OBSTETRICS

Gestational diabetes mellitus is associated with adverse outcomes in twin pregnancies

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BACKGROUND: Among singleton pregnancies, gestational diabetes mellitus is associated with adverse outcomes. In twin pregnancies, this association may be attenuated, given the higher rate of prematurity and the a priori increased risk of some of these complications.

OBJECTIVE: Our aim was to test the hypothesis that gestational diabetes mellitus is less likely to be associated with adverse pregnancy outcomes in twin compared with singleton gestations.

METHODS: This retrospective cohort study comprised all twin and singleton live births in Ontario, Canada, 2012–2016. Pregnancy outcomes were compared between women with vs without gestational diabetes mellitus, analyzed separately for twin and singleton births. Adjusted risk ratios and 95% confidence intervals were generated using modified Poisson regression, adjusting for maternal age, nulliparity, smoking, race, body mass index, preexisting hypertension, and assisted reproductive technology.

RESULTS: A total of 270,843 women with singleton (n = 266,942) and twin (n = 3901) pregnancies met the inclusion criteria. In both the twin and singleton groups, gestational diabetes mellitus was associated with (adjusted risk ratio, [95% confidence interval]) cesarean delivery (1.11 [1.02–1.21] and 1.20 [1.17–1.23], respectively) and preterm birth at $<37^{0/7}$ weeks (1.21 [1.08–1.37] and 1.48 [1.39–1.57]) and at $<34^{0/7}$ weeks (1.45 [1.03–2.04] and 1.25 [1.06–1.47]). In singletons, but not twins, gestational diabetes mellitus was associated with gestational hypertension (1.66 [1.55–1.77]) and preeclampsia. With respect to neonatal outcomes, gestational diabetes mellitus was associated with birthweight greater than the 90th percentile in both twins and singletons, with the risk being 2-fold higher in twins (2.53 [1.52-4.23] vs 1.18 [1.13-1.23], respectively, $P = .004$). Gestational diabetes mellitus was associated with jaundice in both twins (1.56 [1.10–2.21]) and singletons (1.49 [1.37–1.62]) but was associated with the following complications only in singletons: neonatal intensive care unit admission (1.44 [1.38–1.50]), respiratory morbidity (1.09 [1.02–1.16]), and neonatal hypoglycemia (3.20 [3.01–3.40]).

CONCLUSION: In contrast to singleton pregnancies, gestational diabetes mellitus in twins was not associated with hypertensive complications and certain neonatal morbidities. Still, the current study highlights that gestational diabetes mellitus is associated with some adverse pregnancy outcomes including accelerated fetal growth also in twin pregnancies.

Key words: gestational diabetes, pregnancy outcome, singleton, twins

The incidence of gestational diabetes mellitus (GDM) is increasing worldwide because of the increasing prevalence of obesity in women of reproductive age and advanced maternal age.[1] The incidence of GDM may be even greater in twin gestations, a known independent risk factor for GDM.[2,3]

GDM is associated with maternal and neonatal complications in singleton pregnancies.[4–6] However, in twin pregnancies, some of these complications may be either less clinically relevant (eg, macrosomia, shoulder dystocia) or may be common regardless of GDM (eg, preeclampsia, cesarean delivery, hypoglycemia) because of the higher baseline risk of prematurity and hypertensive complications.[7,8]

Data regarding the association of GDM with pregnancy complications in twin pregnancies are conflicting. While some have reported that GDM does not increase the risk for adverse pregnancy outcomes in women with twins,[9] others have found GDM to be associated with an increased risk of hypertensive disorders of pregnancy,[10–12] accelerated fetal growth,[10,12–14] neonatal respiratory complications,[15,16] and admission to the neonatal intensive care unit (NICU).[14,17]

However, these findings were inconsistent across studies,[1] many of which were limited by relatively small sample size[10,11,15–18] and by the lack of adjustment for important confounding variables such as maternal body mass index (BMI)[9,12–14] and race.[10,11] Finally, only a limited number of studies used a control group of singleton pregnancies, which would make it possible to assess the effect of plurality on the clinical consequences of GDM.[12,13,15,17]

Thus, the aim of the current study was to test the hypothesis that GDM is less likely to be associated with adverse pregnancy outcomes in twin compared with singleton gestations using a large population-based cohort.

