Q J Med 2001; **94**:347–356

Original papers

QJM

Maternal and neonatal outcomes in pregestational and gestational diabetes mellitus, and the influence of maternal obesity and weight gain: the DEPOSIT* study

J.G. RAY[1,2], M.J. VERMEULEN[3], J.L. SHAPIRO[4] and A.B. KENSHOLE[1]

From the [1]Department of Medicine, University of Toronto, [2]Department of Clinical Epidemiology and Biostatistics, McMaster University, [3]Sunnybrook Hospital Pre-Hospital Care Programme, Toronto, and [4]Department of Obstetrics and Gynecology, University of Toronto, Toronto, Canada

Received 18 January 2001 and in revised form 14 May 2001

Summary

We prospectively studied pregnancy outcome in 428 women with gestational diabetes mellitus (DM) and 196 women with pregestational DM, with particular reference to the influence of maternal obesity and excessive weight gain. These were consecutive singleton pregnancies delivered in our institution over 5 years. After controlling for multiple risk factors, including maternal BMI and pregnancy weight gain, women with pregestational DM were at increased risk (compared to those with gestational DM) for Caesarean delivery (OR 3.6, 95%CI 2.3–5.6), shoulder dystocia or cephalopelvic disproportion (OR 2.2, 95%CI 1.3–3.6), and gestational hypertension or toxaemia (OR 3.0, 95%CI 1.7–5.4). The offspring of these women were also at increased risk for admission to the neonatal intensive care unit (OR 4.0, 95%CI 2.3–6.8), large-for-gestational-age birthweight (OR 3.5, 95%CI 2.2–5.6), and preterm birth before 37 weeks (OR 3.8, 95%CI 2.5–5.9). Maternal obesity, and, to a lesser degree, excessive weight gain, were also independent risk factors for all these adverse maternal and neonatal outcomes, regardless of the type of DM, except for shoulder dystocia/cephalopelvic disproportion.

Introduction

The presence of maternal diabetes mellitus (DM) during pregnancy has important consequences for both mother and child. Women with DM are at increased risk for pre-eclampsia[1–4] and Caesarian delivery,[5] while their infants tend to experience higher rates of macrosomia[6] and shoulder dystocia.[7,8]

The development of gestational DM[8,9] is directly related to increased maternal body mass index (BMI). For example, the Nurse's Health Study investigators found that a pre-pregnancy BMI of 30 kg/m^2 or greater was a strong risk factor for the development of gestational DM (RR 2.9, 95%CI 2.2–3.9).[9] Others have defined both maternal obesity and excessive weight gain as major risk factors for pre-eclampsia,[10–12] Caesarian section,[10] preterm delivery,[13] fetal macrosomia[14,15] and fetal death.[13] What remains unclear, however, is to what

Address correspondence to Dr J.G. Ray. e-mail: rayjg@mcmaster.ca
**Diabetes Endocrine Pregnancy Outcome Study in Toronto.*

degree the presence of maternal obesity and weight gain among women with DM also contributes to the risk for adverse outcomes. For example, in a prospective study of 2272 women with gestational DM, only maternal BMI predicted neonatal birth weight, while plasma glucose levels did not.[16] In another study, tight glucose control was effective at lowering the risk for adverse perinatal events among obese women with gestational DM, but not among those whose BMI was normal.[17] Similarly, limiting weight gain in the presence of gestational DM was most effective at reducing the number of adverse events within the obese subgroup.[18]

Our current understanding of the influence of DM sub-type, obesity and weight gain on pregnancy outcome is limited by the fact that most data originate from studies comparing women with DM to healthy controls without DM.[18,19] Using such controls may exaggerate the true effect size for adverse obstetrical outcomes compared to the real population, since the latter typically includes women who are obese, or who have undetected DM or concomitant maternal or fetal health problems. Moreover, previous studies rarely controlled for maternal BMI or pregnancy weight gain, while exploring the relationship between DM and adverse obstetrical and neonatal outcomes.

In an attempt to overcome some of these limitations, we studied over 600 women with gestational and pregestational DM, and asked two principal questions: (i) After adjusting for pre-pregnancy BMI and weight gain during pregnancy, do maternal and neonatal morbidity differ among women with gestational compared with pregestational DM? (ii) To what degree do maternal obesity and excess weight gain contribute to the development of adverse outcomes among women with DM during pregnancy?

Methods

Patients and data collection

We included all consecutive women with DM and a singleton pregnancy who delivered at the Women's College Hospital between 1 May 1993 and 31 August 1998. If a woman delivered more than once during this time, her first pregnancy was selected. We included those diagnosed with either pregestational DM (i.e. type 1 and type 2 DM) or gestational DM, according to established criteria.[20] Women without pregestational DM were universally screened at between 24 and 28 weeks gestation using a 1-h 50 g glucose challenge test. Those whose initial screening test was abnormal went on to complete a 3-h 100 g oral glucose tolerance test (OGTT). Gestational DM was confirmed by the presence of at least two abnormal OGTT glucose values.[20] Dietary counselling and capillary blood sugar testing were typically offered to women diagnosed with gestational DM, with the addition of insulin therapy for those whose 2-h PC sugars remained >7.0–8.0 mmol/l. Measurements typically used to assess glycaemic control during pregnancy (e.g. capillary glucose or glycosylated hemoglobin concentrations) were not collected in a systematic fashion for this study, and accordingly, are not reported.

