Observational Study

Medicine

OPEN

Association between gestational diabetes mellitus and adverse obstetric outcomes among women with advanced maternal age

A retrospective cohort study

Lijun Deng, MD[a], Beibei Ning, MM[a], Hailan Yang, MD[a,*]

Abstract

To explore the association of gestational diabetes mellitus (GDM) with maternal and neonatal adverse outcomes among women with advanced maternal age. This retrospective cohort study included 1551,140 eligible pregnant women from the National Vital Statistics System database in 2017 to 2019, and all participants were divided into two groups: GDM group (n = 154,646) and non-GDM group (n = 1396,494). Univariate and multivariate logistic regression analyses were used to assess the association of GDM and maternal and neonatal outcomes; additionally, we also adopted subgroup analysis to analyze the association in detail based on gestational weight gain (GWG) levels. The risk of each adverse outcome was presented by using odds ratio (OR) and 95% confidence interval (CI). After adjusted some covariables, GDM increased the risk of neonatal assisted ventilation (OR = 1.380, 95% CI: 1.345–1.417), neonatal intensive care unit (NICU, OR = 1.436, 95% CI: 1.410–1.463) admission, neonatal low Apgar score at the fifth minutes (OR = 1.034, 95% CI: 1.018–1.051), neonatal high birth weight (OR = 1.132, 95% CI: 1.111–1.153), neonatal premature birth (OR = 1.244, 95% CI: 1.223–1.266), mothers entered intensive care unit (ICU, OR = 1.247, 95% CI: 1.107–1.406), and mothers took cesarean section (OR = 1.193, 95% CI: 1.180–1.207) among women with advanced maternal age. The study findings indicated that GDM was the risk factor for obstetric outcomes among women with advanced maternal age, which will have important implications for the management of GDM in women with advanced maternal age.

Abbreviations: BMI = body mass index, GWG, gestational weight gain, CI = confidence interval, GDM = gestational diabetes mellitus, ICU = intensive care unit, IOM = Institute of Medicine, NCHS = National Center for Health Statistics, NICU = neonatal intensive care unit, NVSS = National Vital Statistics System, OR = odds ratio, SD = standard deviation, WIC = Women, Infants, and Children.

Keywords: gestational diabetes mellitus, NVSS, obstetric outcomes, woman with advanced maternal age

1. Introduction

Gestational diabetes mellitus (GDM), as a common pregnancy complication, is defined as glucose intolerance occurring or first detected during pregnancy, and glucose levels are lower than those diagnosed overt diabetes outside of pregnancy.[1,2] Over the past few decades, the incidence of GDM has increased significantly, especially among women with advanced maternal age (>35 years).[1,3] Globally, GDM affects about 13.9% of pregnancies that the prevalence of GDM in high-risk population reaches almost 27%.[4] Furthermore, the prevalence of GDM rises with gestational age from 25% in 23rd week of gestation,[5] up to 33% in third trimester of pregnancy.[6] GDM poses significant short-term and long-term threat among the mother and their offspring.

It has previously been observed that GDM is liable to have many adverse effects on the pregnancy outcomes of pregnant women and newborns, seriously affecting the maternal and neonatal health.[7,8] In the study of Prakash et al,[9] GDM has been found to be associated with increased risk of complications among mother and newborn, including pregnant women required to take cesarean section, newborns had the high birth weight and required neonatal intensive care unit (NICU) admission. Similarly, Boriboonhirunsarn et al[10] also pointed that the incidence of emergency cesarean section in pregnant women with GDM was significantly higher than normal pregnant women, the possible reason is that GDM patients need to take cesarean sections to avoid complications of macrosomia.[11] Not only that, preterm birth has long been recognized an important cause to affect perinatal mortality and neonatal morbidity[12–14]; a cohort study reported that GDM increased the risk of preterm birth.[13] Nonetheless, to our knowledge, most studies have not considered how GDM on adverse maternal and neonatal outcomes among women with advanced maternal age at present.

With the societal trend for childbearing at a later age,[3] more women are getting pregnant at an older age, which might face higher risk of complications. Therefore, the study of GDM about

The authors have no funding and conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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How to cite this article: Deng L, Ning B, Yang H. Association between gestational diabetes mellitus and adverse obstetric outcomes among women with advanced maternal age: A retrospective cohort study. Medicine 2022;101:40(e30588).

