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Effects of pre-gestational diabetes mellitus and gestational diabetes mellitus on macrosomia and birth defects in Upstate New York

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ABSTRACT

Aims: To evaluate the effects of pre-gestational diabetes mellitus (PGDM) and gestational diabetes mellitus (GDM) on macrosomia and birth defects.

Methods: Existing birth registry data from the Perinatal Data System in Upstate New York was analysed. 650,914 women with a singleton term pregnancy (≥37 weeks) aged 18–55 years from 2004 to 2016 were included.

Results: The prevalence of macrosomia in infants born to women with PGDM and GDM were 26.0% and 16.4%, respectively, higher than that in the controls (11.2%). Compared with the controls (0.8%), the PGDM and GDM groups had higher prevalence of any birth defect (1.8% and 1.0%). The PGDM group had the highest prevalence of cyanotic heart disease (0.6%). Moreover, the PGDM group had higher prevalence of cleft lip and palate, cleft palate alone, hypospadias and limb reduction defect compared to the GDM and control groups ($p < 0.05$). However, these birth defects in the GDM group were similar to those in the controls. Both the PGDM and GDM groups had significantly elevated odds of macrosomia, cyanotic heart disease and any birth defect than controls. The PGDM group had higher odds of cleft lip and palate, cleft palate alone, hypospadias and limb reduction defect.

Conclusions: Using the Perinatal Data System database, PGDM and GDM, especially PGDM, was associated with higher prevalence of macrosomia, cyanotic heart disease and any birth defect in singleton term pregnancy in Upstate New York. PGDM, not GDM had higher prevalence of cleft lip and palate, cleft palate alone, hypospadias and limb reduction defect.

1. Introduction

Diabetes is one of the largest global health emergencies in the 21st century. In 2015, the International Diabetes Federation Diabetes Atlas produced estimates of hyperglycemia in pregnancy, estimating that 20.9 million live births were affected, which accounted for a staggering one in 7 births [1]. Hyperglycemia during pregnancy includes gestational diabetes

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mellitus (GDM) and pre-gestational diabetes mellitus (PGDM) in pregnancy.

GDM increases the frequency of adverse perinatal outcomes, chronic placental insufficiency, pre-eclampsia, premature birth, chronic hypoxia and fetal macrosomia [2–7]. The incidence of type 1 and type 2 diabetes mellitus amongst women of reproductive age is increasing worldwide [8,9]. PGDM was also reported to be associated with increased adverse maternal and neonatal outcomes [8,10,11].

Insulin resistance is the common mechanism in GDM and PGDM. Overweight/obesity, family history of diabetes, and age are the risk factors not only for PGDM, but also for GDM. PGDM and GDM are all associated with adverse pregnancy outcomes. However, studies comparing the impacts of PGDM and GDM on the neonatal outcomes are limited. Perinatal Data System (PDS) is an electronic birth certificate database. The PDS database in Upstate New York was from all counties in the Albany, Syracuse, Rochester, and Buffalo regions [12]. This study is to evaluate the effects of PGDM and GDM on macrosomia, cyanotic congenital heart disease and any birth defect in singleton term births in Upstate New York.

2. Materials and methods

2.1. Subjects

This was a retrospective analysis of existing birth registry data in Upstate New York. Permission was obtained for release of deidentified perinatal data from the New York State PDS files from each of the four Upstate perinatal designated regions. The PDS is mandated by the New York State Department of Health. PDS was designed to obtain information relating to the pregnancy and birth during the 72-hour period immediately following the birth of a live born child in New York State. The Research Subjects Review Board of University of Rochester reviewed this study and determined that it meets federal and University criteria for exemption (RSRB00067936).

All pregnant women aged between 18 and 55 years with a singleton term pregnancy (≥37 weeks) in the dataset were included in this analysis. This retrospective analysis included data from January 1, 2004 to December 31, 2016. This database combined deidentified perinatal data from the four regional databases (Syracuse, Rochester, Albany, and Buffalo). People with missing or incomplete data of glucose tolerance state, neonatal weight, malformation information, twin or multiple gestation, preterm births (<37 weeks) or aged younger than 18-year-old or older than 55 years were excluded.