The Women's College Hospital is a tertiary care facility with an average of 3800 deliveries per year, and is equipped with a High-Risk Obstetrics service, as well as a level 3 neonatal intensive care unit (NICU). The usual practice at this centre was to induce labour at 38 weeks among women with pregestational DM, and to maintain maternal glucose levels at between 3.5 and 7.0 mmol/l during delivery. Each newborn of a mother with DM was evaluated using Apgar scores, a general physical examination, and a capillary blood sugar level. Provided that the Apgar scores were satisfactory and gestational maturity was achieved, most neonates were sent to the level 1 newborn nursery for further glucose monitoring and oral feeding. Although this was the policy, no system had been set up to ensure that this was carried out in practice.

Since May 1993, data were collected on all women who delivered at the Women's College Hospital, regardless of maternal health, mode of delivery, or perinatal outcome. These data were prospectively entered into an on-site computer by the attending nurse, generally within a few hours of delivery. Variables included maternal age at delivery, gravidity and parity, previous obstetrical history (e.g. stillbirth, abortion, preterm birth, neonatal death, Caesarian section), and past medical history, including presence of DM or chronic hypertension. Data related to delivery included placental position, need and reasons for induction of labour, and use of epidural anaesthetic. Baseline perinatal/fetal data included fetal presentation, administration of maternal corticosteroids for fetal lung maturity, and administration of maternal antibiotics during labour.

To complete the data set, two authors (JR and JS) reviewed the standard antenatal sheets of all women included in the study. We collected additional information on pre-pregnancy weight (kg), height (cm) and net weight gain during pregnancy, and calculated the pre-pregnancy body-mass index (kg/m^2). We also verified that the correct DM classification was applied to each patient. If the antenatal records were not available through the hospital

chart, then the primary care obstetrician or family physician was contacted for these data.

Study outcomes

The following maternal and delivery outcomes were assessed: (i) A diagnosis of shoulder dystocia; (ii) a composite of either shoulder dystocia or cephalopelvic disproportion; (iii) all-cause Caesarean section, as well as Caesarean delivery with and without labour; (iv) a composite of either all-cause Caesarian or forceps delivery; (v) development of a second, third or fourth degree vaginal tear; and (vi) development of either gestational hypertension or pre-eclampsia. The composite outcome of shoulder dystocia or cephalopelvic disproportion was chosen because both are attributable to maternal obesity, DM and fetal macrosomia, and both typically necessitate Caesarian delivery.[21,22] Neonatal study outcomes included: (i) admission to the NICU, regardless of cause or duration; (ii) large for gestational age birthweight (LGA), defined as a birthweight greater than two standard deviations above the 50th percentile weight for gestational age;[23] and (iii) preterm delivery before 32 or 37 weeks gestation.

Statistical analysis

The association between DM type (i.e. pregestational vs. gestational) and each study outcome was evaluated using multiple logistic regression analysis. All odds ratio estimates were adjusted for specific covariates, as defined *a priori*. Maternal covariates included maternal age (1 year increments); parity; pre-pregnancy BMI; net weight gain during pregnancy (5 kg increments); history of chronic hypertension; history of preterm delivery before 37 weeks; history of neonatal death or stillbirth; and history of previous Caesarian section or uterine surgery. Fetal presentation (vertex vs. breech) was only included in the analyses of Cesarean delivery outcome. In the analyses of neonatal outcomes, the presence of placenta previa, gestational age at deliver and maternal receipt of betamethasone for fetal lung maturity were included solely in NICU admission.

Baseline maternal characteristics, gestational age at delivery and neonatal birthweight were compared across groups using either an unpaired t-test for continuous variables or the χ^2 test for categorical data. All p values were two-sided, and a significance level of 0.05 was set *a priori*. Statistical analyses were performed using SAS Version 6.12. Permission to conduct this study was granted by the Sunnybrook and Women's College Hospitals' Medical Records Department and the Hospital Research Review Board.

Comparability with other studies

For the Discussion, we compared our results to those of other investigators, and examined whether the rates for Caesarean delivery and LGA have changed with time. We searched MEDLINE for all English language reports published between 1985 and May 2000 that included women with either gestational or pregestational DM. Only studies that presented data on both LGA and all-cause Caesarian delivery were included. For studies that compared different periods of observation, rates were abstracted for the latest period of study. Similarly, when groups were compared for different degrees of glycemic control, data were used for women with the strictest glycaemic control. All rates were presented in graphical form, according to year of publication. Acknowledging its limitations, we calculated crude, non-weighted mean rates for Caesarean section and LGA across the all studies of gestational DM and pregestational DM. In a descriptive manner, we then compared our own results to these crude averages.

Results

Study findings

Between 1 May 1993 and 31 August 1998, 428 women with gestational DM and singleton pregnancies, and 196 women with pregestational DM and singleton pregnancies were delivered at our hospital. Of those with pregestational DM, 146 (74.5%) had type 1 DM and 50 (25.5%) had type 2 DM. Complete data were available on all women, with the exception of BMI, for which height was not measured in 67 (16%) women with gestational DM and in 21 (11%) with pregestational DM. Selected baseline maternal and neonatal characteristics are listed in Table 1. Women with gestational DM were slightly older (33.1 vs. 31.5 years), and there was a higher rate of chronic hypertension in the pregestational DM group (6.1 vs. 1.9%). Although the mean birthweight did not differ between groups, the infants of mothers with pregestational DM were delivered a mean of 1.5 weeks earlier, at a mean gestational age of 36.1 weeks.