Materials and Methods

Study population

We conducted a retrospective population-based study of all women who had a singleton or twin hospital live or stillbirth in Ontario, Canada, between April 2012 and March 2016. Data were obtained from the Better Outcomes Registry and Network (BORN) Ontario (https://www.bornontario.ca/en/about-born/).

BORN Ontario is a registry of all births in the province of Ontario, Canada. For each hospital birth, data are collected by health care providers and hospital staff from charts, clinical forms, and patient

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AJOG at a Glance

Why was this study conducted?

To compare the association between gestational diabetes mellitus (GDM) and adverse pregnancy outcome in twin and singleton gestations.

Key findings

In both the twin and singleton groups, GDM was associated with an increased risk for cesarean delivery and preterm birth. In singletons, but not twins, GDM was associated with gestational hypertension and preeclampsia. GDM was associated with birthweight greater than the 90th percentile and neonatal jaundice in both twins and singletons but was associated with the following complications only in singletons: neonatal intensive care unit admission, respiratory morbidity, and neonatal hypoglycemia.

What does this add to what is known?

In contrast to singleton pregnancies, GDM in twins is not associated with hypertensive complications and certain neonatal morbidities. However, this study highlights that GDM is associated with some adverse pregnancy outcomes also in twin gestation.

interview and then entered into the BORN Information System (either directly or by electronic upload from a hospital's electronic medical records system).

The BORN Information System contains maternal demographics, health behaviors, and reproductive history as well as clinical information related to pregnancy, labor, birth, and fetal and neonatal outcomes. An ongoing program of data verifications, quality checks, and formal training sessions for individuals collecting and entering data assures that a high level of data quality is maintained.

Pregnancy outcomes of women with GDM were compared with those of women without GDM in singletons and twins. Women with any of the following conditions were excluded from both groups: gestational age at birth $<28^{0/7}$ weeks (ie, prior to routine screening and testing for GDM) or $>42^{0/7}$ weeks; high-order multifetal gestations; maternal age <19 years; preexisting diabetes; pregnancies complicated by genetic or structural fetal anomalies; or pregnancies with missing race or prepregnancy BMI data. The study was approved by the Sunnybrook Health Sciences Centre Research Ethics Board.

Diagnosis of GDM

This study spanned 2 time periods with regard to criteria for the diagnosis of GDM in Ontario. Up until April 2013, the criteria for diagnosis were according to 2008 Canadian Diabetes Associations (CDA) guidelines.[19] These guidelines recommended screening for GDM using a 50 g glucose challenge test (GCT), and when positive (>7.8 mmol/L or 140 mg/dL), a 75 g oral glucose tolerance test (OGTT) followed (cutoff values: fasting, ≥5.3 mmol/L or 96 mg/dL; 1 hour, ≥10.6 mmol or 191 mg/dL; 2 hours, ≥ 8.9 mmol/L or 160 mg/dL). GDM was defined as ≥2 abnormal OGTT values or a GCT result of ≥10.3 mmol/L or 185 mg/dL.

The presence of a single abnormal OGTT value was defined as impaired glucose tolerance (IGT). Women with IGT were not considered as GDM for the purpose of this study.

In April 2013, new CDA criteria were published.[20] The new guidelines allowed 2 options for screening/testing for GDM. The preferred option was essentially identical to the CDA 2008 guidelines aside from increasing the diagnostic 50 g GCT value from 10.3 mmol (185 mg/dL) to ≥11.1 mmol (200 mg/dL), and the 2 hour, 75 g OGTT threshold from 8.9 mmol/L (160 mg/dL) to 9.0 mmol/L (162 mg/dL).

The distinction between IGT and GDM was eliminated in these new guidelines. Despite the change in diagnostic criteria, no change in management is anticipated to have occurred because women with both IGT and GDM were referred to specialty clinics for dietary modification and glycemic monitoring.

Definitions

Large for gestational age and small for gestational age were defined as neonatal birth weight >90th and <10th centiles for gestational age, respectively, according to Canadian sex-specific reference.[21]

Composite respiratory morbidity was defined as any of the following events: need for respiratory support in the form of continuous positive airway pressure or mechanical ventilation, a diagnosis of transient tachypnea of the newborn infant, or respiratory distress syndrome.

