Trends in Incidence of Diabetes in Pregnancy and Serious Perinatal Outcomes: A Large, Population-Based Study in Ontario, Canada, 1996–2010

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OBJECTIVE

Women with diabetes in pregnancy have high rates of pregnancy complications. Our aims were to explore trends in the incidence of diabetes in pregnancy and examine whether the risk of serious perinatal outcomes has changed.

RESEARCH DESIGN AND METHODS

We performed a population-based cohort study of 1,109,605 women who delivered in Ontario, Canada, between 1 April 1996 and 31 March 2010. We categorized women as gestational diabetes (GDM) (*n* = 45,384), pregestational diabetes (pre-GDM) (*n* = 13,278), or no diabetes (*n* = 1,050,943). The annual age-adjusted rates of diabetes in pregnancy were calculated, and rates of serious perinatal outcomes were compared between groups and by year using Poisson regression.

RESULTS

The age-adjusted rate of both GDM (2.7–5.6%, $P < 0.001$) and pre-GDM (0.7–1.5%, $P < 0.001$) doubled from 1996 to 2010. The rate of congenital anomalies declined by 23%, whereas the rate of perinatal mortality did not change significantly. However, compared with women with no diabetes, women with pre-GDM and GDM faced an increased risk of congenital anomalies (relative risk 1.86 [95% CI 1.49–2.33] and 1.26 [1.09–1.45], respectively), and perinatal mortality remained elevated in women with pre-GDM (2.33 [1.59–3.43]).

CONCLUSIONS

The incidence of both GDM and pre-GDM in pregnancy has doubled over the last 14 years, and the overall burden of diabetes in pregnancy on society is growing. Although congenital anomaly rates have declined in women with diabetes, perinatal mortality rates remain unchanged, and the risk of both remains significantly elevated compared with nondiabetic women. Increased efforts are needed to reduce these adverse outcomes.

Diabetes in pregnancy is becoming an increasingly growing concern as the prevalence of diabetes continues to rise (1). Women with diabetes who become pregnant have an increased risk of pregnancy complications (2–7), including serious perinatal outcomes such as stillbirth, perinatal mortality, and major congenital malformations. Hyperglycemia in the period around conception and the first weeks

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postconception is a particular concern as it carries a substantially higher risk of congenital anomalies (8). Studies have demonstrated reduced rates of congenital malformations and perinatal mortality with preconception counseling, where glycemic control is optimized, and comorbidities such as hypertension and diabetes complications are treated appropriately prior to and during pregnancy (9,10).

Numerous advances over the last decade have the potential to reduce the rates of serious outcomes in women with diabetes. Such advances include the use of insulin analogs (11), continuous glucose monitoring (12), and the development of preconception clinics (9). There is little data on whether the rates of these serious outcomes have changed over time in women with diabetes. Only two studies have looked at trends in outcomes in women with diabetes over the last decade, in Germany (data up to 2004) and the U.K. (data up to 2007), and both failed to find significant decreases in perinatal mortality or congenital anomalies (13,14). Using unique population-based databases that link maternal and fetal health records, the aim of this population-based study was to compare rates of serious perinatal outcomes between women with and without diabetes in pregnancy, explore whether these rates have changed over time, and relate these rates to the underlying trends in rates of diabetes in pregnancy over the past 14 years. A secondary objective was to identify demographic and health care factors that predict serious outcomes in this population.

RESEARCH DESIGN AND METHODS

Ethics Statement

This study was approved by the institutional review board at Sunnybrook Health Sciences Centre in Toronto.

Study Design and Data Sources

We conducted a population-based cohort study using administrative health claims to examine the rate of diabetes in pregnancy (gestational diabetes [GDM] and pregestational diabetes [pre-GDM]) in all women who gave birth in Ontario from 1 April 1996 to 31 March 2010, the rate of congenital anomalies and perinatal mortality among newborns, and the predictors of these serious perinatal outcomes. We have a unique dataset that uses the Canadian Institute for Health Information Discharge Abstract Database on all inpatient admissions to link the delivering mother to her newborn where each record corresponds to a mother-child pair. Ontario is a large, diverse multicultural province in Canada with ~12 million residents. Each resident is covered by a provincial health insurance plan for all medically necessary services across a full spectrum of providers and hospitals that is paid for by the Government of Ontario.