Medical data were from maternal medical record [13]. PGDM was defined as having glucose intolerance requiring treatment before pregnancy diagnosed by a physician. GDM was defined as having glucose intolerance, diagnosed during this pregnancy by a physician. Women without the history of PGDM nor GDM were set as controls. Macrosomia was diagnosed when the infant weight was over 4,000 g. Birth defects were diagnosed by a physician. Birth defects included cyanotic congenital heart disease, anencephaly, cleft lip and palate, cleft palate alone, diaphragmatic hernia, Down syndrome, gastroschisis, hypospadias, limb reduction defect, meningomyelocele spina bifida, omphalocele, and suspected chromosomal disorder. Cyanotic congenital heart disease was defined if any of the following conditions had been diagnosed by a physician: transposition of the great arteries (vessels), teratology of Fallot, pulmonary or pulmonic valvular atresia, tricuspid atresia, truncus arteriosus, total or partial anomalous pulmonary venous return with or without obstruction. Limb reduction defect was defined if any of the following conditions had been diagnosed by a physician: a missing hand, arm, foot, or leg, or any portion of it, excluding congenital amputation and dwarfing syndromes. Any birth defect was defined as having any least one of above twelve birth defects, including multiple birth defects. Drinking during pregnancy means that the mother used alcohol during the pregnancy. Smoking during pregnancy means that the mother smoked cigarettes during each trimester of the pregnancy or during the three months prior to conception.

2.2. Statistical analysis

All statistical analyses were performed using SPSS version 17.0 (SPSS Inc., USA). Chi-Square test and Fisher's exact test were used for categorical data. Analysis of Variance was used for continuous variables. Logistic regression was performed. 95% confidence intervals (CI) were also calculated. A multiple hierarchical logistic regression was also performed to find the independent effects of GDM and PGDM on the neonatal outcomes after adjusting the confounding variables. Purposeful model selection method was used to select potential confounding covariates in the model. Hosmer and Lemeshow goodness-of-fit statistics were used to examine the goodness of fit of the data to the model. A p-value <0.05 is considered statistically significant. A p-value ≤0.017 is considered statistically significant in any two groups' comparison in multiple groups testing according to the Bonferroni method for multiplicity adjustment.

3. Results

3.1. Demographic characteristics

There were 650,914 pregnant women aged over 18-year-old who met the inclusion criteria in the PDS database. The prevalence of PGDM and GDM was 0.6% (4,134/650,914) and 5.0% (32,605/650,914) respectively. There were 614,175 (94.4%) women who had no history of PGDM or GDM. Women in the PGDM and GDM groups were older compared with women in the control group (30.36 ± 5.95, 30.62 ± 5.59, and 27.91 ± 5.71 years respectively, $p < 0.001$). The prevalence of women aged over 35 years in the control, GDM, and PGDM group were 13.8%, 25.4%, and 25.9%, respectively ($P < 0.001$, Table 1). The body mass index (BMI) in the control, GDM and PGDM group was 26.71 ± 6.56, 30.84 ± 8.04, and 32.94 ± 8.77 kg/m^2 ($p < 0.001$). Compared with women in the control group, women in the PGDM and GDM groups had higher prevalence of overweight and obesity (Table 1). Differences in education, race, drinking during pregnancy, smoking during pregnancy, pregnancy related hypertension, pre-pregnancy hypertension and depression were also statistically significant among these three groups ($p < 0.05$, Table 1).

Table 1 – Demographic characteristic of women in different groups.