The diagnosis of hypertensive disorders in pregnancy in Ontario is based on the guidelines published by the Canadian Hypertensive Disorders of Pregnancy Working Group.[22] Preexisting hypertension is defined as hypertension that develops either before pregnancy, at $<20^{+0}$ weeks' gestation or that persists for >3 months after birth. Gestational hypertension is defined as hypertension that develops for the first time at $\geq 20^{+0}$ weeks' gestation, and preeclampsia is defined as gestational hypertension with new onset of proteinuria or the involvement of one of the following organ systems: the central nervous system or the cardiorespiratory, hematological, renal, hepatic, or fetoplacental system.[22]

Data analysis

Baseline characteristics and pregnancy outcomes were compared between women with and without GDM for singletons and twins separately. Standardized differences were used to compare mean and proportions, with an absolute value of ≥0.10 denoting an important difference. Standardized differences reflect the mean difference as a percentage of the standard deviation. The rationale for using standardized differences as opposed to *P* values is that the standardized differences are not as sensitive to sample size, and therefore, given the large cohort in the current study, the use of *P* values would not be informative.

In addition, in contrast to standardized differences, *P* values do not provide an indication of the relative magnitude

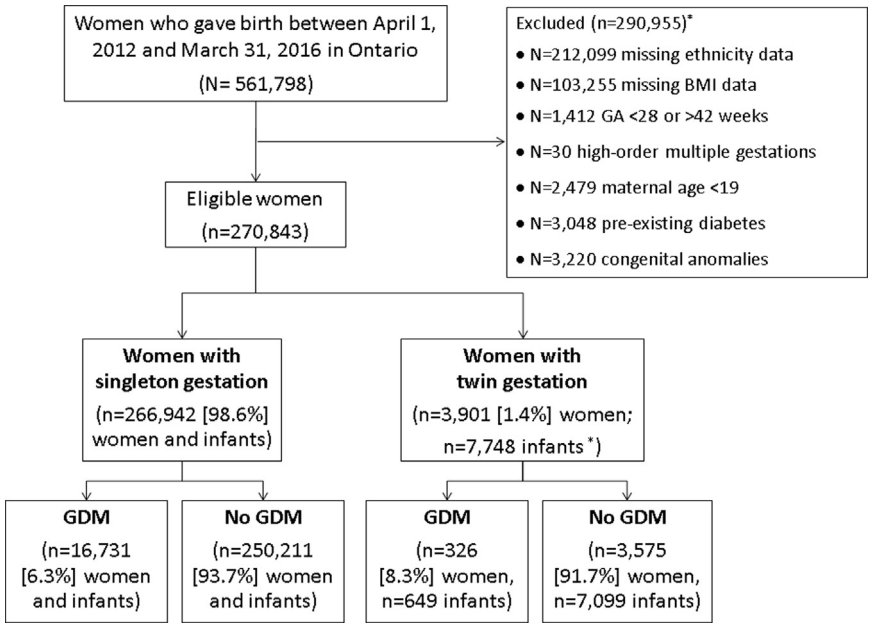
of the difference. Standardized differences of greater than 0.1 are typically believed to be meaningful. The threshold of 0.10 was chosen because it has been previously suggested to indicate a meaningful difference.[23,24]

Modified Poisson regression analysis with robust error variance was used to calculate the adjusted risk ratio (aRR) for each adverse pregnancy outcome in women with GDM (using women without GDM as reference) among twins and singletons while adjusting for confounders, identified a priori, which were informed by the literature and clinical expertise.

This analysis was performed separately for twins and singletons, and the associations of GDM with each of the outcomes (expressed as aRR) were compared between the singleton and twin groups as per the methodology described by Altman and Bland (2003).[25] Models for twin neonates were generated using generalized estimating equations to account for the correlation within twin pairs.

Data were analyzed using the SAS statistical software, version 9.4 (SAS Institute, Cary, NC, USA).

FIGURE 1
Selection of the study group



Asterisk indicates that exclusion criteria are not mutually exclusive.

BMI, body mass index; *GA*, gestational age.