Study Population and Eligibility

We identified all women aged 15–50 years who delivered in an Ontario hospital from 1 April 1996 to 31 March 2010 using the Canadian Institute for Health Information Discharge Abstract Database. The hospital admission date during their delivery was used as the index date. For women who had multiple pregnancies during this time period, one pregnancy was chosen at random to be the index episode from which the outcomes would be determined. Women with a diagnosis of diabetes in the 280 days prior to the index date were defined as having GDM based on their hospitalization records and outpatient data from physician services claims (see Supplementary Material). Women with pre-GDM were those who were diagnosed with diabetes >280 days prior to the index date using the Ontario Diabetes Database, an administrative data-derived registry of Ontario residents diagnosed with nongestational diabetes. The registry was validated against patient charts and was shown to have a sensitivity of 86% and a specificity of >97% (15). We restricted the cohort to women that reside in Ontario and those with known postal codes. Women were linked across the health administrative databases using a unique identifier (health care number). Women who could not be linked due to an invalid unique identifier and those with no record in the mother-baby database were excluded.

Outcome Measures

We calculated the annual rates of GDM and pre-GDM by age-group in the study population and compared the rates across fiscal years. For numerators, we identified all women with GDM and pre-GDM who delivered that year, and the denominators were all women who delivered that respective year.

Newborns were followed up to 1 year after the index date for major congenital anomalies, defined as any congenital anomaly with ICD-9 diagnosis codes 740 to 759 or any ICD-10 diagnosis codes Q00.0 to Q99.9 (including cardiac, neural tube defect, central nervous system, gastrointestinal, and renal anomalies). Minor anomalies were excluded (Supplementary Table 1). Perinatal mortality was defined as any intrauterine stillbirth (not including miscarriage) and any postnatal newborn death (including those with congenital anomalies) within 28 days of the baby's birth date.

Covariates

Demographic and physician services were gathered from administrative data to be applied to the multivariable models. Demographic information was obtained using the Registered Persons Database, which contains demographic and residential information on all residents of Ontario. Data on prior physician visits were obtained using the Ontario Health Insurance Plan, which contains all physician service claims. Having a primary care physician before pregnancy was defined as having at least one visit to a family physician/general practitioner in the 21- to 9-month period before the index date. Having a regular care provider before pregnancy was defined as having half or more of their primary care visits to the same primary care physician in the 21- to 9-month period before the index date. A prior visit to an obstetrician during pregnancy was defined as women who had at least one visit to an obstetrician within 280 days of the index date. A similar definition was used for a prior visit to an endocrinologist/internist.

Statistical Analysis

Age-adjusted rates of GDM and pre-GDM by study year and age-group and rates of congenital anomalies and perinatal mortality among those with GDM and pre-GDM and women without diabetes in pregnancy were calculated using a Poisson model. We fitted Poisson regression models, relating the variables of interest to *1*) the number of women with GDM and pre-GDM in separate

models and *2*) the number of congenital anomalies and perinatal mortalities among women with GDM and pre-GDM and women without diabetes in pregnancy in one model, using the given population of women that delivered that year as the offset. We tested for a two-way interaction between diabetes status at pregnancy and year to determine whether any changes in congenital anomalies and perinatal deaths differed on the basis of diabetes status over the years. Predicted age-adjusted rates were calculated from the age-adjusted regression model for diabetes during pregnancy, and predicted serious outcome rates included the two-way diabetes × year interaction term. We used a multivariable logistic regression analysis to identify predictors of congenital anomalies and perinatal mortality stratified by diabetes status.