Shoulder dystocia was diagnosed among 3.0% of women with gestational DM and 4.1% of those with pregestational DM (OR 1.8, 95%CI 0.6–5.1). Compared to those with gestational DM, women with pregestational DM were at significantly increased risk for shoulder dystocia

or cephalopelvic disproportion (OR 2.2, 95%CI 1.3–3.6), and were at even greater risk for all-cause Caesarian section (rate 60.2%; OR 3.6, 95%CI 2.3–5.6) (Table 2). The risk for Caesarean delivery among women with pregestational compared to gestational DM was more pronounced for the subgroup who did not experience labour (OR 4.4, 95%CI 2.2–9.0) than for those who did labour (OR 3.3, 95%CI 2.0–5.4). After adjusting for DM type and other potential confounders, it appeared that the risk for all-cause Caesarian section rose progressively with increasing pre-pregnancy BMI, and was highest among those whose BMI was >30.0 kg/m^2 (rate 55.3%; OR 3.5, 95%CI 1.4–8.6). This was evident despite the absence of a relationship between higher BMI and the development of either shoulder dystocia or cephalopelvic disproportion (OR 1.2, 95%CI 0.4–3.4). Weight gain conferred a slightly increased risk for both all-cause Caesarean delivery (OR 1.2 for each 5 kg increment, 95%CI 1.0–1.4) and the composite of all-cause Caesarian or forceps delivery (OR 1.2, 95%CI 1.0–1.4) (Table 2).

There was no significant difference in the rate of second, third or fourth degree vaginal tears between women with gestational vs. pregestational DM, nor with higher maternal BMI or weight gain (Table 2). However, compared to those with gestational DM, women with pregestational DM experienced higher rates of gestational hypertension and toxaemia (20.4%; OR 3.0, 95%CI 1.7–5.4). A non-significant association with the hypertensive disorders of pregnancy was seen with increasing BMI, but weight gain was a significant risk factor for this outcome (OR 1.4 for each 5 kg increment, 95%CI 1.2–1.7) (Table 2).

Neonatal outcomes are presented in Table 3. The rate of admission to the NICU was significantly higher among the offspring of women with pregestational (83.7%) than gestational (45.8%) DM (OR 4.0; 95%CI 2.3–6.8). There was also a graded increase in risk for NICU admission according to increasing maternal BMI, with the highest risk among those whose BMI was >30.0 kg/m^2 (OR 2.4, 95%CI 1.0–5.9). Weight gain during pregnancy also conferred an increased risk for NICU admission (OR 1.2 for each 5 kg increment, 95%CI 1.0–1.4).

LGA infants were born more commonly to women with pregestational DM (rate 37.2%; OR 3.5, 95%CI 2.2–5.6) (Table 3). Both maternal obesity (OR 3.3, 95%CI 1.0–10.6) and 5 kg interval weight gain (OR 1.3, 95%CI 1.1–1.6) were independent predictors of LGA birthweight. The

Table 1 Characteristics of singleton women with gestational and pregestational diabetes mellitus, as well as gestational age and neonatal birthweight at delivery

Characteristic	Gestational diabetes mellitus ($n=428$)	Pregestational diabetes mellitus ($n=196$)	Statistical comparison between groups
Mean (SD) maternal age (years)	33.1 (4.5)	31.5 (4.9)	$p<0.001$
No. (%) primigravidae	226 (52.8)	116 (59.2)	$p=0.2$
No. (%) prior Caesarian section*	50 (24.8)	30 (37.5)	$p=0.3$
No. (%) prior preterm delivery before 37 weeks*	41 (20.3)	14 (17.5)	$p=0.4$
No. (%) previous stillbirth or neonatal death*	33 (16.3)	14 (17.5)	$p=0.9$
No. (%) chronic hypertension	8 (1.9)	12 (6.1)	p=0.01
Mean (SD, 95%CI) pre-pregnancy BMI (kg/m^2)	26.6 (6.3, 25.9–27.2)	26.2 (5.5, 25.4–27.0)	p=0.4
No. (%)**			
BMI <20.0	33 (9.1)	10 (5.7)	NA
BMI 20.0–24.9	138 (38.2)	80 (45.7)	NA
BMI 25.0–29.9	106 (29.4)	46 (26.3)	NA
BMI $\geqslant 30.0$	84 (23.3)	39 (22.3)	NA
Mean (SD, 95%CI) weight gain during current pregnancy (kg)	12.9 (7.0, 12.2–13.6)	12.2 (6.1, 11.3–13.1)	$p=0.2$
Mean (SD, 95%CI) gestational age at current delivery (weeks)	37.6 (2.8, 37.3–37.8)	36.1 (2.5, 35.7–36.4)	$p<0.001$
Mean (SD, 95%CI) neonatal birthweight at current delivery (g)	3265.4 (785.6, 3200.8–3350.1)	3266.6 (877.2, 3143.0–3390.2)	$p=1.0$

*Excludes all primigravidae. **BMI data were unavailable for 67 (16%) women with gestational DM and 21 (11%) with pregestational DM. BMI, body mass index; NA, not applicable.