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Results

Characteristics of the study population

A total of 561,798 women gave birth in Ontario, Canada, during the study period. Of the 270,843 women who met inclusion criteria, 266,942 had a singleton pregnancy and 3901 (7748 neonates) had a twin pregnancy (Figure 1). The incidence of GDM in the twin and singleton groups was 8.3% and 6.3%, respectively.

The characteristics of women with and without GDM in the twin and singleton groups are presented in Table 1. Compared with women without GDM, women with GDM were older, were less likely to be white and more likely to be of Asian race, and had a higher BMI in both the twin and singleton groups (Table 1). In the singleton group, women with GDM were more likely to have a history of preexisting hypertension and were less likely to be nulliparous compared with women without GDM (Table 1). In the twin group, women with GDM were more likely to conceive following in vitro fertilization treatments compared with women without GDM.

Association of GDM with maternal complications

The risk of maternal complications in women with and without GDM in the singleton and twin groups is presented in Table 2. As in the singleton group, women carrying twins who had GDM had a higher risk of cesarean delivery and preterm birth at $<37^{0/7}$ and $<34^{0/7}$ weeks as compared with women without GDM (Table 2).

In contrast to singleton gestations, women with twins who had GDM did not have a higher risk of gestational hypertension, preeclampsia, and induction of labor compared with women without GDM (Table 2). As expected, the absolute rates of hypertensive complications were higher in twins compared with singletons, irrespective of GDM.

Association of GDM with neonatal complications

As in singletons, birthweight in the twins group was higher in women with GDM compared with women without GDM when stratified by gestational age at birth (Figure 2).

The risk of neonatal complications in women with and without GDM in the singleton and twin groups is presented in Table 3. As in the singleton group, infants of women with twins and GDM were more likely to be large for gestational age, and the risk was about 2-fold higher in twins compared with singletons (aRR, 2.53 vs 1.18, respectively, $P = .004$), although the absolute rates were considerably lower in twins compared with singletons (Table 3). In addition, as in singletons, infants of women with twins and GDM were more likely to have jaundice requiring phototherapy compared with infants of women without GDM (Table 3).

In contrast to singleton gestations, twin infants of women with GDM were not at a higher risk of composite respiratory morbidity, admission to NICU, and hypoglycemia compared with infants of women without GDM (Table 3). However, the absolute rates of these complications were higher in twins. For example, the rate of neonatal

TABLE 1
Characteristics of the singleton and twin groups

Characteristic	Singleton group			Twin group		
	GDM (n = 16,731)	No GDM (n = 250,211)	Standardized difference	GDM (n = 326)	No GDM (n = 3575)	Standardized difference
Maternal age, y	33.1 ± 4.8	31.0 ± 5.0	0.43[a]	34.0 ± 5.3	32.3±5.0	0.33[a]
≥35	6428 (38.4)	61,141 (24.4)	0.30[a]	155 (47.5)	1167 (32.6)	0.31[a]
Race						
White	7257 (43.4)	163,085 (65.2)	−0.45[a]	170 (52.1)	2491 (69.7)	−0.37[a]
Asian	7482 (44.7)	58,404 (23.3)	0.46[a]	115 (35.3)	636 (17.8)	0.40[a]
Black	937 (5.6)	15,521 (6.2)	−0.03	16 (4.9)	249 (7.0)	−0.09
Other	1055 (6.3)	13,201 (5.3)	0.04	25 (7.7)	199 (5.6)	0.08
Nulliparity	6776 (40.5)	113,748 (45.5)	−0.10[a]	152 (46.6)	1681 (47.0)	−0.01
Prepregnancy BMI, kg/m^2	27.8 ± 7.1	27.4 ± 6.5	0.43[a]	27.4 ± 6.5	25.7 ± 6.3	0.26[a]
<18.5	468 (2.8)	13,613 (5.4)	−0.13[a]	8 (2.5)	149 (4.2)	−0.10[a]
18.5–24.9	6492 (38.8)	139,625 (55.8)	−0.35[a]	134 (41.1)	1895 (53.0)	−0.24[a]
25–29.9	4605 (27.5)	57,605 (23.0)	0.10[a]	94 (28.8)	862 (24.1)	0.11[a]
30–34.9	2703 (16.2)	23,361 (9.3)	0.21[a]	51 (15.6)	373 (10.4)	0.16[a]
≥35	2463 (14.7)	16,007 (6.4)	0.27[a]	39 (12)	296 (8.3)	0.12[a]
Preexisting hypertension	314 (1.9)	1831 (0.7)	0.10[a]	7 (2.1)	36 (1.0)	0.09
Smoking	1106 (6.6)	20,166 (8.1)	−0.06	20 (6.1)	248 (6.9)	−0.03
Fertility treatments						
In vitro fertilization	440 (2.6)	4010 (1.6)	0.07	79 (24.2)	646 (18.1)	0.15[a]
Ovulation induction	491 (2.9)	4156 (1.7)	0.09	30 (9.2)	337 (9.4)	−0.01

Data are presented as mean ± SD or n (percentage).