	Control group (n = 614,175)	GDM group (n = 32,605)	PGDM group (n = 4,134)	P value
Age (years)	27.91 ± 5.71	30.62 ± 5.59**	30.36 ± 5.95**##	<0.001
Age ≥ 35 years, n (%)	84,626 (13.8%)	8268 (25.4%)**	1071 (25.9%)**	<0.001
Pre- pregnancy BMI (kg/m^2)	26.71 ± 6.56	30.84 ± 8.04**	32.94 ± 8.77**##	<0.001
BMI >=25 kg/m^2, n (%)	299,776 (48.8%)	22,999 (70.5%)**	3142 (76.0%)**##	<0.001
BMI >=30 kg/m^2, n (%)	148,265 (24.1%)	15,171 (46.5%)**	2295 (55.5%)**##	<0.001
Delivery BMI (kg/m^2)	31.99 ± 6.33	35.24 ± 7.59**	37.67 ± 8.32**##	<0.001
Education				<0.001
< 8 years, n (%)	10,785 (1.8%)	621 (1.9%)	97 (2.4%)	
9–11 years, n (%)	67,989 (11.1%)	2751 (8.5%)	484 (11.8%)	
12 years, n (%)	152,806 (25.0%)	7645 (23.6%)	1041 (25.3%)	
13–15 years, n (%)	190,444 (31.1%)	10,865 (33.5%)	1505 (36.6%)	
16 < years, n (%)	189,550 (31.0%)	10,569 (32.6%)	990 (24.0%)	
Employed during pregnancy	383,757 (62.5%)	20,626 (63.3%)**	2355 (57.0%)**##	<0.001
Race				<0.001
White, n (%)	506,840 (83.3%)	25,814 (80.2%)	3199 (78.3%)	
Black, n (%)	57,660 (9.5%)	2763 (8.6%)	521 (12.8%)	
Asian/Pacific Islander, n (%)	18,744 (3.1%)	2192 (6.8%)	115 (2.8%)	
American Indian/Native Alaskan, n (%)	2235 (0.4%)	174 (0.5%)	40 (1.0%)	
Other (Other/Native Hawaiian, n (%)	11,821 (1.9%)	705 (2.2%)	107 (2.6%)	
Multiple races, n (%)	10,976 (1.8%)	530 (1.6%)	103 (2.5%)	
Drinking during pregnancy, n (%)	5202 (0.8%)	250 (0.8%)	48 (1.2%)*##	0.025
Smoking during pregnancy, n (%)	90,414 (14.7%)	4095 (12.6%)**	686 (16.6%)**##	<0.001
Pregnancy related hypertension, n (%)	22,186 (3.6%)	2735 (8.4%)**	414 (10.0%)**##	<0.001
Pre-pregnancy hypertension, n (%)	7910 (1.3%)	1306 (4.0%)**	542 (13.1%)**##	<0.001
Depression, n (%)	162,796 (30.1%)	8700 (30.0%)	1298 (35.3%)**##	<0.001

GDM: gestational diabetes mellitus, PGDM: pre-gestational diabetes mellitus.
Compared to the control group * p < 0.05, ** p < 0.01; compared to the GDM group # p < 0.05, ## p < 0.01.

3.2. *Macrosomia and birth defects*

There were 75,387 infants with macrosomia, accounting for 11.6% of all singleton births. The prevalence of macrosomia in the GDM and PGDM groups was 16.4% (5,344/32,605) and 26.0% (1076/4134) respectively, significantly higher than that in the control group (11.2%, Table 2).

The overall prevalence of any birth defect was 0.8% (5316 /650,914). Compared with the controls, the PGDM and GDM groups had higher prevalence of any birth defect. The prevalence of any birth defect in the PGDM group was 1.8%, higher than that in the GDM group (1.2%, Table 2).

The overall prevalence of cyanotic congenital heart disease was 0.1% (755/650,914). The PGDM group had the highest prevalence of cyanotic congenital heart disease (0.6%, Table 2).

The PGDM had higher prevalence of cleft lip and palate, cleft palate alone, hypospadias and limb reduction defect

Table 2 – The prevalence of neonatal outcomes in different groups.

	Control group (n = 614,175)	GDM group (n = 32,605)	PGDM group (n = 4,134)	Total	P value
Macrosomia, n (%)	68,967 (11.2%)	5344 (16.4%)**	1076 (26.0%)**##	75,387 (11.6%)	<0.001
Any birth defect, n (%)	4920 (0.8%)	320 (1.0%)**	76 (1.8%)**##	5,316 (0.8%)	<0.001
Cyanotic heart disease, n (%)	680 (0.1%)	50 (0.2%)*	25 (0.6%)**##	755 (0.1%)	<0.001
Anencephaly, n (%)	37 (0.0%)	1 (0.0%)	0 (0.0%)	38 (0.0%)	0.702
Cleft lip and palate, n (%)	417 (0.1%)	22 (0.1%)	7 (0.2%)*#	446 (0.1%)	0.046
Cleft palate alone, n (%)	195 (0.0%)	10 (0.0%)	5 (0.1%)**##	210 (0.0%)	0.006
Diaphragmatic hernia, n (%)	99 (0.0%)	8 (0.0%)	1 (0.0%)	108 (0.0%)	0.480
Down Syndrome, n (%)	424 (0.1%)	30 (0.0%)	1 (0.1%)	455 (0.1%)	0.167
Gastroschisis, n (%)	94 (0.0%)	1 (0.0%)	0 (0.0%)	95 (0.0%)	0.157
Hypospadias, n (%)	690 (0.1%)	46 (0.1%)	11 (0.3%)**	747 (0.1%)	0.005
Limb reduction defect, n (%)	172 (0.0%)	13 (0.0%)	4 (0.1%)**	189 (0.0%)	0.018
Meningomyelocele Spina Bifida, n (%)	94 (0.0%)	5 (0.0%)	2 (0.0%)	101 (0.0%)	0.235
Omphalocele, n (%)	31 (0.0%)	3 (0.0%)	1 (0.0%)	35 (0.0%)	0.149
Suspected chromosomal disorder, n (%)	269 (0.0%)	15 (0.0%)	4 (0.1%)	288 (0.0%)	0.269