Table 2 Rates and adjusted odds ratios (OR) for delivery and maternal health outcomes among women with pregestational and gestational diabetes mellitus

Maternal characteristic	Shoulder dystocia or cephalopelvic disproportion		All-cause Caesarian delivery		All-cause Caesarian or forceps delivery		Second, third or fourth degree vaginal tear		Hypertensive disorders of pregnancy**	
	Rate (%)	OR (95%CI)	Rate (%)	OR* (95%CI)	Rate (%)	OR (95%CI)	Rate (%)	OR (95%CI)	Rate (%)	OR (95%CI)
Diabetes mellitus type										
Gestational	14.2	1.0	34.1	1.0	40.6	1.0	23.5	1.0	8.9	1.0
Pregestational	25.5	2.2 (1.3–3.6)	60.2	3.6 (2.3–5.6)	66.3	3.3 (2.1–5.1)	18.4	0.8 (0.5–1.3)	20.4	3.0 (1.7–5.4)
Pre-pregnancy BMI (kg/m^2)										
<20.0	14.0	1.0	30.2	1.0	41.9	1.0	25.6	1.0	4.6	1.0
20.0–24.9	21.1	1.5 (0.6–3.8)	39.0	1.2 (0.5–2.8)	45.4	0.9 (0.4–2.0)	21.1	0.7 (0.3–1.6)	10.6	1.8 (0.4–8.1)
25.0–29.9	16.4	1.3 (0.5–3.5)	43.4	1.3 (0.6–3.3)	50.7	1.1 (0.5–2.5)	27.0	1.3 (0.6–2.9)	13.2	2.6 (0.6–11.8)
$\geqslant 30.0$	15.4	1.2 (0.4–3.4)	55.3	3.5 (1.4–8.6)	58.5	2.3 (1.0–5.4)	14.6	0.4 (0.2–1.1)	17.1	4.1 (0.9–18.9)
Weight gain (5 kg increments)	–	1.1 (0.9–1.3)	–	1.2 (1.0–1.4)	–	1.2 (1.0–1.4)	–	0.9 (0.8–1.1)	–	1.4 (1.2–1.7)

*All odds ratios were adjusted for DM class (gestational or pregestational), maternal age, parity, pre-pregnancy BMI, net weight gain during pregnancy, history of chronic hypertension, history of preterm delivery before 34 weeks, history of neonatal death or stillbirth, history of prior Caesarian section or uterine surgery, and the presence of placenta previa. Fetal presentation was added to the analysis of Caesarean delivery. **Defined as either gestational hypertension, pre-eclampsia or the HELLP (Haemolysis, Elevated Liver enzymes, Low Platelets) syndrome. BMI, body mass index.

Table 3 Rates and adjusted odds ratios (OR) for neonatal outcomes among women with pregestational and gestational diabetes mellitus

Maternal characteristics	NICU admission		LGA		Preterm birth <32 weeks		Preterm birth <37 weeks	
	Rate (%)	OR* (95%CI)	Rate (%)	OR (95%CI)	Rate (%)	OR (95%CI)	Rate (%)	OR (95%CI)
Diabetes mellitus type								
Gestational	45.8	1.0	15.9	1.0	4.7	1.0	19.2	1.0
Pregestational	83.7	4.0 (2.3–6.8)	37.2	3.5 (2.2–5.6)	7.1	2.1 (0.8–5.1)	43.4	3.8 (2.5–5.9)
Pre-pregnancy BMI (kg/m^2)								
<20.0	39.5	1.0	9.3	1.0	4.6	1.0	7.0	1.0
20.0–24.9	54.1	1.2 (0.5–2.7)	24.8	2.5 (0.8–7.7)	3.2	0.6 (0.1–3.3)	28.0	5.0 (1.4–17.6)
25.0–29.9	61.8	1.9 (0.8–4.4)	24.3	2.6 (0.8–8.2)	4.6	0.9 (0.2–4.6)	28.3	5.5 (1.5–19.4)
⩾30.0	65.0	2.4 (1.0–5.9)	26.0	3.3 (1.0–10.6)	6.5	0.8 (0.4–4.4)	27.6	5.1 (1.4–18.6)
Weight gain (5 kg increments)	–	1.2 (1.0–1.4)	–	1.3 (1.1–1.6)	–	0.9 (0.6–1.3)	–	1.0 (0.8–1.2)

*All odds ratios were adjusted for DM class (gestational or pregestational), maternal age, parity, pre-pregnancy BMI, net weight gain during pregnancy, history of chronic hypertension, history of preterm delivery before 34 weeks, history of neonatal death or stillbirth, and history of prior Caesarian section or uterine surgery. The presence of placenta previa, gestational age at delivery and maternal receipt of betamethasone were added to the analysis of NICU admission. NICU, neonatal intensive care unit; LGA, large-for-gestational-age birthweight; BMI, body mass index.

risk for preterm delivery before 32 weeks was not significantly associated with DM type, BMI, or weight gain; however, infants born to mothers with pregestational DM were at increased risk for preterm birth before 37 weeks (OR 3.8, 95%CI 2.5–5.9). Compared with a BMI of <20.0 kg/m^2, each BMI group above this value had a significant association with preterm delivery before 37 weeks regardless of DM type (OR 5.0–5.5) (Table 3).

