,730	38,283 (23.18)	266,761 (22.73)	2,362,686 (15.06)
Obesity II	1,308,583	28,855 (17.47)	163,715 (13.95)	1,116,013 (7.11)
Obesity III	934,203	31,664 (19.17)	140,835 (12.00)	761,704 (4.86)
History of preterm birth				
Yes	595,092	15,199 (9.20)	58,759 (5.01)	521,134 (3.32)
No	10,254,960	95,428 (57.79)	726,691 (61.92)	9,432,841 (60.12)

Table 1 (continued)

Variable	N	Pre-pregnancy diabetes n (%)	Gestational diabetes n (%)	Non diabetes n (%)
Nulliparous	6,177,740	54,510 (33.01)	388,219 (33.08)	5,735,011 (36.55)
Infant sex				
Male	8,712,567	84,424 (51.12)	607,940 (51.80)	8,020,203 (51.12)
Female	8,315,225	80,713 (48.88)	565,729 (48.20)	7,668,783 (48.88)
Preterm birth				
Yes	1,374,286	42,658 (25.83)	133,689 (11.39)	1,197,939 (7.64)
No	15,653,506	122,479 (74.17)	1,039,980 (88.61)	14,490,450 (92.36)

Table 2 Associations of Pre-existing Diabetes and Gestational Diabetes with Preterm Birth by Race/ethnicity

Variables	Non-diabetes	Gestational diabetes	Pre-pregnancy diabetes	P for interaction
Preterm Birth				
Hispanic	1.00 (ref)	1.48 (1.46–1.50)	3.02 (2.95–3.09)	< 0.0001
non-Hispanic white	1.00 (ref)	1.44 (1.43–1.45)	4.01 (3.94–4.09)	
non-Hispanic black	1.00 (ref)	1.45 (1.42–1.47)	3.16 (3.08–3.24)	
non-Hispanic Asian	1.00 (ref)	1.38 (1.35–1.40)	2.22 (2.11–2.34)	
Other	1.00 (ref)	1.39 (1.35–1.44)	3.36 (3.19–3.53)	
Moderately preterm birth				
Hispanic	1.00 (ref)	1.57 (1.53–1.62)	3.12 (2.95–3.31)	0.0002
non-Hispanic white	1.00 (ref)	1.56 (1.52–1.59)	4.10 (3.93–4.29)	
non-Hispanic black	1.00 (ref)	1.56 (1.50–1.63)	3.37 (3.16–3.59)	
non-Hispanic Asian	1.00 (ref)	1.48 (1.41–1.56)	2.16 (1.90–2.46)	
Other	1.00 (ref)	1.43 (1.33–1.54)	3.17 (2.79–3.61)	
Very preterm birth				
Hispanic	1.00 (ref)	1.25 (1.13–1.38)	3.24 (2.78–3.79)	0.0002
non-Hispanic white	1.00 (ref)	1.09 (1.01–1.19)	3.52 (3.09–4.02)	
non-Hispanic black	1.00 (ref)	1.19 (1.07–1.33)	3.32 (2.89–3.83)	
non-Hispanic Asian	1.00 (ref)	1.23 (1.05–1.44)	2.18 (1.51–3.16)	
Other	1.00 (ref)	1.32 (1.06–1.64)	2.88 (2.04–4.09)	
Extremely preterm birth				
Hispanic	1.00 (ref)	–	1.88 (1.52–2.32)	< 0.0001
non-Hispanic white	1.00 (ref)	–	2.55 (2.14–3.05)	
non-Hispanic black	1.00 (ref)	–	2.03 (1.17–2.40)	
non-Hispanic Asian	1.00 (ref)	–	1.99 (1.27–3.11)	
Other	1.00 (ref)	–	1.73 (1.09–2.73)	

Maternal age, race/ethnicity, parity, education levels, smoking during pregnancy, previous history of preterm birth, marital status, infant sex, initiation of prenatal care, and pre-pregnancy BMI were adjusted in models. Maternal race/ethnicity and pre-pregnancy BMI category were not adjusted for when used as a stratified variable, respectively

The defect values in the table indicated that gestational diabetes had not been screened when extremely preterm birth occurred

[a] OR; 95% CI in parentheses (all such values)

those with GDM, and then by those with normal glucose levels, across all racial/ethnic groups. However, as pre-pregnancy BMI increased, the association between pre-pregnancy diabetes and preterm birth decreased for non-Hispanic Black women, while it showed an increasing trend for non-Hispanic Asians. For Hispanic women, a U-shaped relationship was observed. There were no significant differences in the risk of preterm birth among White women with pre-pregnancy diabetes at different pre-pregnancy BMI levels. Additionally, the relationship between GDM and preterm birth demonstrated a U-shaped trend from underweight to obesity III, and this pattern was relatively consistent across all racial groups. Joint analyses showed that non-Hispanic Black