Received: 8 April 2022 / Received in final form: 11 August 2022 / Accepted: 15 August 2022

http://dx.doi.org/10.1097/MD.0000000000030588

women with advanced maternal age should be paid more attention. Our study aimed to explore the association of GDM with adverse maternal and neonatal outcomes among women with advanced maternal age based on the National Vital Statistics System (NVSS).

2. Methods

2.1. Study design and data sources

All data of this longitudinal study were obtained from the NVSS,[15,16] which provides the most complete data on births and deaths in the United States. In the United States, all births need to fill out a birth certificate, and death certificates also are registered. The NVSS is the result of a cooperation between the National Center for Health Statistics (NCHS) and states to provide statistical information obtained from birth and death certificates, which make the NVSS become successful example of inter-governmental data sharing in Public Health.

2.2. Study eligibility criteria

In the present study, we collected data of pregnant women with advanced maternal age (referred to ≥35 years in this article) from the NVSS database between 2017 and 2019. The inclusion criteria were as follows: participants were ≥35 years; participants had no a history of pre-pregnancy diabetes. The exclusion criteria: participants were infected during this pregnancy (n = 30,054); participants had pre-pregnancy hypertension or gestational hypertension or eclampsia or infertility treatment or neonatal limb deformity (n = 314,119); participants had incomplete baseline information (n = 150,299). The final analysis included 1551,140 eligible pregnant women. These women with advanced maternal age were divided into two groups: GDM group (n = 154,646) and non-GDM group (n = 1396,494). Considering that our data were obtained from a publicly available database and desensitized, there was no need of ethic approval and informed consent.

2.3. Measurement of variables

2.3.1. Primary exposure variable and covariates. Primary exposure variable was GDM in this study; maternal GDM was defined as a newly diagnosed diabetes during pregnancy.[2] Covariates included maternal age, ethnicity, educational background, pre-pregnancy body mass index (BMI), gestational weight gain (GWG), number of prenatal visits, smoking status before pregnancy, smoking status during the first trimester, smoking status during the second trimester, smoking status during the third trimester, plurality, birth order, WIC (The Special Supplemental Nutrition Program for Women, Infants, and Children) food use history, preterm birth history, number of cesarean sections in the past, gestational age, and newborn gender.

2.3.2. Outcome variables. The adverse obstetric outcomes refer to neonatal and the maternal adverse outcomes. Neonatal adverse outcomes were defined as the presence of the following: birth weight, neonatal assisted ventilation, NICU admission, low Apgar score at the fifth minutes, preterm birth. Maternal adverse outcomes were considered as entering intensive care unit (ICU) and taking cesarean section. Low birth weight is considered to <2500 g, high birth weight: ≥4000 g.[17] Apgar score at the fifth minutes ranges from 0 to 10 is a measure of the neonatal condition based on heart rate, respiration, muscle tone, reflex stimuli and color; Apgar scores at the fifth minutes was divided into 4 groups: Apgar 0 to 3, Apgar 4 to 6, Apgar 7 to 8, and Apgar 9 to 10.[18] Preterm birth pointed the birth of a live infant before 37 weeks of gestation.[19] Furthermore, GWG levels were divided into less GWG, normal GWG and excess GWG based on the standard, normal GWG pointed the gain of 28 to 40 lb for underweight women [BMI < 18.5]; 25 to 35 lb for normal-weight women [BMI: 18.5–24.9]; 15 to 25 lb for overweight women [BMI: 25–29.9]; and 11 to 20 lb for obese women [BMI ≥ 30] according to the Institute of Medicine (IOM) guidelines.[20]

2.4. Statistical analysis

Kolmogorov–Smirnov was used to conduct normality test for quantitative data. The continuous variable of normally distributed was exhibited as mean ± standard deviation (Mean ± SD), and *t* test was used for comparison between groups. The non-normally distributed quantitative data were analyzed by median and interquartile range, and the comparison between groups adopted rank sum test. Categorical variables were used to describe the number and percentage of each category. χ^2 test was used for comparison between groups.