There were 17 (2.7%) congenital defects detected at birth in our study. The number of anomalies that may have resulted in a either spontaneous or therapeutic termination before birth was not available. Five (2.6%) anomalies were seen in the offspring of mothers with pregestational DM, of whom four had type 1 DM. The remaining 12 (2.8%) congenital anomalies arose in the offspring of mothers with gestational DM.

Discussion

We studied the pregnancy outcomes of 428 women with gestational DM and 196 women with pregestational DM. After controlling for multiple risk factors, including maternal BMI and pregnancy weight gain, we observed that women with pregestational DM were at an increased risk for operative delivery, shoulder dystocia or cephalopelvic disproportion, and gestational hypertension or pre-eclampsia. The offspring of these women were also at a significantly increased risk for NICU admission, LGA birthweight, and preterm birth. We also found maternal obesity, and, to a lesser degree, excessive weight gain, to be independent risk factors for adverse maternal and neonatal outcomes.

There were several limitations to our study. First, due to the absence of a control group without DM, we did not compare the risk for adverse events between women with and without DM. This decision was made on the basis that previous studies have clearly established this point.[1–8] Second, we did not define or control for maternal ethnicity, which is a known risk factor for the development of both gestational[9] and type 2[24] DM. A third limitation is that neither the nurses nor physicians in our study were blinded to the patients' DM subtype, past medical and obstetrical history, or fetal status. Furthermore, we did not control for maternal co-morbidity, such as the presence of diabetic nephropathy.[25] Each of these factors may have influenced the endocrinologists' and obstetricians' choice regarding timing and mode of delivery, and the pediatricians' decision to admit a newborn to the NICU.

In the current study, we did not collect data on maternal insulin use or glycemic control in pregnancy, both of which may influence perinatal outcome.[2] We chose to omit the use of the glycosylated haemoglobin concentration as a marker of early pregnancy glycemic control, because this test is rarely ordered in women with gestational DM. Although we might have used the mean serum glucose values in both groups of women, we knew that fewer results would be available for those

with gestational DM, and the majority would have been collected after 32 weeks gestation. Had we incorporated these data, knowing the degree to which they were imbalanced, we might have introduced, rather than attenuated, study bias. Finally, some clinicians may challenge our decision to classify women with type 1 and type 2 DM together, since they differ in terms of pathophysiology and maternal complications. However, others have found little or no difference between individuals with type 1 and type 2 DM, in terms of rates for Caesarean section, shoulder dystocia or LGA birthweight.[26]

The strengths of the DEPOSIT study lie in its originality, modest sample size, and the adjustment for several important maternal confounders. We are not aware of other investigations of the relative contributions of pregestational and gestational DM to both maternal and neonatal complications that also consider the concomitant impact of pre-pregnancy BMI and weight gain.

The observation that pregestational DM confers a higher risk for obstetrical complications compared to gestational DM, independent of baseline weight and weight gain, may be explained by one or more factors. For example, fetal exposure to the hyperglycaemic milieu of pregestational DM is typically more prolonged and severe, and hence, may be more pathogenic, than with gestational DM.[27] This is paralleled by higher fetal production of endogenous insulin and C-peptide.[28] The fact that we did not record either insulin dosing or adequacy of glycemic control for all of our participants precludes us from addressing this issue more directly, however.

The rates for LGA birthweight and Caesarean section in our study compared with other studies are presented in Figures 1 and 2. The frequency of Caesarean delivery observed in our population was appreciably higher than the crude mean across all studies of both gestational DM (34% vs. 25%) (Figure 1) and pregestational DM (60% vs. 49%) (Figure 2). However, the rate of LGA in our study approximated the crude mean rate for all studies of gestational DM (16% vs. 19%) and pregestational DM (37% vs. 34%). We caution against drawing strong conclusions from these comparisons, however, since these crude mean rates were derived from studies comprising different populations at different periods, and were not based on formal meta-analytical principles.[57]

Using year of publication as a reference point, Figures 1 and 2 suggest that the rates of LGA and Caesarean section have not declined appreciably over time. We acknowledge that the year of publication was only an approximate indicator of the period of study. Nonetheless, the fact that we and others have demonstrated that women with pregestational DM remain at greatest risk for operative delivery, independent of several maternal covariates or the presence of an LGA infant, is an important one. Caesarian delivery is associated with increased health care costs,[58,59] as well as higher maternal[59] and neonatal morbidity.[60] Furthermore, relative to those with gestational DM, we have found that women with pregestational DM are even more likely to undergo Caesarean delivery without labour. One can speculate as to whether such behaviour reflects a 'play it safe' strategy among obstetricians who care for women with pregestational DM, an observation already noted for women with gestational DM.[25]

We were most interested to find a higher risk for Caesarian delivery related to maternal obesity despite little association between elevated BMI and the diagnosis of shoulder dystocia or cephalopelvic disproportion. Future research should attempt to identify the reasons for Caesarian delivery in these women, including the preferences of both obstetricians and patients,[61] as well as the limitations of ultrasonography for accurately predicting the presence of fetal macrosomia at birth.[62] This may enhance our understanding of ways to reduce the rate of complications among women with DM who undergo a trial of labour,[63] especially in terms of progression to Caesarean delivery. There also remains an urgent need to evaluate whether policies aimed at the appropriate use of elective Caesarean delivery[59,63] can be safely applied to women with DM.