GDM: gestational diabetes mellitus, PGDM: pre-gestational diabetes mellitus.
Compared to the control group * p < 0.05, ** p < 0.01, compared to the GDM group # p < 0.05, ## p < 0.01.

compared to the GDM and the control group (0.2%, 0.1%, 0.3%, and 0.1%, respectively, Table 2). The prevalence of cleft palate alone in the PGDM group was statistically significant compared to that in the GDM group ($p < 0.01$, Table 2). However, these birth defects in the GDM group were similar to those in the control group ($p > 0.05$, Table 2).

There was no significant difference in the prevalence of anencephaly, diaphragmatic hernia, Down syndrome, gastroschisis, meningomyelocele spina bifida, omphalocele, and suspected chromosomal disorder among these three groups ($p > 0.05$, Table 2).

3.3. *Risk factors for neonatal macrosomia and birth defects*

Logistic regression was conducted to compare the difference between the PGDM and GDM groups in their association with neonatal macrosomia and birth defects, using the controls as reference (Table 3). Results from unadjusted logistic regression analysis showed that both the PGDM (OR = 2.78, 95% CI: 2.59–2.98, $p < 0.001$) and GDM (OR = 1.55, 95% CI: 1.50–1.60, $p < 0.001$) groups had significantly elevated odds of macrosomia than the control group.

Results from unadjusted logistic regression analysis showed that both the PGDM (OR = 2.32, 95% CI: 1.85–2.92, $p < 0.001$) and GDM groups (OR = 1.23, 95% CI: 1.10–1.38, $p < 0.001$) had significantly elevated odds of any birth defect than the control group. Moreover, both the PGDM (OR = 5.49, 95% CI: 3.68–8.19, $p < 0.001$) and GDM groups (OR = 1.39, 95% CI: 1.04, 1.85, $p = 0.026$) had significantly elevated odds of cyanotic congenital heart disease than the control group in the logistic regression analysis.

After adjusting the confounding variables, these associations persisted. The adjusted ORs for macrosomia, cyanotic congenital heart disease and any birth defect were 2.29 (95% CI: 2.11–2.47), 4.97 (95% CI: 3.20–7.70), and 2.18 (95% CI: 1.69, 2.80, p all < 0.001) in the PGDM group. The adjusted ORs for macrosomia, cyanotic congenital heart disease and any birth defect were 1.25 (95% CI: 1.21–1.29), 1.42 (95% CI: 1.05–1.92), and 1.21 (95% CI: 1.07, 1.37, p all < 0.05, Table 3) in the GDM group.

In the logistic regression, the PGDM group had higher odds of cleft lip and palate, cleft palate alone, hypospadias and limb reduction defect (crude ORs were 2.50 (1.18–5.27), 3.81 (1.57–9.27), 2.37 (1.31–4.31), and 3.46 (1.28–9.32), respectively, p all < 0.05). After adjusting the confounding variables, these associations persisted (adjusted ORs were 2.89 (1.37–6.12), 3.75 (1.39–10.11), 2.02 (1.04–3.92), and 3.95 (1.46–10.67), respectively, p all < 0.05). However, the GDM group did not show any association with these birth defects ($p > 0.05$, Table 4).

4. Discussion

In this retrospective study using the PDS database, PGDM and GDM, especially PGDM seemed to be associated with higher prevalence of macrosomia, cyanotic congenital heart disease and any birth defect in singleton term pregnancy in the Upstate New York region. After adjusting the confounding variables, these associations remained. Moreover, PGDM, not GDM was associated with cleft lip and palate, cleft palate alone, hypospadias and limb reduction defect.