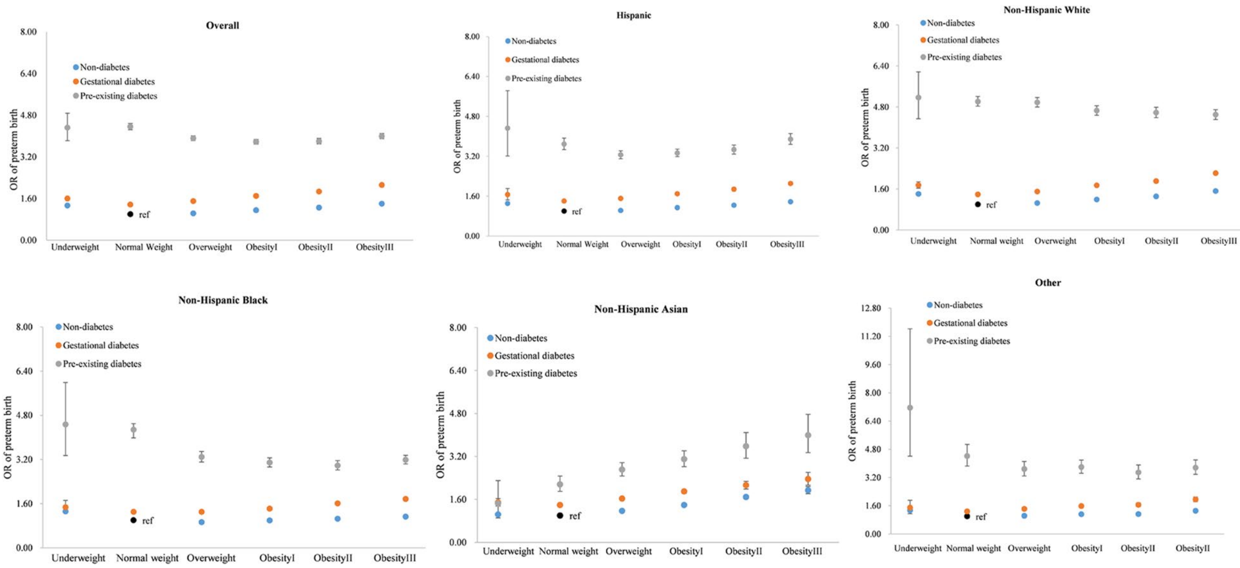

Fig. 1 Joint effects of diabetes and BMI on the risk of preterm birth in different race/ethnicity

individuals with normal blood sugar levels have a higher risk of preterm birth than non-Hispanic White individuals with GDM. Asian pregnant women with obesity, as well as Hispanic pregnant women with obesity II and obesity III, also have a higher risk of preterm birth than white women with GDM.

We found that maternal diabetes (pre-pregnancy diabetes and GDM) was associated with the increased risk of preterm birth, and the risk of preterm birth was the highest for pre-pregnancy diabetes, followed by GDM, compared with non-diabetic women. This is consistent with previous findings [13, 22]. Our further examination of the joint effect of maternal diabetes and race/ethnicity on preterm birth showed that the association between pre-pregnancy diabetes and preterm birth was the highest among non-Hispanic blacks compared with non-Hispanic whites. Moreover, we for the first time examined the association between pre-pregnancy diabetes and preterm birth among non-Hispanic Asians, and found that they had the lowest risk of preterm birth compared with other races/ethnicities group.

More importantly, we examined the association between preterm birth and maternal diabetes combined with various obesity severity overall and in different race/ethnic groups. Consistent with the limited previous studies [23, 24], we found that the risk of preterm birth increases for women with GDM with obesity severity increases. Moreover, we found that this pattern was the same across all races and ethnic groups. However, for women with pre-pregnancy diabetes, the risk of preterm birth did not change linearly with the increase severity of pre-pregnancy obesity. Previous studies regarding the association of preterm birth with maternal diabetes in combination with various BMI strata are limited [6, 7]. A Swedish population-based study found that the risk of preterm birth was similar for normal weight, overweight, and obese women with type 1 diabetes [6]. Besides, a Finnish study showed that the ORs of preterm birth for pre-pregnancy diabetes were similar across all maternal BMI strata [7]. It was worth noting that the majority of the populations included in these two studies are white, and their results were actually consistent with our stratified findings in whites. Our study added to the understanding of the joint effect of maternal diabetes and pre-pregnancy obesity on preterm birth across different racial/ethnic groups. Specifically, we, for the first time, found that the risk of preterm birth among women with pre-pregnancy diabetes increased with increasing obesity severity among non-Hispanic Asians, but decreased with increasing obesity severity among non-Hispanic Blacks. This finding suggested that recommendations should be tailored when addressing different racial/ethnic groups.