Firstly, we performed an analysis of differences between groups to select statistically significant variables. Then all variables were included in the multivariate analysis for stepwise regression, which explored the association between neonatal and maternal adverse outcome variables with GDM, respectively. In addition, it is reported that GWG, as an important index for the health of women and their fetuses, was associated with pregnancy complications and neonatal adverse outcomes,[21] thus we adopted subgroup analysis based on GWG levels to explore the maternal and neonatal adverse outcomes among women with advanced maternal age. The risk of each adverse outcome was presented by using odds ratio (OR) and 95% confidence interval (CI). Statistical analyses were performed by using SAS (version 9.4) (CI). Statistical analyses were performed by using SAS (version 9.4, Institute Inc., Cary, NC, USA) software. All statistical tests were conducted by bilateral test. $P < .05$ was considered as statistically significant.

3. Results

3.1. Baseline characteristics

A total of 1551,140 women with advanced maternal age were enrolled in our study eventually, which were divided into two groups: GDM group (n = 154,646) and non-GDM group (n = 1396,494). Table 1 displayed the baseline information of all participants. In this population, the average age of mothers was 37.34 ± 2.29; 62,769 pregnant women had preterm birth history and 364,337 had caesarean section in the past. Compared with pregnant women without GDM, pregnant women with GDM were older, had lower GWG, and had caesarean section more frequently, detailed baseline information was given in Table 1. Similarly, we also summarized the distribution of maternal and neonatal outcome variables in the population. Just as Table 2 suggested, 325 pregnant women need to enter into the ICU and 73,570 pregnant women required to take caesarean section; the average Apgar score at the fifth minutes for newborns was 8.82 ± 0.69; 7478 infants need to use assisted ventilation immediately, and 10,703 were low birth weight. Detailed information was shown in Table 2.

3.2. The association of GDM and adverse obstetric outcomes among women with advanced maternal age by multivariate logistic regression

As shown in Table 3, after adjusted covariates, including maternal age, ethnicity, pre-pregnancy BMI, educational background, GWG, number of prenatal visits, smoking status before pregnancy and during the first trimester, plurality, birth order, WIC food use history, preterm birth history, newborn gender, the results showed that GDM was associated with the increased risk of premature birth (OR = 1.244, 95% CI: 1.223–1.266);

Table 1

Baseline characteristics of all included participants.