Macrosomia has been demonstrated to be the predominant adverse outcome in cases of GDM [9,14]. Macrosomia is typically defined as a birth weight above the 90th percentile for gestational age or $\geq$4000 g [15]. Maternal hyperglycemia, maternal obesity, gestational age at delivery, maternal pre-pregnancy BMI, hypertension and cigarette smoking all had effects on fetal macrosomia [15–17]. GDM has proved to be an independent risk factor for newborn macrosomia in a meta-analysis [18]. As shown in other studies [19], we found that PGDM and GDM were all independently associated with macrosomia after adjusting BMI, age, hypertension, and smoking in this study. However, we found that PGDM had greater effect on infant macrosomia than GDM. In a prospective pregnancy cohort using data from the Avon longitudinal study, PGDM and GDM had similar effect on infant macrosomia [19]. Different criteria for macrosomia may relate with different results. In a population-based cohort study in South Australia assessing the risk of congenital anomalies in infants born to women with maternal diabetes, the increasing prevalence of macrosomia was only found in women with PGDM, not in women with GDM, when macrosomia is defined as a birth weight above the 90th percentile [20]. Maternal BMI is another important risk factor for macrosomia besides PGDM and GDM. However, the South Australia study did not control for the maternal BMI effect. In our study, the means of pre-

Table 3 – The odds ratio and 95% confidence intervals of pre-gestational diabetes mellitus and gestational diabetes mellitus related to macrosomia, any birth defects and cyanotic congenital heart disease in the hierarchical logistic regression analysis.

	Macrosomia			Any birth defect			Cyanotic Congenital heart disease		
	Odds Ratio	95% CI	p value	Odds Ratio	95% CI	p value	Odds Ratio	95% CI	P value
Model 1									
PGDM	2.78	2.59, 2.98	<0.001	2.32	1.85, 2.92	<0.001	5.49	3.68, 8.19	<0.001
GDM	1.55	1.50, 1.60	<0.001	1.23	1.10, 1.38	<0.001	1.39	1.04, 1.85	0.026
Model 2									
PGDM	2.29	2.11, 2.47	<0.001	2.18	1.69, 2.80	<0.001	4.97	3.20, 7.70	<0.001
GDM	1.25	1.21, 1.29	<0.001	1.21	1.07, 1.37	0.003	1.42	1.05, 1.92	0.022

Model 1: unadjusted.
Model 2: adjusted for age (35 years or not), smoking during pregnancy, drinking during pregnancy, race, education, employed during pregnancy, pre-pregnancy BMI, depression, hypertension (pre-pregnancy and gestational hypertension).
PGDM: pre-gestational diabetes mellitus; GDM: gestational diabetes mellitus; CI: confidence intervals.

Table 4 – The odds ratio and 95% confidence intervals of pre-gestational diabetes mellitus and gestational diabetes mellitus related to congenital cleft lip and palate, cleft palate alone, hypospadias and limb reduction defect in the hierarchical logistic regression analysis.

	Cleft lip and palate			Cleft palate alone			Hypospadias			Limb reduction defect		
	Odds Ratio	95% CI	p value	Odds Ratio	95% CI	P value	Odds Ratio	95% CI	p value	Odds Ratio	95% CI	P value
Model 1												
PGDM	2.45	1.18, 5.27	0.016	3.81	1.57, 9.27	0.003	2.37	1.31, 4.31	0.005	3.46	1.28, 9.32	0.014
GDM	0.99	0.65, 1.53	0.977	0.97	0.51, 1.82	0.915	1.26	0.93, 1.69	0.135	1.42	0.81, 2.50	0.219
Model 2												
PGDM	2.89	1.37, 6.12	0.005	3.75	1.39, 10.11	0.009	2.02	1.04, 3.92	0.037	3.95	1.46 10.67	0.007
GDM	1.04	0.65, 1.65	0.880	1.06	0.54, 2.08	0.856	1.27	0.93, 1.74	0.133	1.15	0.59, 2.26	0.679

Model 1: unadjusted.
Model 2: adjusted for age (35 years or not), smoking during pregnancy, drinking during pregnancy, race, education, employed during pregnancy, pre-pregnancy BMI, depression, hypertension (pre-pregnancy and gestational hypertension).
PGDM: pre-gestational diabetes mellitus; GDM: gestational diabetes mellitus; CI: confidence intervals.

pregnancy BMI in the GDM and PGDM group were over 30 kg/m^2, which was found to have increased the risk of neonatal macrosomia.

Congenital heart disease was the other infant outcome associated with diabetes mellitus. In a meta-analysis using data from the Texas Birth Defects Registry and statewide vital records for deliveries between 1999 and 2009, PGDM and GDM were all found to be associated with cyanotic congenital heart disease. While PGDM had an even stronger association with the presence of most congenital heart disease phenotypes and categories [21]. Other studies also found stronger associations between congenital heart disease and PGDM than between congenital heart disease and GDM [20,22,23]. In our study, PGDM had much stronger association with congenital heart disease compared with GDM, even adjusted the other confounding risk factors such as age and BMI.