RESULTS

Diabetes in Pregnancy

From 1 April 1996 to 31 March 2010, there were 1,109,605 women who delivered in Ontario, Canada. Crude rates of diabetes in pregnancy are presented in the Supplementary Material. There were 45,384 women with GDM and 13,278 with pre-GDM. In 1996, the age-adjusted prevalence of diabetes in pregnancy was 2.7% for women with GDM and 0.7% for women with pre-GDM. These figures doubled by 2010: 5.6% for GDM ($P < 0.001$) and 1.5% for pre-GDM ($P < 0.001$) (Supplementary Table 1). Rates of diabetes in pregnancy were consistently higher among women aged 30 years and older than women aged 15–29 years; this pattern pertained both to GDM (3.6 vs. 1.7% in 1996 and 7.4 vs. 3.5% in 2010, $P < 0.001$) and pre-GDM (0.9 vs. 0.5% in 1996 and 1.9 vs. 0.9% in 2010, $P < 0.001$) (Fig. 1). By 2010, the rate of diabetes in pregnancy was almost 1 in every 10 pregnant women >30 years of age (9.3%; 7.4% for GDM and 1.9% in women with pre-GDM). Diabetes in pregnancy rose in all age-groups; however, women >40 years of age had the highest rate of diabetes in pregnancy (13.0% in women with GDM and 3.2% in women with pre-GDM) (Supplementary Fig. 1*A* and *B*).

Serious Perinatal Outcomes

Compared with women without diabetes in pregnancy, women with pre-GDM and GDM had a higher risk of offspring with congenital anomalies, and women with pre-GDM experienced the greatest risk (absolute risk [AR] 62.4 per 1,000 births in women with pre-GDM, AR 37.5 per 1,000 births in women with GDM, and AR 29.04 per 1,000 births in nondiabetic women). Over the study period, the rate of congenital anomalies declined by 23% in women with pre-GDM (from 7.1 to 5.5%, $P = 0.017$) and by 20% in women with GDM (from 4.6 to 3.7%, $P = 0.099$) (Fig. 2). The relative risk (RR) of congenital anomalies significantly narrowed by 31 and 34% ($P = 0.003$ and $P = 0.031$) for women with GDM and pre-GDM, respectively. Although the risk has narrowed, women with diabetes in pregnancy continued to face an increased risk of serious perinatal outcomes compared with women without diabetes. In 2010, offspring of women with pre-GDM experienced an almost twofold increased risk of congenital anomalies (RR 1.86 [95% CI 1.49–2.33]), and women with GDM were at a 26% increased risk of having an offspring with a congenital anomaly (1.26 [1.09–1.45]) compared with women without diabetes (Fig. 2).

The adjusted rate of perinatal mortality did not significantly change over the years for infants of women with GDM and pre-GDM ($P = 0.249$ for interaction between year and diabetes status). In 2010, infants of women with pre-GDM continued to be at a significantly higher risk of having a perinatal death (RR for women with pre-GDM, 2.33 [95% CI 1.59–3.43]) compared with those of women without diabetes. Women with GDM were at a lower risk of having a perinatal death (RR 0.63 [0.43–0.93]) compared with women without diabetes (AR for pre-GDM, 19.4 per 1,000 births; AR for GDM, 5.66 per 1,000 births; and AR for nondiabetic women, 6.97 per 1,000 births).

Predictors of Serious Perinatal Outcomes

Baseline covariates by diabetes status are presented in Table 1. Women with

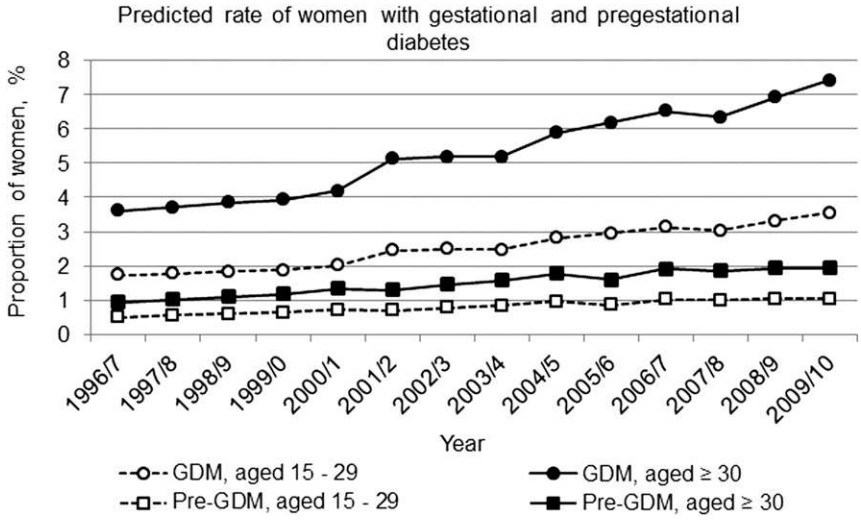

Figure 1—Predicted rate by age of pregnancies with GDM and pre-GDM in Ontario from 1996 to 2010. Circles represent women with GDM, and squares represent women with pre-GDM. Dashed lines represent women aged 15–29 years, and solid lines represent women aged 30 years and over.