Variables	Total (n = 1551,140)	Non-GDM group (n = 1396,494)	GDM group (n = 154,646)	Statistics	P
Maternal age, yr, mean ± SD	37.34 ± 2.29	37.31 ± 2.27	37.66 ± 2.43	$t = -53.93$	<.001
Maternal ethnicity, n (%)				$\chi^2 = 6574.526$	<.001
White	1,148,378 (74.03)	1,042,013 (74.62)	106,365 (68.78)		
Black	189,918 (12.24)	172,731 (12.37)	17,187 (11.11)		
Asian	177,716 (11.46)	150,444 (10.77)	27,272 (17.64)		
Others	35,128 (2.26)	31,306 (2.24)	3822 (2.47)		
Maternal education background, n (%)				$\chi^2 = 9299.624$	<.001
8th grade or less	73,190 (4.72)	61,591 (4.41)	11,599 (7.50)		
9th through 12th grade with no diploma	85,425 (5.51)	73,424 (5.26)	12,001 (7.76)		
High school graduate or GED completed	220,381 (14.21)	193,953 (13.89)	26,428 (17.09)		
Some college credit, but not a degree	219,552 (14.15)	195,568 (14.00)	23,984 (15.51)		
Associate degree	129,563 (8.35)	115,362 (8.26)	14,201 (9.18)		
Bachelor's degree	444,990 (28.69)	407,252 (29.16)	37,738 (24.40)		
Master's degree	277,089 (17.86)	255,499 (18.30)	21,590 (13.96)		
Doctorate or professional degree	100,950 (6.51)	93,845 (6.72)	7105 (4.59)		
Pre-pregnancy BMI, kg/m^2, n (%)				$\chi^2 = 29079.97$	<.001
Underweight	33,101 (2.13)	31,243 (2.24)	1858 (1.20)		
Normal	684,209 (44.11)	640,845 (45.89)	43,364 (28.04)		
Overweight	441,230 (28.45)	395,064 (28.29)	46,166 (29.85)		
Obesity I	230,484 (14.86)	196,952 (14.10)	33,532 (21.68)		
Obesity II	100,532 (6.48)	82,882 (5.94)	17,650 (11.41)		
Extremely obesity III	61,584 (3.97)	49,508 (3.55)	12,076 (7.81)		
GWG, lb, M (Q1, Q3)	28.00 (20.00, 37.00)	29.00 (20.00, 37.00)	26.00 (18.00, 36.00)	$Z = -39.384$	<.001
Smoking before pregnancy, n (%)				$\chi^2 = 138.850$	<.001
No	1,477,460 (95.25)	1,331,095 (95.32)	146,365 (94.65)		
Yes	73,680 (4.75)	65,399 (4.68)	8281 (5.35)		
Smoking 1st trimester, n (%)				$\chi^2 = 32.629$	<.001
No	1,495,622 (96.42)	1,346,907 (96.45)	148,715 (96.16)		
Yes	55,518 (3.58)	49,587 (3.55)	5931 (3.84)		
Smoking 2nd trimester, n (%)				$\chi^2 = 7.633$	.006
No	1,503,032 (96.90)	1,353,361 (96.91)	149,671 (96.78)		
Yes	48,108 (3.10)	43,133 (3.09)	4975 (3.22)		
Smoking 3rd trimester, n (%)				$\chi^2 = 6.183$	.013
No	1,505,076 (97.03)	1,355,180 (97.04)	149,896 (96.93)		
Yes	46,064 (2.97)	41,314 (2.96)	4750 (3.07)		
Plurality, n (%)				$\chi^2 = 17.844$	<.001
Single	1,501,037 (96.77)	1,351,591 (96.78)	149,446 (96.64)		
Twin	49,031 (3.16)	43,920 (3.15)	5111 (3.30)		
Triplet	1035 (0.07)	946 (0.07)	89 (0.06)		
Quadruplet	37 (0.00)	37 (0.00)	0 (0.00)		
Number of prenatal visits, n (%)				$\chi^2 = 3610.775$	<.001
12	987,683 (63.67)	899,996 (64.45)	87,687 (56.70)		
>12	563,457 (36.33)	496,498 (35.55)	66,959 (43.30)		
nBirth order, n (%)				$\chi^2 = 1506.530$	<.001
3	954,412 (61.53)	866,305 (62.03)	88,107 (56.97)		
>3	596,728 (38.47)	530,189 (37.97)	66,539 (43.03)		
WIC food use history, n (%)				$\chi^2 = 5672.594$	<.001
No	1,187,320 (76.54)	1,080,854 (77.40)	106,466 (68.84)		
Yes	363,820 (23.46)	315,640 (22.60)	48,180 (31.16)		
Gestational age, wk, mean ± SD	38.59 ± 2.12	38.62 ± 2.12	38.28 ± 2.08	$t = 61.73$	<.001
Number of cesarean sections in the past, n (%)				$\chi^2 = 1074.140$	<.001
0	1,186,803 (76.51)	1,073,665 (76.88)	113,138 (73.16)		
>0	364,337 (23.49)	322,829 (23.12)	41,508 (26.84)		
Preterm birth history, n (%)				$\chi^2 = 921.557$	<.001
No	1,488,371 (95.95)	1,342,215 (96.11)	146,156 (94.51)		
Yes	62,769 (4.05)	54,279 (3.89)	8490 (5.49)		
Newborn gender, n (%)				$\chi^2 = 16.617$	<.001
Female	758,271 (48.88)	683,433 (48.94)	74,838 (48.39)		
Male	792,869 (51.12)	713,061 (51.06)	79,808 (51.61)		

BMI = body mass index, GDM = gestational diabetes mellitus, GED = general equivalent diploma, GWG = gestational weight gain, SD = standard deviation, WIC = Women, Infants, and Children.

when the calibrated covariates were also included smoking status during the second trimester and the third trimester, the results indicated that GDM could increase the risk of neonatal outcomes of assisted ventilation (OR = 1.380, 95% CI: 1.345–1.417), NICU admission (OR = 1.436, 95% CI: 1.410–1.463), low Apgar score at the fifth minutes (On a scale of 10 to 0, OR = 1.034, 95% CI: 1.018–1.051), and high birth weight (OR = 1.132, 95% CI: 1.111–1.153). Likewise, the effect of GDM on maternal adverse outcomes was presented in the Table 4; after adjusted maternal age, ethnicity, pre-pregnancy BMI, educational background, GWG, number of prenatal visits, smoking status during the first trimester, plurality, birth order,

Table 2

The population distribution of adverse outcomes between groups.