BMI, body mass index; *GDM*, gestational diabetes mellitus.

[a] Standardized differences ≥0.10.

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hypoglycemia was higher among twins, regardless of GDM (10.5% and 9.2% for twins with and without GDM, respectively), compared with only 2.3% among singletons without GDM (Table 3).

Comment

Principal findings of the study

In the current study, we aimed to test the hypothesis that the association of GDM with adverse pregnancy outcomes is less prominent in twin compared with singleton gestations. We found that GDM was associated with several adverse pregnancy outcomes in both twin and singleton gestations including preterm birth, cesarean delivery, accelerated fetal growth (in which the association was even greater in twins), and neonatal jaundice requiring phototherapy. However, in support of our hypothesis, we found that certain adverse outcomes were more common in twins, irrespective of GDM, and were associated with GDM only in singleton but not in twin gestations, including hypertensive complications, induction of labor, NICU admission, neonatal respiratory morbidity, and neonatal hypoglycemia.

Results of the study in the context of other observations

Several studies have explored the association between GDM and adverse outcome in twin gestations.[1,9-12,14–16] However, only a limited number of studies included a control group of singleton pregnancies that would allow direct comparison of the associations of GDM with adverse pregnancy outcomes between twins and singletons.[12,13,15,17]

Our finding, that GDM is associated with hypertensive complications in singleton but not in twin gestations, contrasts with several previous studies.[10–12] It should be noted that in these studies the results were not adjusted for maternal BMI[12] or race,[10,11] both of which are significant risk factors for gestational hypertension and preeclampsia.[26–28]

One possible reason for the lack of such an association in twins may be the a priori increased risk for hypertensive disorders in twins[29] which may mask the potential small effect of GDM that was observed in singletons. In addition, it is possible that our study was underpowered to detect these associations.

TABLE 2
Pregnancy outcomes in women with and without gestational diabetes in singletons and twins

Outcome	Singleton group				Twin group			
	GDM (n = 16,731)	No GDM (n = 250,211)	Crude RR (95% CI)	Adjusted RR (95% CI)[a]	GDM (n = 326)	No GDM (n = 3575)	Crude RR (95% CI)	Adjusted RR (95% CI)[a]
Hypertensive complications	1312 (7.8)	10,153 (4.1)	1.93 (1.83–2.04)[c]	1.56 (1.47–1.66)[c]	38 (11.7)	311 (8.7)	1.34 (0.98–1.84)	1.41 (1.00–1.98)
Gestational hypertension	1135 (6.8)	8322 (3.3)	2.04 (1.92–2.17)[c]	1.66 (1.55–1.77)[c]	27 (8.3)	203 (5.7)	1.46 (0.99–2.14)	1.47 (0.96–2.24)
Preeclampsia	177 (1.1)	1831 (0.7)	1.45 (1.24–1.69)[c]	1.26 (1.06–1.50)[c]	11 (3.4)	108 (3.0)	1.12 (0.61–2.06)	1.44 (0.76–2.74)
Induction of labor	6536 (39.1)	58,174 (23.2)	1.68 (1.65–1.71)[c]	1.68 (1.65–1.72)[c]	68 (20.9)	1070 (29.9)	0.70 (0.56–0.87)[c]	0.71 (0.55–0.91)[c]
Instrumental delivery	1540 (9.2)	24,182 (9.7)	0.95 (0.91–1.0)	0.98 (0.93–1.04)	22 (6.7)	394 (11.0)	0.61 (0.40–0.93)[c]	0.73 (0.47–1.15)
Cesarean delivery	6183 (37.0)	67,211 (26.9)	1.38 (1.35–1.4)[c]	1.20 (1.17–1.23)[c]	229 (70.2)	2121 (59.3)	1.18 (1.10–1.28)[c]	1.11 (1.02–1.21)[c]
Gestational age at birth, wks[b]	38.7 (1.5)	39.4 (1.5)	N/A	N/A	36.0 (2.0)	36.4 (2.0)	N/A	N/A
<37	1395 (8.3)	13,146 (5.3)	1.59 (1.51–1.67)[c]	1.48 (1.39–1.57)[c]	184 (56.4)	1737 (48.6)	1.2 (1.07–1.35)[c]	1.21 (1.08–1.37)[c]
<34	225 (1.3)	2451 (1.0)	1.37 (1.20–1.57)[c]	1.25 (1.06–1.47)[c]	50 (15.3)	394 (11.0)	1.39 (1.06–1.83)[c]	1.45 (1.03–2.04)[c]
<32	71 (0.4)	1046 (0.4)	1.02 (0.80–1.29)	0.99 (0.74–1.31)	16 (4.9)	137 (3.8)	1.28 (0.77–2.12)	1.24 (0.59–2.59)