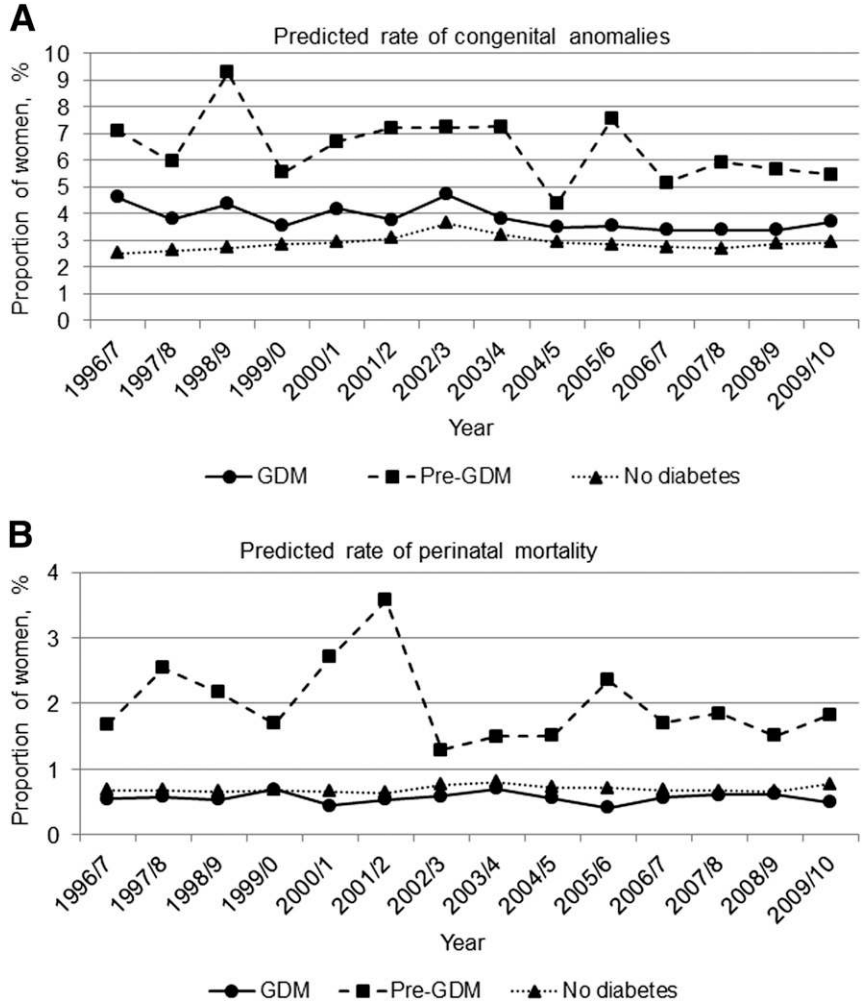

Figure 2—Predicted rate of serious outcomes between women with GDM and pre-GDM compared with women without diabetes in pregnancy in Ontario, Canada, from 1996 to 2010. *A*: Congenital anomalies. *B*: Perinatal mortality. Solid circles on a solid line represent women with GDM, solid squares on a dashed line represent women with pre-GDM, and solid triangles on a dotted line represent women with no diabetes.

both GDM and pre-GDM were more likely to be older, be of lower socioeconomic status, and have more physician visits. In the stratified multivariable logistic regression analysis, among women with pre-GDM, older age reduced the likelihood of a congenital anomaly (odds ratio [OR] 0.81 [95% CI 0.70–0.94]), whereas living in a rural community increased the likelihood (1.55 [1.24–1.93]) (Table 2). Women with pre-GDM who saw an endocrinologist or internist during pregnancy were more likely to have had an offspring with congenital anomaly and perinatal mortality. Among women with GDM, those of higher socioeconomic status were less likely to have had a perinatal mortality, and seeing an endocrinologist or internist reduced the likelihood of a congenital anomaly and perinatal mortality in offspring of women with GDM. Having at least one prenatal obstetrician visit reduced the odds of perinatal mortality in women with both GDM and pre-GDM (OR 0.52 [0.36–0.76] and 0.52 [0.34–0.79], respectively) (Table 2).