Variables	Total (n = 1551,140)	Non-GDM group (n = 1396,494)	GDM group (n = 154,646)	Statistics	*P*
Maternal outcomes					
Admitted to ICU, n (%)				$\chi^2 = 27.849$	<.001
No	1,548,668 (99.84)	1,394,347 (99.85)	154,321 (99.79)		
Yes	2472 (0.16)	2147 (0.15)	325 (0.21)		
Mode of delivery, n (%)				$\chi^2 = 25565.25$	<.001
Eutocia	948,365 (61.14)	899,871 (62.97)	48,494 (39.73)		
Caesarean section	602,775 (38.86)	529,205 (37.03)	73,570 (60.27)		
Neonatal outcomes					
Preterm birth, n (%)				$\chi^2 = 1019.848$	<.001
Yes	164,926 (10.63)	144,810 (10.37)	20,116 (13.01)		
No	1,386,214 (89.37)	1,251,684 (89.63)	134,530 (86.99)		
Apgar 5 min, mean ± SD	8.83 ± 0.69	8.83 ± 0.69	8.82 ± 0.69	$t = 8.55$	<.001
Apgar 5 min grade, n (%)				$Z = -8.296$	<.001
0–3	5355 (0.35)	4887 (0.35)	468 (0.30)		
4–6	17,393 (1.12)	15,495 (1.11)	1898 (1.23)		
7–8	172,080 (11.09)	153,991 (11.03)	18,089 (11.70)		
9–10	1,356,312 (87.44)	1,222,121 (87.51)	134,191 (86.77)		
Assisted ventilation, n (%)				$\chi^2 = 689.339$	<.001
No	1,494,556 (96.35)	1,347,388 (96.48)	147,168 (95.16)		
Yes	56,584 (3.65)	49,106 (3.52)	7478 (4.84)		
NICU admission, n (%)				$\chi^2 = 1974.531$	<.001
No	1,429,076 (92.13)	1,291,064 (92.45)	138,012 (89.24)		
Yes	122,064 (7.87)	105,430 (7.55)	16,634 (10.76)		
Birth weight, g, n (%)				$\chi^2 = 182.408$	<.001
Low birth weight	101,314 (6.53)	90,611 (6.49)	10,703 (6.92)		
Normal birth weight	1,305,557 (84.17)	1,177,214 (84.30)	128,343 (82.99)		
High birth weight	144,269 (9.30)	128,669 (9.21)	15,600 (10.09)		

GDM = gestational diabetes mellitus, ICU = intensive care unit, NICU = neonatal intensive care unit.

Table 3

The association of GDM and neonatal adverse outcomes among women with advanced maternal age by multivariate logistic regression.

	Model 1		Model 2		Model 3	
Neonatal outcomes	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***
Assisted ventilation	1.394 (1.360–1.429)	<.001	1.419 (1.384–1.455)	<.001	1.380 (1.345–1.417)#	<.001
NICU admission	1.476 (1.451–1.502)	<.001	1.475 (1.449–1.501)	<.001	1.436 (1.410–1.463)#	<.001
Low Apgar 5 min	1.068 (1.051–1.085)	<.001	1.080 (1.064–1.097)	<.001	1.034 (1.018–1.051)#	<.001
Birth weight						
Normal birth weight	Ref		Ref		Ref#	
High birth weight	1.112 (1.093–1.132)	<.001	1.160 (1.140–1.181)	<.001	1.132 (1.111–1.153)#	.001
Low birth weight	1.083 (1.061–1.106)	<.001	1.069 (1.047–1.092)	<.001	1.017 (0.994–1.041)#	.142
Preterm birth	1.293 (1.272–1.313)	<.001	1.283 (1.263–1.304)	<.001	1.244 (1.223–1.266)*	<.001

Model 1: unadjusted. Model 2: adjusted maternal age, ethnicity, and newborn gender. Model 3: # adjusted maternal age, ethnicity, pre-pregnancy BMI, educational background, GWG, number of prenatal visits, smoking status before pregnancy, smoking status during the first trimester and the second trimester and the third trimester, plurality, birth order, WIC food use history, preterm birth history, newborn gender. * adjusted maternal age, ethnicity, pre-pregnancy BMI, educational background, GWG, number of prenatal visits, smoking status before pregnancy and during the first trimester, plurality, birth order, WIC food use history, preterm birth history, and newborn gender.