The mechanisms underlying these racial/ethnic differences are not clear. We found consistent evidence across different racial/ethnic groups that the risk of preterm birth was higher in women with maternal diabetes followed by those with GDM, compared to women with normal glucose levels [22]. This may reflect the impact of the duration and severity of individual glucose abnormalities on offspring [25]. The pattern of the relationship between maternal diabetes and preterm birth varies across different pre-pregnancy BMI groups among various racial/ethnic groups. This variation may be due to the different metabolic characteristics. A previous study showed that for the equivalent age-adjusted and sex-adjusted incidence of type 2 diabetes at a BMI of 30·0 kg/m^2 in White populations, the BMI cutoffs were 23·9 kg/m^2 in south Asian populations, 28·1 kg/m^2 in Black populations, 26·9 kg/m^2in Chinese populations [26].. Additionally, black women had the highest risk of preterm birth, which is even higher than that of White women with GDM. This may be related to factors such as socioeconomic status, stress, and health awareness. It has been reported that non-Hispanic black women generally had lower socioeconomic status and higher psychosocial stress compared to Whites [27]. These factors may lead to less access to prenatal care and poor diabetes management [28, 29], ultimately increasing the risk of preterm birth [28, 30]. In addition, non-Hispanic black women are less likely to screen and manage lipid health during pregnancy [31], and Asian women had greater odds of having low HDL-C compared to non-Hispanic White women [32]. Lipid health is also a key component in the pathophysiology of preterm birth [33, 34]. Racial/ethnic disparities in biological factors may play a role, at least partially. For example, compared to non-Hispanic whites, non-Hispanic Blacks have higher levels of c-reactive protein (CRP) and interleukin (IL)−6, non-Hispanic Asians have lower levels of CRP and IL-6 [35]. These two inflammation markers were strongly associated with preterm birth [35]. More research with abundant clinical data and biomarker test results is needed to understand the underlying mechanisms of racial/ethnic disparities in the association of maternal diabetes, GDM, and pre-pregnancy obesity with preterm birth.

While limited studies have explored the relationship between diabetes, obesity, and preterm birth, this research is the first to investigate racial disparities in the impact of these significant risk factors using the large-scale data from the NVSS. This study has significant clinical and public health implications. The findings underscore the urgent necessity for tailored guidelines during pregnancy, considering factors such as maternal diabetes, pre-pregnancy BMI, and racial/ethnic background together, to precisely assess the risk of preterm delivery. For example, non-diabetic black women with healthy BMI exhibited a higher risk of preterm birth then White women with GDM. Further studies are required to enhance these recommendations.

Strengths and limitations

The main strength of this study is the large sample size that allowed us to perform comprehensive analyses to, for the first time, investigate the racial/ethnic disparity in the joint association of maternal diabetes and maternal BMI strata with preterm birth. There are several limitations of our study. First, NVSS does not have information about the type, severity, and treatment of diabetes, which restricting our ability to identify their effects. Future studies with more comprehensive clinical data are needed to further investigate the effects of these factors, including types of diabetes, blood glucose levels, as well as treatment approaches, on the association of diabetes, obesity, and race/ethnicity with preterm birth. Secondly, maternal BMI was calculated from self-reported weight and height, which may suffer from recall bias. However, a previous study demonstrated that most women of reproductive age remained classified in the appropriate BMI categories according to self-reported height and weight [36]. Finally, although we have adjusted for many confounders in our analyses, we cannot rule out the effects of unknown or unmeasured factors.

Conclusions

In conclusion, while both pre-pregnancy diabetes and GDM were significantly associated with preterm birth, the associations varied by race/ethnicity. The risk of preterm birth for GDM increased with increasing BMI in all race/ethnicity groups. However, the pattern of the joint association of pre-pregnancy diabetes and BMI levels with preterm birth differed by race/ethnicity. Future studies on the underlying mechanisms of the racial/ethnic disparities in the association of diabetes and obesity with preterm birth are needed.

Abbreviations

BMI	Body Mass Index
GDM	Gestational Diabetes Mellitus
NCHS	The National Center for Health Statistics
NVSS	The US National Vital Statistics System

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12884-025-07352-2.

Supplementary Material 1.

Acknowledgements

Not applicable.

Authors' contributions

Buyun Liu and Wei Bao conceived the idea. Juan Xie and Buyun Liu analyzed the data. Juan Xie wrote the manuscript. All other authors (Yuxiang Yan, Ziyi Ye, Yuxiao Wu, Yongfu Yu, Yangbo Sun, Shuang Rong, Donna A. Santillan, Kelli Ryckman and Linda G. Snetselaar) critically revised the drafts of the manuscript. Buyun Liu and Wei Bao supervised all tasks. All authors approved the current version of the manuscript.

Funding

No funding.

Data availability

Buyun Liu and Wei Bao had full access to all the data in the study. Data ia available from the authors on direct request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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Received: 29 August 2024 Accepted: 19 February 2025
Published online: 21 March 2025

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