PGDM and GDM were risks not only for fetal congenital heart disease but also for other birth defects [22,24,25]. An observational study recruited pregnant women between 2002 and 2010 and reported that the birth defect rate was greater in the type 2 diabetes mellitus group than that in the general population [24]. Another observation study using the Swedish Medical Birth Registry database found that the total defect rate in PGDM was higher than that in GDM, however, the rate in GDM was similar to the population rate [22]. Schaefergraf et al. [25] reported that major birth defects were higher in the type 2 diabetes mellitus group than that in the GDM group.

Congenital cleft lip and palate were birth defect associated with diabetes mellitus. It was reported that diabetes, either PGDM or GDM, would increase the risk of orofacial cleft [26]. In our study, cleft lip and palate and cleft palate alone were much more be seen in women with PGDM than in women with GDM and control group. PGDM, not GDM might increase the risk of cleft lip and palate and cleft palate alone by 2.9 to 3.7 fold. Similar results were found in the analysis of hypospadias and limb reduction defect.

In our study, similar result was found that PGDM showed a stronger positive association with major birth defects compared with GDM. PGDM/GDM may be related to different physiopathological mechanisms. Whether GDM will increase the risk of fetal congenital malformation varied in different studies. PGDM and GDM have similar risk factors, such as age and being overweight/obese. Age may also relate to some kinds of birth defects. Being overweight/obese may be accompanied with other metabolic disorders, which may increase the risk of birth defect. This may contribute to the result that birth defect rate in GDM was higher than that in the general population. We found that compared to women without history of diabetes, women with PGDM and GDM was older, having higher BMI and higher prevalence of hypertension. After adjusting age, BMI, hypertension, and other variables, PGDM and GDM remained to be associated with fetal defects. Moreover, PGDM had a stronger association with birth defects compared to GDM, which might be caused by PDGM accompanying the whole period of fetal development process. However, GDM always manifests after 24th–28th weeks of pregnancy.

The mechanisms underlying the association between GDM and birth defects are not well known. It is commonly

known that hyperglycemia plays an important role. It was postulated that insulin resistance might exist during the whole pregnancy even GDM manifested after the 24th weeks of pregnancy [27]. Insulin resistance-associated oxidative stress, abnormal cytokine and adipokines may relate to birth defects, which need further experimental and prospective studies. Besides hyperglycemia, pre-gestational overweight/obese is another risk factor, which had been found to be associated with birth defects [28]. In the study, women with GDM or PGDM were elder than the controls. Age is another risk factor for birth defects.

There were some limitations in this study. First, there was no HbA1c or glucose control data. It was well known that glucose control was associated with macrosomia and fetal congenital malformation [25]. Second, there was no information on the type of PGDM, the treatment and the duration of diabetes, e.g. PGDM was not categorized as type 1 diabetes or type 2 diabetes mellitus. Third, this analysis included data between 2004 and 2016. The diagnose threshold for GDM had changed during this period. The American Diabetes Association criterion was accepted in 2006. The International Association of Diabetes in Pregnancy Study Groups issued the diagnostic criterion in 2010 and was widely accepted in 2013 [29]. However, there was no related information about which criteria for diagnosis GDM was selected between 2004 and 2016 in the PDS. The diagnosis of PGDM and GDM were all self-reported. Fourth, we mainly aimed to compare the risk of both macrosomia and birth defects between PGDM and GDM in full-term babies. Thus, we excluded the preterm birth, which may increase the risk for birth defects. The percentage of birth defects might be underestimated in this study. In addition, PDS was designed to obtain information relating to the pregnancy and birth during the 72-hour period immediately following the birth of a live born child. The suspected chromosomal disorders were not confirmed by further examinations. This percentage of suspected chromosomal disorder in this study might be overestimated.

In this secondary analysis on PDS database from 2004 to 2016, PGDM and GDM, especially PGDM, seemed to be associated with higher prevalence of macrosomia, cyanotic congenital heart disease and any birth defect in singleton term pregnancy in Upstate New York. Moreover, PGDM had higher odds of congenital cleft lip and palate, cleft palate alone, hypospadias and limb reduction defect. Even after adjusting the confounding variables, these associations remained. Screening PGDM and GDM may be helpful for decreasing the risk of macrosomia and any birth defect in infants, especially for women aged over 35 or with higher BMI.

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Declaration of Competing Interest

None.

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