BMI = body mass index, CI = confidence interval, GDM = gestational diabetes mellitus, GWG = gestational weight gain, NICU = neonatal intensive care unit, OR = odds ratio, WIC = Women, Infants, and Children.

preterm birth history, newborn gender, the results showed that GDM were related to an increased risk of mothers entered ICU (OR = 1.247, 95% CI: 1.107–1.406); when the calibrated covariates excluded smoking status during the first trimester and contained smoking status before pregnancy and WIC food use history, GDM significantly enhanced the risk of mother needed to take cesarean section (OR = 1.193, 95% CI: 1.180–1.207).

3.3. Subgroup analysis based on the GWG levels

We performed a subgroup analysis for less GWG, normal GWG and excess GWG which in terms of the criteria of pre-pregnancy BMI and GWG. Aimed to analysis of neonatal adverse outcomes, the variables of pre-pregnancy BMI and GWG need be excluded based on the calibrated variables in the previous neonatal outcomes, the findings described (Table 5) that GDM was risk factor of neonatal assisted ventilation (OR = 1.397, 95% CI: 1.332–1.465), NICU admission (OR = 1.285, 95% CI: 1.242–1.329), low Apgar score at the fifth minutes (OR = 1.035, 95% CI: 1.005–1.067), high birth weight (OR = 1.246, 95% CI: 1.191–1.303), premature birth (OR = 1.084, 95% CI: 1.052–1.118) in the less GWG group; nevertheless, GDM became a protective factor for low birth weight with OR = 0.937 (95% CI: 0.903–0.971). Among normal and excess GWG group, GDM enhanced a risk for infant outcomes, such as assisted ventilation, NICU admission, low

Apgar score at the fifth minutes, high birth weight, low birth weight, premature birth. The maternal adverse outcomes were also performed by subgroup analysis, Model 3 also needs to exclude the interference of pre-pregnancy BMI and GWG on the basis of the previous maternal outcome calibration (Model 3 in Table 4); after adjusting for variables, Table 6 reveals that GDM was a risk factor for both ICU admission and caesarean section delivery for less and normal GWG group. GDM only as risk factor to cesarean section (OR = 1.441, 95% CI: 1.416–1.467) with respect to excess GWG group.

Table 4

The association of GDM and maternal adverse outcomes among women with advanced maternal age by multivariate logistic regression.

	Model 1		Model 2		Model 3	
Maternal outcomes	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***
Admitted to ICU	1.368 (1.217–1.537)	<.001	1.309 (1.164–1.471)	<.001	1.247 (1.107–1.406)#	<.001
Mode of delivery						
Eutocia	Ref		Ref		Ref*	
Caesarean section	1.310 (1.296–1.324)	<.001	1.290 (1.276–1.304)	<.001	1.193 (1.180–1.207)*	<.001

Model 1: unadjusted. Model 2: adjusted maternal age and ethnicity. Model 3: # adjusted the maternal age, ethnicity, educational background, pre-pregnancy BMI, GWG, number of prenatal visits, smoking status during the first trimester, plurality, birth order and preterm birth history. * adjusted maternal age, ethnicity, educational background, pre-pregnancy BMI, GWG, number of prenatal visits, smoking status before pregnancy, plurality, birth order, WIC food use history, preterm birth history, and newborn gender.

CI = confidence interval, Eutocia = normal/spontaneous vaginal births, GDM = gestational diabetes mellitus, ICU = intensive care unit, OR = odds ratio, WIC = Women, Infants, and Children.

4. Discussion

Currently, the number of women with advanced maternal age is increasing and likely to continue to increase in the next few years. Due to the complicated clinical process and difficult treatment, the mortality rate of mothers and infants is still high, GDM might bring several adverse effects on the pregnancy outcome. Therefore, we must pay high attention to GDM. Several researches[6,22,23] have shown that the relationship between GDM and adverse obstetric outcomes; nevertheless, there were few studies to concern the association of GDM with adverse obstetric outcomes for women with advanced maternal age. This study aimed to examine the effects of GDM on the risk of adverse maternal and neonatal adverse outcomes with respect to women with advanced maternal age. The finding manifested that GDM was significantly associated with the increased risk of mother admitted to ICU, mother took cesarean section, neonatal high birth weight, neonatal assisted ventilation, neonatal NICU admission, neonatal low Apgar score at the fifth minutes, and neonatal preterm birth after controlling for some covariates. We believed that these results would be beneficial to alert clinicians about risks potentially related to GDM among women with advanced maternal age.