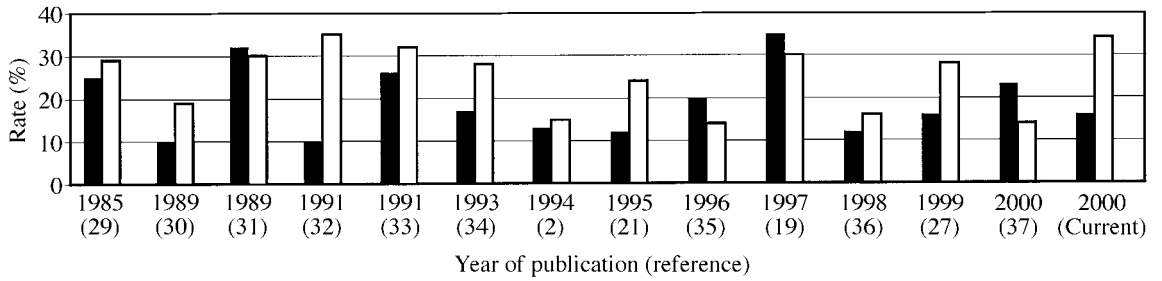

Figure 1. Rates for Caesarian delivery (empty bars) and LGA birthweight (solid bars) from published studies of women with gestational diabetes mellitus.

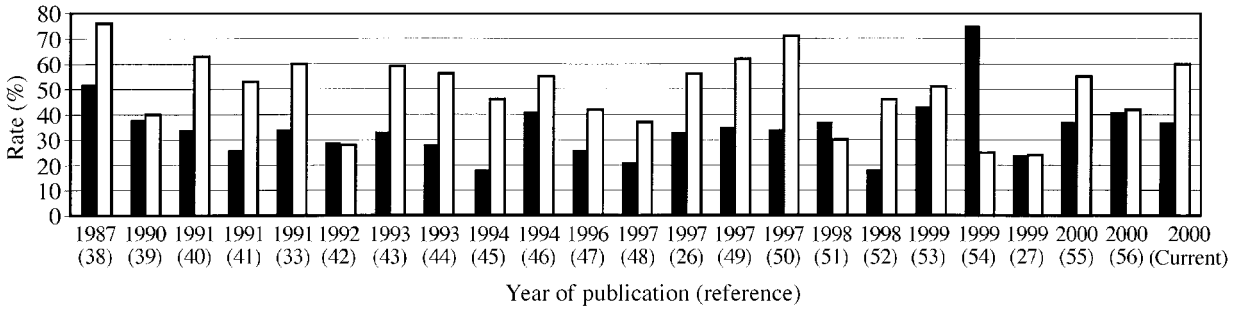

Figure 2. Rates for Caesarian delivery (empty bars) and LGA birthweight (solid bars) from published studies of women with pregestational diabetes mellitus.

In our population of women with DM, both pregestational and gestational, we found pre-pregnancy obesity to be independently and strongly associated with both LGA and birth before 37 weeks, while net weight gain during pregnancy had a more modest effect. Others have observed a strong association between pre-pregnancy BMI and adverse perinatal events within non-diabetic populations, despite little or no influence from pregnancy weight gain.[64,65] Furthermore, among women with pregestational DM, the development of LGA has been mostly attributed to the level of glycaemic control during the early[66] and late[67,68] first trimester, but not at subsequent gestational periods. Together, these data suggest that the timing for the development of LGA among the infants of women with DM may depend on the presence of periconceptual insulin resistance[69] as well as concomitant hyperglycemia.[66] Future clinical research should evaluate whether limiting weight gain during pregnancy can reduce the risk for adverse perinatal events among women with all forms of DM,[70] and more specifically, whether there is any benefit from a preconceptual weight reduction program among obese women with DM who are planning to conceive.[66,71]

In our study, we found that the infants of mothers with gestational and pregestational DM were admitted to NICU at rates of 46% and 84%, respectively. The risk for NICU admission was even more pronounced among the offspring of obese mothers, as noted previously in a population of women without known DM,[72] and was independent of gestational age. Although we did not assess the duration of stay in our study, a single day in the NICU is associated with high health care costs[73,74] and parental stress.[76] Our own institutional policy was to admit these infants selectively; nonetheless, the admission rate remained high. Others have observed NICU admission rates of 25% among the offspring of mothers with gestational DM,[2] and respective rates of 43% and 70% among the infants of mothers with White Class B and Class F/R DM.[76] Again, future research is needed to determine the latest gestational age at which delivery is safest for both mother and child, while minimizing the need for NICU admission. There also remains an urgent need to further define the effect of maternal obesity on fetal growth and maturation in the heterogeneous group of women who share DM in common.

Acknowledgements

A grant-in-aid was provided by the Physicians' Services Incorporated Foundation, Toronto, Ontario.