Data are presented as mean (SD), n (percentage), or risk ratios (95% confidence interval).

GDM, gestational diabetes mellitus; *N/A*, nonapplicable; *RR*, risk ratio.

[a] Values reflect the results of a Poisson regression model using women without GDM as the reference. Model for gestational hypertension is adjusted for maternal age, smoking, nulliparity, race groups, maternal prepregnancy body mass index, and assisted reproductive technology. All other models are adjusted for maternal age, smoking, nulliparity, preexisting hypertension, race groups, maternal prepregnancy body mass index, and assisted reproductive technology; [b] Gestational age was significantly lower in the GDM compared with the non-GDM group for both singleton (standardized difference, −0.47) and twin (standardized difference, −0.19) groups; [c] Significant associations.

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We found that GDM is associated with accelerated fetal growth, one of the main consequences of GDM,[30,31] in both twins and singletons and that the association was actually greater in twins. This is in agreement with our prior observation in twin pregnancies with GDM,[32] in which we found that not only the rate of large for gestational age but also the rate of asymmetric growth (as reflected by the abdominal circumference/head circumference ratio) is higher in twins with GDM and is related to the degree of glucose intolerance.[32]

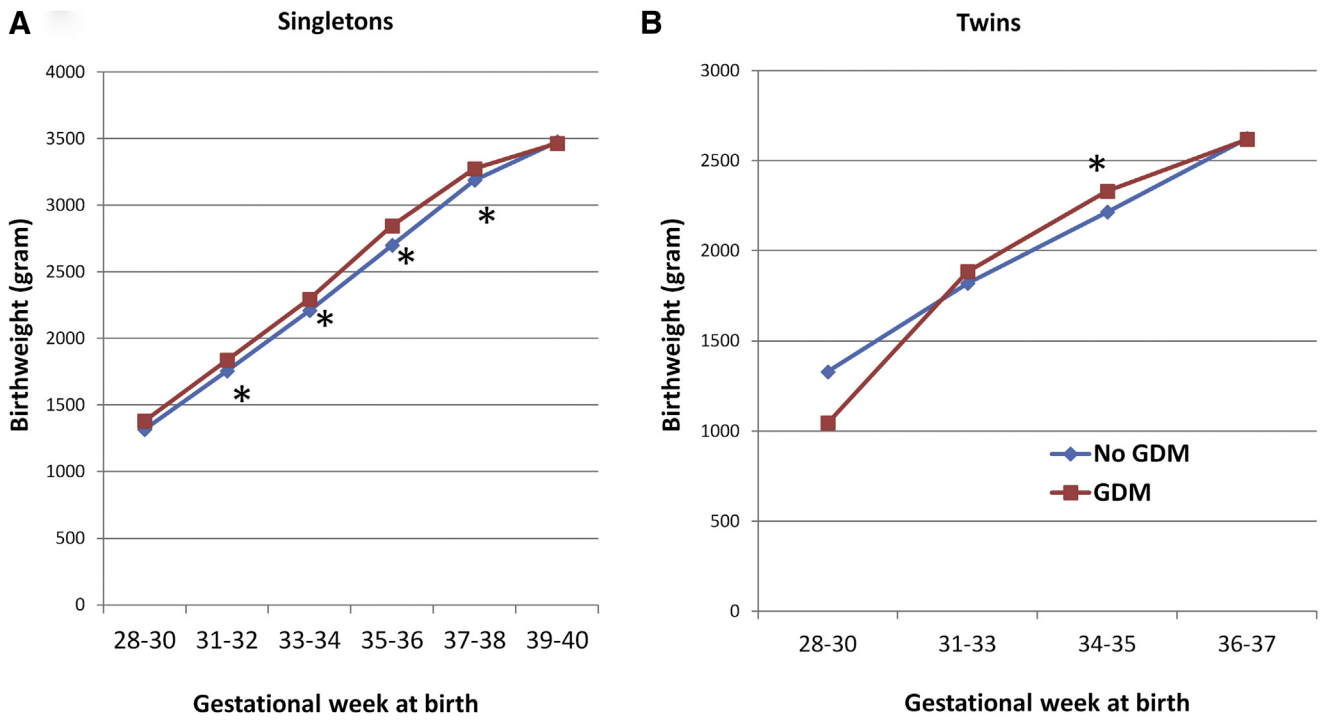
It may be argued that the GDM-induced accelerated fetal growth observed in twins should not be of concern because it is unlikely to result in neonatal complications such as shoulder dystocia and birth trauma and may actually have a beneficial or protective role, given the slower growth of twins during the third trimester,[33,34] and the increased risk of fetal growth restriction in twins.[35,36] Nonetheless, accelerated fetal growth may be associated with fetal programming and long-term metabolic complications similar to those reported among singletons including obesity, diabetes, and cardiovascular disease.[37–41] Long-term follow-up studies in twin infants are needed to address this question.