CONCLUSIONS

This large, population-based study documented a significant rise in diabetes in pregnancy rates over the last 14 years. From 1996 to 2010, we found a doubling of the age-adjusted rate of both GDM and pre-GDM. By 2010, almost 1 in every 10 pregnant women >30 years of age had diabetes in pregnancy. Although congenital anomaly rates have declined over the last decade by 20–23% in offspring of women with GDM and pre-GDM, respectively, the risk of these complications remains significantly elevated in both groups. Perinatal mortality is also significantly higher among offspring of women with pre-GDM, and sadly, this risk has not significantly changed. Living in a rural community increased the risk of both congenital anomalies and perinatal mortality in offspring of women with pre-GDM, and seeing an obstetrician reduced the risk of mortality in offspring of women with both GDM and pre-GDM. With a doubling in the incidence of both GDM and pre-GDM over the last 14 years, the overall burden of diabetes in pregnancy on society is growing (Supplementary Table 1). Increased efforts are needed to reduce these serious adverse outcomes.

We found that the rates of GDM more than doubled over the 14 years of follow-up. Other studies have also found that GDM rates are increasing (16–20). Possible reasons for the rising rates of GDM

Table 1—Demographic and prepregnancy physician visits of women by diabetes status in pregnancy in Ontario, Canada, from 1996 to 2010

Characteristic	GDM	Pre-GDM	No diabetes
n	45,384	13,278	1,050,943
Age			
Mean ± SD	32.3 ± 5.3	32.0 ± 5.3	29.7 ± 5.6
Median (IQR)	32 (29–36)	32 (28–36)	30 (26–34)
Age-group (years)			
15–29	13,220 (29.1%)	4,190 (31.6%)	492,136 (46.8%)
≥30	32,164 (70.9%)	9,088 (68.5%)	558,807 (53.2%)
Socioeconomic status			
1 Lowest	12,541 (27.6%)	3,302 (24.9%)	237,533 (22.6%)
2	9,951 (21.9%)	2,675 (20.1%)	213,937 (20.4%)
3	9,243 (20.4%)	2,748 (20.7%)	211,373 (20.1%)
4	8,045 (17.7%)	2,673 (20.1%)	210,466 (20.0%)
5 Highest	5,383 (11.9%)	1,808 (13.6%)	174,033 (16.6%)
Rural residence	2,996 (6.6%)	1,218 (9.2%)	113,215 (10.8%)
Prepregnancy visits			
Primary care physician	38,529 (84.9%)	12,458 (93.8%)	875,259 (83.3%)
Regular care provider	34,187 (75.3%)	10,862 (81.8%)	778,184 (74.0%)
Visits during pregnancy			
Obstetrician	42,302 (93.2%)	12,341 (92.9%)	856,639 (81.5%)
Endocrinologist or internist	31,800 (70.1%)	7,494 (56.4%)	38,446 (3.7%)

A primary care physician before pregnancy was defined as having at least one visit to a family physician/general practitioner in the 21- to 9-month period before the index date. A regular care provider before pregnancy was defined as having half or more of their primary care visits to the same primary care physician in the 21- to 9-month period before the index date.

may include increasing rates of obesity (21), decreased physical activity (22), and increased saturated fat content in diets (23). GDM rates are often reflective of the rate of type 2 diabetes in the background population, and these rates are also rising in our population (1). The rate of pre-GDM also doubled to 1.5 per 100 women. This rise is consistent with other studies in the U.S. (16,24) and the U.K. (13), where rates of pre-GDM are increasing. We found that women >30 years of age had the highest prevalence of GDM (7.4%) and pre-GDM (1.9%), such that, for women >30 years of age, almost 10% of all pregnancies have diabetes. The average age of first pregnancy in Canada in 2012 was >29 years (25), a trend that has resulted in an alarming rate of diabetes in pregnancy in our population.