In our present study, newborns born to GDM women with advanced maternal age were more likely to require assisted

Table 5

Subgroup analysis of neonatal adverse outcomes based on different GWG levels.

	Model 1		Model 2		Model 3	
Neonatal outcomes	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***
Less GWG						
Assisted ventilation	1.197 (1.142–1.253)	<.001	1.231 (1.175–1.290)	<.001	1.397 (1.332–1.465)#	<.001
NICU admission	1.120 (1.084–1.157)	<.001	1.136 (1.100–1.173)	<.001	1.285 (1.242–1.329)#	<.001
Low Apgar 5 min	0.957 (0.929–0.985)	.003	0.976 (0.948–1.005)	.106	1.035 (1.005–1.067)#	.021
Birth weight						
Normal birth weight	Ref		Ref		Ref#	
High birth weight	1.221 (1.169–1.276)	<.001	1.271 (1.216–1.328)	<.001	1.246 (1.191–1.303)#	.001
Low birth weight	0.830 (0.802–0.859)	<.001	0.835 (0.807–0.865)	<.001	0.937 (0.903–0.971)#	<.001
Preterm birth	0.958 (0.931–0.986)	.034	0.967 (0.939–0.995)	.022	1.084 (1.052–1.118)*	<.001
Normal GWG						
Assisted ventilation	1.410 (1.347–1.475)	<.001	1.434 (1.370–1.501)	<.001	1.474 (1.407–1.544)#	<.001
NICU admission	1.492 (1.447–1.540)	<.001	1.491 (1.445–1.538)	<.001	1.522 (1.474–1.573)#	<.001
Low Apgar 5 min	1.066 (1.036–1.096)	<.001	1.078 (1.048–1.109)	<.001	1.085 (1.055–1.116)#	<.001
Birth weight						
Normal birth weight	Ref		Ref		Ref#	
High birth weight	1.236 (1.195–1.278)	<.001	1.280 (1.237–1.324)	<.001	1.271 (1.228–1.315)#	<.001
Low birth weight	1.076 (1.036–1.117)	<.001	1.066 (1.026–1.107)	<.001	1.053 (1.010–1.097)#	<.001
Preterm birth	1.297 (1.261–1.334)	<.001	1.290 (1.254–1.328)	<.001	1.307 (1.268–1.347)*	<.001
Excess GWG						
Assisted ventilation	1.518 (1.460–1.579)	<.001	1.528 (1.469–1.589)	<.001	1.519 (1.460–1.580)#	<.001
NICU admission	1.728 (1.682–1.776)	<.001	1.709 (1.663–1.756)	<.001	1.693 (1.646–1.741)#	<.001
Low Apgar 5 min	1.156 (1.128–1.184)	<.001	1.158 (1.130–1.187)	<.001	1.142 (1.114–1.170)#	<.001
Birth weight						
Normal birth weight	Ref		Ref		Ref#	
High birth weight	1.230 (1.200–1.259)	<.001	1.264 (1.233–1.295)	<.001	1.282 (1.251–1.314)#	<.001
Low birth weight	1.231 (1.186–1.277)	<.001	1.208 (1.164–1.254)	<.001	1.125 (1.080–1.173)#	<.001
Preterm birth	1.523 (1.484–1.562)	<.001	1.497 (1.459–1.536)	<.001	1.466 (1.426–1.506)*	<.001

Model 1: unadjusted. Model 2: adjusted maternal age, ethnicity and newborn gender. Model 3: # adjusted maternal age, ethnicity, educational background, number of prenatal visits, smoking status before pregnancy, smoking status during the first trimester and the second trimester and the third trimester, plurality, birth order, WIC food use history, preterm birth history, newborn gender. * adjusted maternal age, ethnicity, educational background, number of prenatal visits, smoking status before pregnancy and during the first trimester, plurality, birth order, WIC food use history, preterm birth history, and newborn gender.

CI = confidence interval, GWG = gestational weight gain, NICU = neonatal intensive care unit, OR = odds ratio, WIC = Women, Infants, and Children.

Table 6

Subgroup analysis of maternal adverse outcomes based on different GWG levels.