References

1. Garner PR, D'Alton ME, Dudley DK, Huard P, Hardie M. Preeclampsia in diabetic pregnancies. *Am J Obstet Gynecol* 1990; **163**:505–8.
2. Langer O, Rodriguez DA, Xenakis EM, McFarland MB, Berkus MD, Arredondo F. Intensified versus conventional management of gestational diabetes. *Am J Obstet Gynecol* 1994; **170**:1036–47.
3. Suhonen L, Teramo K. Hypertension and pre-eclampsia in women with gestational glucose intolerance. *Acta Obstet Gynecol Scand* 1993; **72**:269–72.
4. Kvetny J, Poulsen HF, Damgaard DW. Results from screening for gestational diabetes mellitus in a Danish county. *Dan Med Bull* 1999; **46**:57–9.
5. Naylor CD, Sermer M, Chen E, Sykora K. Cesarean delivery in relation to birth weight and gestational glucose tolerance. *JAMA* 1996; **275**:1165–70.
6. Kieffer EC, Alexander GR, Kogan MD, Himes JH, Herman WH, Mor JM, *et al*. Influence of diabetes during pregnancy on gestational age-specific newborn weight among US black and US white infants. *Am J Epidemiol* 1998; **147**:1053–61.
7. Bradley RJ, Nicolaides KH, Brudenell JM. Are all infants of diabetic mothers 'macrosomic'? *BMJ* 1988; **297**:1583–4.
8. Godwin M, Muirhead M, Huynh J, Helt B, Grimmer J. Prevalence of gestational diabetes mellitus among Swampy Cree women in Moose Factory, James Bay. *CMAJ* 1999; **160**:1299–302.