We found that in both twins and singleton gestations, GDM was associated with jaundice requiring phototherapy. However, other outcomes such as NICU admission, neonatal respiratory morbidity, and neonatal hypoglycemia were associated with GDM only in singletons. The lack of association between GDM and these latter outcomes in twin gestations may once again be attributed to the a priori higher rate of these complications in twins,[12,15,42] which are likely driven by the higher rate of prematurity in twins compared with singletons.[43,44]

Indeed, we found that the rate of neonatal hypoglycemia in twins (either with or without GDM) was similar to that of singletons with GDM and considerably higher than that of singletons without GDM.

The reason for the association of GDM with cesarean delivery in twin

FIGURE 2
Relationship between GDM and birthweight in twins and singletons



Data are presented for singleton **(A)** and twin **(B)** pregnancies. Asterisk indicates a value of $P < .05$.

GDM, gestational diabetes mellitus.

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pregnancies is unclear but may be attributed to the increased risk of prematurity in twins with vs without GDM. In addition, it is important to note that although the association between GDM and cesarean delivery was statistically significant, mainly because of the large sample size, the absolute value of the relative risk was small (1.20 for singletons and 1.11 for singletons), which questions the clinical significance of this association.

Strengths and limitations

The main strengths of our study are the population-based nature of the study and the large sample size. The inclusion of a comparison group of women with singleton pregnancy allowed us to directly compare the association of GDM and adverse pregnancy outcomes in twins with that observed in singletons. Finally, another important point is the availability of data on important confounding variables such as maternal BMI and race, which were not adjusted for in some of the previous studies on this topic.[10–12]

Our study has several limitations. Because of its retrospective nature, information on several potentially confounding variables such as the degree of glycemic control, a history of GDM, a history of polycystic ovary syndrome, and gestational weight gain was not available. In addition, given that information on IGT is not available in the BORN database, women with IGT were considered as controls despite the fact they had some degree of glucose intolerance. Moreover, interpretation of the findings of the current study should take into account that the diagnosis of GDM in our cohort was based on a 2 hour rather than 3 hour glucose challenge test and that two different protocols for the diagnosis of GDM were used during the study period; still it should be noted that these changes equally affected twin and singleton pregnancies.

Another limitation is the potential for selection bias, given the fact that about 50% of the initial population was excluded because of missing data on prepregnancy BMI or race. To address this issue, we compared the characteristics of women who were excluded because of missing data with those included in the current study and overall found them to be similar (data not shown).

