Prepregnancy Diabetes and Risk of Placental Vascular Disease

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Maternal diabetes before pregnancy is associated with adverse maternal and perinatal outcomes, including acquired hypertension during pregnancy (1–3). The maternal placental syndromes preeclampsia and abruption or infarction of the placenta (4) are also more prevalent in women with insulin resistance, diabetes, and the metabolic syndrome (3,5–8). We evaluated the risk of placental vascular disease in association with prepregnancy diabetes.

RESEARCH DESIGN AND METHODS

We completed a retrospective population-based study of all women who underwent antenatal maternal serum screening (MSS) in Ontario, Canada, between 1993 and 2000, as described elsewhere (9). Those with a multiple gestation pregnancy at the time of MSS were excluded.

Maternal characteristics (Table 1) were recorded on a standardized form and completed by the patients' caregivers at the time of MSS. Data on obstetrical outcomes and the health status of each newborn were also linked to the Discharge Abstract Database of the Canadian Institute for Health Information, providing up to eight ICD-9 diagnostic codes for each woman and each newborn (see the online appendix [available at http://dx.doi.org/10.2337/dc07-0364]).

The primary study outcome was a diagnosis of either preeclampsia and abruption or infarction, according to the relevant ICD-9 codes recorded at the delivery hospital (online appendix). Secondary study outcomes included an individual diagnosis of preeclampsia and abruption or infarction, maternal preeclampsia/eclampsia, and poor fetal growth or fetal growth restriction.

Statistical analysis

The association between prepregnancy diabetes and study outcomes was analyzed using logistic regression analysis and expressed as a crude odds ratio (OR) and 95% CI. The ORs were further adjusted for those variables listed in the footnote of Table 1. All statistical analyses were done using SAS (version 9.1), and statistical significance was set at a two-sided P value <0.05.

The study research protocol was originally approved through the Ministry of Health and Longterm Care in Ontario, Canada, and by the research ethics board of St. Michael's Hospital.

RESULTS

There were 386,323 singleton pregnancies included during the period of study, and 1,717 (0.44%) women had a diagnosis of prepregnancy diabetes. Most maternal characteristics were similar among women with and without prepregnancy diabetes (Table 1). Fewer women with prepregnancy diabetes were of nonwhite ethnicity (21.7 vs. 27.4%); however, they weighed more at the time of MSS (74.6 vs. 66.9 kg).

The rate of preeclampsia was ~12% in women with prepregnancy diabetes and ~3% in those without diabetes (adjusted OR 3.4 [95% CI 2.9–4.0]) (Table 1). Preeclampsia and abruption or infarction was diagnosed among 2.2% of women with prepregnancy diabetes and 1.8% of those without diabetes (1.1 [0.79–1.5]) (Table 1).

CONCLUSIONS

Despite having a more than three times greater risk of preeclampsia, women with prepregnancy diabetes did not appear to be at elevated risk for preeclampsia and infarction or abruption. A nonsignificantly higher risk of fetal growth restriction was seen among the women with prepregnancy diabetes.

How do we explain the higher observed risk of preeclampsia but not preeclampsia and abruption or infarction in association with prepregnancy diabetes? The current study had >90% statistical power to detect at least a 1.5 times higher risk of preeclampsia and abruption or infarction between groups; thus, a type II statistical error is unlikely. Poor coding and ascertainment of preeclampsia and abruption or infarction in a database originally designed to focus on congenital and chromosomal anomalies may be one explanation, and the ICD-9 codes for preeclampsia and abruption and infarction have not been properly validated. The Ontario birth record contains a mandatory field whereby the delivering physician or midwife describes the gross appearance of the placenta and should therefore record the presence of preeclampsia and abruption or infarction. Because women with prepregnancy diabetes are more likely delivered electively by Cesarean section (10), a factor not controlled for herein, they might be at lower risk of preeclampsia and abruption precipitated during labor (11). At the same time, we did find an association between preeclampsia and prepregnancy diabetes, as expected, and the 3% rate of preeclampsia and 0.85% rate of preeclampsia and abruption among nondiabetic con-

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Abbreviations: MSS, maternal serum screening.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Characteristics of women with and without prepregnancy diabetes and risk of adverse placental and perinatal outcomes*