	Model 1		Model 2		Model 3	
Maternal outcomes	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***
Less GWG						
Admitted to ICU	1.277 (1.040–1.567)	<.001	1.259 (1.025–1.547)	.028	1.321 (1.073–1.627)#	.009
Mode of delivery						
Eutocia	Ref		Ref		Ref#	
Caesarean section	1.190 (1.167–1.214)	<.001	1.184 (1.160–1.208)	<.001	1.199 (1.174–1.223)*	<.001
Normal GWG						
Admitted to ICU	1.435 (1.166–1.766)	<.001	1.361 (1.105–1.676)	.004	1.337 (1.084–1.649)#	.007
Mode of delivery						
Eutocia	Ref		Ref		Ref#	
Caesarean section	1.369 (1.343–1.395)	<.001	1.337 (1.312–1.363)	<.001	1.334 (1.308–1.359)*	<.001
Excess GWG						
Admitted to ICU	1.318 (1.083–1.605)	.006	1.254 (1.029–1.528)	.025	1.193 (0.978–1.456)#	.081
Mode of delivery						
Eutocia	Ref		Ref		Ref#	
Caesarean section	1.474 (1.449–1.499)	<.001	1.441 (1.417–1.466)	<.001	1.441 (1.416–1.467)*	<.001

Model 1: unadjusted. Model 2: adjusted maternal age and ethnicity. Model 3: # adjusted the maternal age, ethnicity, educational background, number of prenatal visits, smoking status during the first trimester, plurality, birth order and preterm birth history. * adjusted maternal age, ethnicity, educational background, number of prenatal visits, smoking status before pregnancy, plurality, birth order, WIC food use history, preterm birth history, and newborn gender.

CI = confidence interval, Eutocia = normal/spontaneous vaginal births, GWG = gestational weight gain, OR = odds ratio, ICU = intensive care unit, WIC = Women, Infants, and Children.

ventilation and NICU admission. Not only that, GDM women with advanced maternal age was associated with the risk of infant high birth weight and low Apgar score at the fifth minutes. Previous studies also reported that GDM could lead to the high birth weight of newborns; therefore, the reason might be explained that GDM pregnant women have higher blood sugar levels, and persistent hyperglycemia is able to enter into the fetal body through the placenta, making fetus to overdevelop.[8,24–26] Moreover, high blood sugar environment also makes fetus in a long-term hyperinsulinemia environment,[27] which promotes the synthesis of protein and fat. Of concern is that preterm birth was also observed in this study when women with advanced maternal age suffered GDM. This is mainly that with the maternal blood sugar increases, excessive glucose enters into the fetus through the placenta, and thus fetus would produce hyperglycemia and hyperosmotic diuresis, resulting in the increased of urine excretion,[28–30] which caused the result of pregnant women with excessive amniotic fluid, during the late pregnancy, premature rupture of membranes more likely to occur and triggered preterm birth; similarly, these processes can also increase the probability of cesarean section and affect the recovery of pregnant women after delivery,[29,31] which was consistent with our finding, namely advanced age mothers with GDM were more likely to have their babies born via cesarean section.

In addition, notably, our study concluded that GDM was a protective factor for low birth weight of newborns among less GWG groups. The current studies on the relationship between GDM and low birth weight of newborns are not particularly clear and lack of clinical evidence and mechanism studies. More studies still need to be discussed in the future.

The strengths of our study included that our large sample size, which provided high statistical power to analyze the association of the GDM with maternal and neonatal adverse outcomes. In addition, there are few studies about association of GDM with maternal and infant adverse outcomes among women with advanced maternal age at present, the findings could provide an effective reference for the prevention of GDM among women with advanced maternal age. Nevertheless, limitations of this study should be taken into account. Firstly, the NVSS database only included demographic information and no clinical indicators. Secondly, our study lacked the adjustment of blood glucose control in pregnant women, which may have an impact on maternal and neonatal outcomes as well. More studies are needed to explore the effect of blood glucose control among women with advanced maternal age on maternal and neonatal outcomes. Besides since the data were retrospective cohort study, there may be unavoidable information bias.

5. Conclusion

In conclusion, this study aimed to provide the association of GDM with maternal and neonatal adverse outcomes among women with advanced maternal age. We believed that these results will have important implications for the management of GDM in women with advanced maternal age to improve maternal and neonatal outcomes.

Author contributions

LD and HY designed the study. LD and BN collected data. LD performed the statistical analysis and wrote the manuscript. HY critically reviewed, edited, and approved the manuscript. All authors read and approved the final manuscript.

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