Conclusion

In contrast to singleton pregnancies, GDM in twins is not associated with hypertensive complications and certain neonatal morbidities, possibly because of the higher baseline risk of prematurity, hypertensive complications, and cesarean delivery in twin pregnancies. Nevertheless, the current study highlights that GDM is associated with accelerated fetal growth and certain adverse maternal and neonatal outcomes also in twin pregnancies.

TABLE 3
Neonatal outcomes of infants born to women with and without gestational diabetes in singletons and twins

Outcome	Singleton group				Twin group			
	GDM (n = 16,731)	No GDM (n = 250,211)	Crude RR (95% CI)	Adjusted RR (95% CI)[a]	GDM (n = 649)	No GDM (n = 7099)	Crude RR (95% CI)	Adjusted RR (95% CI)[a]
Birthweight, g[b]	3315 ± 543	3382 ± 537	N/A	N/A	2452 ± 517	2491 ± 505	N/A	N/A
>90th percentile[c]	2188 (13.1)	22,770 (9.1)	1.44 (1.38–1.50)[e]	1.18 (1.13-1.23)[e]	21 (3.2)	90 (1.3)	2.55 (1.60–4.08)[e]	2.53 (1.52–4.23)[e]
<10th percentile[c]	1514 (9.0)	23,069 (9.2)	0.98 (0.93–1.03)	1.01 (0.95–1.07)	152 (23.4)	1865 (26.3)	0.89 (0.77–1.03)	0.95 (0.79–1.14)
Five minute Apgar <7	296 (1.8)	4094 (1.6)	1.08 (0.96–1.22)	0.95 (0.84–1.09)	21 (3.2)	282 (4.0)	0.81 (0.53–1.26)	0.87 (0.50–1.51)
Admission to NICU	2799 (16.7)	25,983 (10.4)	1.61 (1.55–1.67)[e]	1.44 (1.38–1.50)[e]	349 (53.8)	3287 (46.3)	1.16 (1.08–1.25)[e]	1.12 (1.00–1.25)
Composite respiratory morbidity[d]	1189 (7.1)	14,906 (6.0)	1.19 (1.13–1.26)[e]	1.09 (1.02–1.16)[e]	130 (20.0)	1343 (18.9)	1.06 (0.90–1.24)	0.93 (0.75–1.16)
Jaundice requiring phototherapy	708 (4.2)	6629 (2.6)	1.60 (1.48–1.72)[e]	1.49 (1.37–1.62)[e]	69 (10.6)	474 (6.7)	1.59 (1.25–2.02)[e]	1.56 (1.10–2.21)[e]
Neonatal hypoglycemia	1510 (9.0)	5859 (2.3)	3.85 (3.65–4.07)[e]	3.20 (3.01–3.40)[e]	68 (10.5)	652 (9.2)	1.14 (0.90–1.45)	1.15 (0.84–1.59)

Data are presented as mean (SD), n (percentage), or risk ratios (95% confidence interval).

GDM, gestational diabetes mellitus; *NICU*, neonatal intensive care unit; *RR*, risk ratio.

[a] Modified Poisson regression model is used to calculate the adjusted risk ratios with general estimating equations to account for correlation among twins. All models were adjusted for maternal age, nulliparity, prepregnancy body mass index, maternal smoking, assisted reproductive technology, maternal preexisting hypertension, and mode of delivery; [b] Birthweight was significantly lower in the GDM compared with the non-GDM group for singletons (standardized difference, −0.13) but not for twins (standardized difference, −0.08); [c] Based on the Canadian birthweight reference of Kramer et al[21] (2001). The adjusted risk ratio for birthweight greater than the 90th percentile in twins was significantly higher than the corresponding adjusted risk ratio for singletons ($P = .004$); [d] Defined as any of the following: need for respiratory support in the form of continuous positive airway pressure or mechanical ventilation, a diagnosis of transient tachypnea of the newborn infant, or respiratory distress syndrome; [e] Significant associations.

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Further studies are needed to determine whether GDM and the associated accelerated fetal growth of twin fetuses has long-term implications for the infant similar to those reported in singleton pregnancies. Until then, we believe that clinicians should view GDM in twin pregnancies to be as a pathological condition that requires monitoring and treatment similar to the practice in singleton pregnancies. ■

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