	Prepregnancy diabetes		OR (95% CI)	
	Present (n = 1,717)	Absent (n = 384,606)	Crude	Adjusted
Maternal characteristics				
Age (years)	30.0 ± 5.1	29.7 ± 5.0	—	—
Gestational age at the time of MSS (weeks)	16.5 ± 1.1	16.7 ± 1.1	—	—
Nonwhite ethnicity	362 (21.7)	101,670 (27.4)	—	—
Median gravidity	2.0	2.0	—	—
Median parity	1.0	1.0	—	—
Weight at the time of MSS (kg)	74.6 ± 17.6	66.9 ± 14.4	—	—
Preeclampsia or eclampsia at delivery	205 (11.9)	11,410 (3.0)	—	—
Gestational hypertension at delivery	117 (6.8)	7,071 (1.8)	—	—
Hypertension outside of pregnancy (coded at delivery)	8 (0.47)	148 (0.040)	—	—
Tobacco use at delivery	1 (0.060)	951 (0.25)	—	—
Drug dependence at delivery	0 (0.00)	221 (0.060)	—	—
Study outcomes				
Placental abruption or infarction	38 (2.2)	7,120 (1.8)	1.2 (0.87–1.7)	1.1 (0.79–1.5)*
Placental infarction	19 (1.1)	3,998 (1.0)	1.4 (0.88–2.1)	1.2 (0.74–1.8)*
Placental abruption	20 (1.2)	3,274 (0.85)	1.1 (0.68–1.7)	1.0 (0.66–1.6)*
Poor fetal growth or fetal growth restriction	17 (0.99)	2,000 (0.52)	1.9 (1.2–3.1)	1.5 (0.94–2.5)*
Preeclampsia	205 (11.9)	11,410 (3.0)	4.4 (3.8–5.1)	3.4 (2.9–4.0)†

Data are means ± SD or *n* (%) unless otherwise indicated. *Adjusted for maternal age, nonwhite ethnicity, parity, and body weight at the time of MSS, as well as preeclampsia/eclampsia, gestational hypertension, gestational diabetes, tobacco use, and drug dependence at the time of delivery. †Adjusted for maternal age, nonwhite ethnicity, parity, and maternal body weight at the time of MSS, as well as gestational diabetes and tobacco use at the time of delivery.

trol subjects are comparable with rates of other studies (5,11). Thus, it appears that the current database may have captured and classified at least some study outcomes. This does not rule out an association between prepregnancy diabetes and preeclampsia and abruption or infarction, however.

With respect to study strengths, this was a large cohort of ~400,000 women who delivered over a 7-year period. The study exposure—the presence of prepregnancy diabetes—was determined before all outcomes, and baseline maternal data were collected using a standardized method, enabling us to adjust for several potential confounding variables. Whereas we could not distinguish between women with type 1 and type 2 diabetes, we did adjust for maternal body weight in early pregnancy, which is a major determinant of type 2 diabetes (12).

There is a direct relationship between abnormal glucose metabolism before or in early pregnancy and the development of preeclampsia (1–3), and the current study confirms this. Although hypertensive disorders of pregnancy are a major risk factor for preeclampsia and abruption or infarction (13,14), a link between prepregnancy diabetes and preeclampsia and abruption or infartction was not found in the original observation. It has been postulated that longer duration of exposure of the placental vessels to a hyperglycemic and hypertensive environment is harmful (15,16). In one prospective study of 290 pregnant women with type 1 diabetes, an elevated A1C at 24 weeks' gestation was associated with a significantly higher risk of preeclampsia (17). However, as in our study, there are no data on glycemic control in pregnancy and the risk of preeclampsia and abruption or infarction.

A prospective study can address the issue of maternal glycemic control and the risk of preeclampsia, preeclampsia and abruption, or preeclampsia and infarction. Both preeclampsia and abruption and infarction might be captured not only at delivery, with a systematic examination of the placenta, but also before delivery using ultrasonography. The gestational age at onset of the preeclampsia and preeclampsia and abruption or preeclampsia and infarction, as well as the mode of delivery, should also be documented.

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