Congenital anomaly rates declined in our population, and the RR among offspring of women with diabetes in pregnancy did narrow significantly compared with nondiabetic women. This is very encouraging and may be due to increased preconception counseling and awareness by physicians and patients that excellent glycemic control prior to pregnancy can decrease anomaly rates to rates similar to those of the general population (10). The rates, however, remain substantially elevated compared with nondiabetic women, with an almost twofold increased risk in women with pre-GDM. Women with pre-GDM who have congenital anomalies tend to be younger. This may reflect reduced pregnancy planning in this group. Increased efforts to educate young women with diabetes, even those in their teens, regarding the need to seek preconception care is needed, and may improve rates of anomalies in the offspring of young women. Increased efforts are also needed to educate and empower women with type 2 diabetes, who have the lowest rates of attendance for preconception care (19 vs. 35% in women with type 1 diabetes) (26). Women with type 2 diabetes tend to be of lower socioeconomic status and include many ethnic minorities and new immigrants, making the challenges of preconception awareness and care more difficult (27). Diabetes outcomes are consistently worse in those of lower socioeconomic status (28,29), and the increased rates of serious outcomes in women may also be due to non–health care factors, such as poor nutrition and smoking. Seeing an endocrinologist or internist during pregnancy increased the rates of congenital anomalies and perinatal mortality, but this observation may simply reflect referral bias or reverse causality. We did not look at the rates of anomalies in women who saw an endocrinologist prior to pregnancy, but given that preconception counseling and attendance to preconception clinics have been shown to reduce the rates of anomalies, we would expect that seeing an endocrinologist prior to pregnancy would be associated with reduced rates of anomalies (9,10).

Of concern, we also found that women with GDM have an 86% increased risk of offspring with congenital anomalies. This elevated rate may be due partly to inclusion of women with undiagnosed type 2 diabetes. Given that women with GDM have an increased risk of developing diabetes postpartum (30), they may have developed diabetes prior to their next pregnancy, which had gone undetected. Therefore, we need to increase efforts to screen women with prior GDM for diabetes so that appropriate treatment can be pursued prior to the next pregnancy. As well, women with GDM are often obese, and folic acid levels tend to be lower in obese women, possibly also contributing to the increased rate of congenital anomalies in these women (31). Information on obesity would help clarify this in future studies.

We found that women with pre-GDM continue to have a significantly higher rate of perinatal mortality, and this rate has not declined despite lower rates of congenital anomalies. This is consistent with other studies that continue to show elevated perinatal mortality rates in women with pre-GDM captured past 2003 (13,14,32). Two studies that looked at the trend over time showed a nonsignificant decline in stillbirths/perinatal mortality (13,14). Poor glycemic control and its associated morbidity may account for the majority of deaths (33). Obesity is also an independent risk factor for perinatal mortality (21) and may be playing a role along with hyperglycemia, especially in women with type 2 diabetes in pregnancy who are often obese and have been reported to have higher rates of perinatal mortality than women with type 1 diabetes (26). Our study adds to this literature by identifying risk factors for adverse outcomes and

Table 2—Multivariable models of the predictors of congenital anomalies and perinatal mortality in offspring of women by diabetes status in pregnancy in Ontario, Canada, from 1996 to 2010

Characteristic	Congenital anomalies OR (95% CI)	Perinatal death OR (95% CI)
Among women with GDM		
Age (years)		
15–29	1.00 Ref	1.00 Ref
≥30	0.90 (0.81–0.99)	1.13 (0.86–1.48)
Socioeconomic status		
1 Lowest	1.00 Ref	1.00 Ref
2	0.99 (0.86–1.14)	0.64 (0.45–0.91)
3	1.02 (0.89–1.18)	0.58 (0.40–0.84)
4	1.05 (0.90–1.21)	0.67 (0.47–0.97)
5 Highest	0.84 (0.71–1.01)	0.57 (0.36–0.89)
Rural residence (Ref: urban)	1.09 (0.89–1.32)	0.94 (0.58–1.53)
Primary care physician	0.99 (0.81–1.21)	1.19 (0.73–1.95)
Regular care provider	1.00 (0.85–1.18)	0.88 (0.59–1.32)
Obstetrician	1.31 (1.06–1.62)	0.52 (0.36–0.76)
Endocrinologist or internist	0.85 (0.77–0.95)	0.68 (0.52–0.88)
Among women with pre-GDM		
Age (years)		
15–29	1.00 Ref	1.00 Ref
≥30	0.81 (0.70–0.94)	0.91 (0.70–1.18)
Socioeconomic status		
1 Lowest	1.00 Ref	1.00 Ref
2	0.97 (0.79–1.19)	0.77 (0.54–1.10)
3	0.85 (0.69–1.05)	0.72 (0.50–1.03)
4	0.70 (0.56–0.88)	0.67 (0.46–0.98)
5 Highest	0.92 (0.73–1.16)	0.80 (0.54–1.20)
Rural residence (Ref: urban)	1.55 (1.24–1.93)	1.57 (1.08–2.29)
Primary care physician	1.00 (0.72–1.39)	1.15 (0.65–2.04)
Regular care provider	0.88 (0.71–1.09)	0.78 (0.55–1.12)
Obstetrician	0.85 (0.64–1.13)	0.52 (0.34–0.79)
Endocrinologist or internist	1.56 (1.24–1.93)	1.68 (1.28–2.22)

A primary care physician before pregnancy was defined as having at least one visit to a family physician/general practitioner in the 21- to 9-month period before the index date. A regular care provider before pregnancy was defined as having half or more of their primary care visits to the same primary care physician in the 21- to 9-month period before the index date.

potential protective factors. We found nearly 50% lower perinatal mortality among women who were seen by an obstetrician. This may be due to the increased surveillance of these high-risk pregnancies (34). Finally, rural residence increased the risk of both congenital anomalies and perinatal mortality. Decreased education and awareness regarding pregnancy planning, along with reduced access to care, may be playing a role in this observed risk. This gap surely needs to be addressed. Finally, women with GDM had a lower rate of perinatal mortality compared with nondiabetic women. This is a somewhat surprising finding. One possible explanation may be that women with GDM are seen more often by obstetricians during pregnancy than non-DM women. We found that seeing obstetricians predicted lower perinatal mortality in both GDM and pre-GDM women.

Strengths of this study include the large number of deliveries (>1 million), allowing enough power to detect differences in rare events; the use of a validated database to distinguish women with GDM from pre-GDM (15); the generalizability given the population-based nature of the data in a province with health coverage for all residents, allowing for valid incidence rates; and the long follow-up of 14 years, allowing for assessment of trends. We were also able to detect some important predictors of poor outcomes, including young age and rural residence, while controlling for socioeconomic status, prepregnancy primary care visits, and pregnancy visits to obstetricians and internists. Some limitations include the fact that we were not able to differentiate women with type 1 diabetes from women with type 2 diabetes. This does limit our ability to fully interpret the data. However, with the increasing rates of type 2 diabetes outside of pregnancy and the declining age of onset of type 2 diabetes into the child-bearing age, much of this rise is likely due to an increase in type 2 diabetes in pregnancy (35). This hypothesis is supported by surveys of diabetic pregnancies conducted in the U.K. (13) and the U.S. (16), where observed increases in the prevalence of pre-GDM were found to be driven mainly by a rise in type 2 diabetes. We were also unable to examine important risk factors such as glycemic control, obesity, and ethnicity as predictors of serious perinatal outcomes.

With the steadily increasing rates of diabetes in pregnancy, and the serious nature of perinatal complications, the burden of these high-risk pregnancies is increasing. Although we have come a long way in improving care for women with diabetes in pregnancy, further efforts are needed to reverse the trend toward increased type 2 diabetes in women of child-bearing age and to decrease the prevalence of these serious perinatal outcomes in women with diabetes through improved preconception and perinatal care.

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version of the manuscript to be published. D.S.F. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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