9. Solomon CG, Willett WC, Carey VJ, Rich-Edwards J, Hunter DJ, Colditz GA, *et al*. A prospective study of pregravid determinants of gestational diabetes mellitus. *JAMA* 1997; 1078–83.
10. Sermer M, Naylor CD, Gare DJ, Kenshole AB, Ritchie JWK, Farine D, Cohen HR, McArthur K, Holzapfel S, Biringer A, Chen E. Impact of increasing carbohydrate intolerance on maternal-fetal outcomes in 3637 women without gestational diabetes. The Toronto Tri-Hospital Gestational Diabetes Project. *Am J Obstet Gynecol* 1995; **173**:146–56.
11. Brost BC, Goldenberg RL, Mercer BM, lams JD, Meis PJ, Moawad AH, *et al*. The Preterm Prediction Study: association of caesarean delivery with increases in maternal weight and body mass index. *Am J Obstet Gynecol* 1997; **177**:333–7.
12. Sibai BM, Ewell M, Levine RJ, Klebanoff MA, Esterlitz J, Catalano PM, Goldenberg RL, Joffe G. Risk factors associated with preeclampsia in healthy nulliparous women. The Calcium for Preeclampsia Prevention (CPEP) Study Group. *Am J Obstet Gynecol* 1997; **177**:1003–10.
13. Cnattingius S, Bergstrom R, Lipworth L, Kramer MS. Prepregnancy weight and the risk of adverse pregnancy outcomes. *N Engl J Med* 1998; **338**:147–52.
14. Cameron M, Feng T, Newman M. Infants of obese class A1 diabetics are at increased risk for fetal macrosomia. *Am J Obstet Gynecol* 1998:S57.
15. Sunehag A, Berne C, Lindmark G, Ewald U. Gestational diabetes-perinatal outcome with a policy of liberal and intensive insulin therapy. *Ups J Med Sci* 1991; **96**:185–98.
16. Jacobson JD, Cousins L. A population-based study of maternal and perinatal outcome in patients with gestational diabetes. *Am J Obstet Gynecol* 1989; **161**:981–6.
17. Hod M, Rabinerson D, Kaplan B, Peled Y, Bar J, Shindel B, *et al*. Perinatal complications following gestational diabetes mellitus: how 'sweet' is ill? *Acta Obstet Gynecol Scand* 1996; **75**:809–15.
18. Lauszus FF, Paludan J, Klebe JG. Birthweight in women with potential gestational diabetes mellitus—an effect of obesity rather than glucose intolerance? *Acta Obstet Gynecol Scand* 1999; **78**:520–5.
19. Casey BM, Lucas MJ, Mcintire DD, Leveno KJ. Pregnancy outcomes in women with gestational diabetes compared with the general obstetric population. *Obstet Gynecol* 1997; **90**:869–73.
20. National Diabetes Data Group. Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. *Diabetes* 1979; **28**:1039–57.
21. De Veciana M, Major CA, Morgan MA, Asrat T, Toohey JS, Lien JM, *et al*. Postprandial versus preprandial blood glucose monitoring in women with gestational diabetes mellitus requiring insulin therapy. *N Engl J Med* 1995; **333**:1237–41.
22. Jensen H, Agger AO, Rasmussen KL. The influence of prepregnancy body mass index on labor complications. *Acta Obstet Gynecol Scand* 1999; **78**:799–802.
23. Usher R, McLean F. Intrauterine growth of liveborn Caucasian infants at sea level: standards obtained from measurements in seven dimensions of infants born between 25 and 44 weeks gestation. *Pediatrics* 1969; **74**:901–10.
24. American Diabetes Association. Screening for type 2 diabetes. *Diabetes Care* 1999; **22**:S20–3.
25. Gordon M, Landon MB, Samuels P, Hissrich S, Gabbe SG. Perinatal outcome and long-term follow-up associated with modern management of diabetic nephropathy. *Obstet Gynecol* 1996; **87**:401–9.
26. Sacks DA, Chen W, Greenspoon JS, Wolde-Tsadik G. Should the same glucose values be targeted for type 1 as for type 2 diabetics in pregnancy? *Am J Obstet Gynecol* 1997; **177**:1113–19.
27. Nachum Z, Ben-Shlomo I, Weiner E, Shalev E. Twice daily versus four times daily insulin dose regimens for diabetes in pregnancy: randomised controlled trial. *Br Med J* 1999; **319**:1223–7.
28. Schwartz R, Gruppuso PA, Petzold K, Brambilla D, Hiilesmaa V, Teramo KA. Hyperinsulinemia and macrosomia in the fetus of the diabetic mother. *Diabetes Care* 1994; **17**:640–8.
29. Philipson EH, Kalhan SC, Rosen MG, Edelberg SC, Williams TG, Riha MM. Gestational diabetes mellitus: is further improvement necessary? *Diabetes* 1985; **34**:55–60.
30. Nordlander E, Hanson U, Persson B. Factors influencing neonatal morbidity in gestational diabetic pregnancy. *Br J Obstet Gynaecol* 1989; **96**:671–8.
31. Jacobson JD, Cousins L. A population-based study of maternal and perinatal outcome in patients with gestational diabetes. *Am J Obstet Gynecol* 1989; **161**:981–6.
32. Goldman JA, Dicker D, Feldberg D, Yeshaya A, Samuel N, Karp M. Pregnancy outcome in patients with insulin-dependent diabetes mellitus with preconceptual diabetic control: a comparative study. *Am J Obstet Gynecol* 1986; **155**:293–7.
33. GDDF (Gestation and Diabetes in France Study Group). Multicenter survey of diabetic pregnancy in France. *Diabetes Care* 1991; **14**:994–1000.
34. Kjos SL, Henry OA, Montoro M, Buchanan TA, Mestman JH. Insulin-requiring diabetes in pregnancy: a randomized trial of active induction of labor and expectant management. *Am J Obstet Gynecol* 1993; **169**:611–15.
35. Nasrat H, Fageeh W, Abalkhail B, Yamani T, Ardawi M. Determinants of pregnancy outcome in patients with gestational diabetes. *Int J Gynaecol Obstet* 1996; **53**:117–23.
36. Hod M, Bar J, Peled Y, Fried S, Katz I, Itzhak M, *et al*. Antepartum management protocol. Timing and mode of delivery in gestational diabetes. *Diabetes Care* 1998; **21 (Suppl. 2)**:B113–7.
37. Griffin ME, Coffey M, Johnson H, Scanlon P, Foley M, Stronge J, *et al*. Universal vs. risk factor-based screening for gestational diabetes mellitus: detection rates, gestation at diagnosis and outcome. *Diabet Med* 2000; **17**:26–32.
38. Goldkrand JW, Lin JY. Large for gestational age: dilemma of the infant of the diabetic mother. *J Perinatol* 1987; **7**:282–7.
39. Peck RW, Price DE, Lang GD, MacVicar J, Hearnshaw JR. Birthweight of babies born to mothers with type 1 diabetes: is it related to blood glucose control in the first trimester? *Diabet Med* 1991; **8**:258–62.
40. Tchobroutsky C, Vray MM, Altman JJ. Risk/benefit ratio of changing late obstetrical strategies in the management of insulin-dependent diabetic pregnancies. A comparison between 1971–1977 and 1978–1985 periods in 389 pregnancies. *Diabete Metab* 1991; **17**:287–94.
41. Gregory R, Scott AR, Mohajer M, Tattersall RB. Diabetic pregnancy 1977–1990: have we reached a plateau? *J R Coll Physicians Lond* 1992; **26**:162–6.
42. Rasmussen MJ, Firth R, Foley M, Stronge JM. The timing of delivery in diabetic pregnancy: a 10-year review. *Aust N Z J Obstet Gynaecol* 1992; **32**:313–17.

43. Hunter DJ, Burrows RF, Mohide PT, Whyte RK. Influence of maternal insulin-dependent diabetes mellitus on neonatal morbidity. *CMAJ* 1993; **149**:47–52.
44. Nielsen GL, Nielsen PH. Outcome of 328 pregnancies in 205 women with insulin-dependent diabetes mellitus in the county of Northern Jutland from 1976 to 1990. *Eur J Obstet Gynecol Reprod Biol* 1993; **50**:33–8.
45. Cnattingius S, Berne C, Nordstrom ML. Pregnancy outcome and infant mortality in diabetic patients in Sweden. *Diabet Med* 1994; **11**:696–700.
46. Aucott SW, Williams TG, Hertz RH, Kalhan SC. Rigorous management of insulin-dependent diabetes mellitus during pregnancy. *Acta Diabetol* 1994; **31**:126–9.
47. Persson B, Hanson U. Fetal size at birth in relation to quality of blood glucose control in pregnancies complicated by pregestational diabetes mellitus. *Br J Obstet Gynaecol* 1996; **103**:427–33.
48. Zhu L, Nakabayashi M, Takeda Y. Statistical analysis of perinatal outcomes in pregnancy complicated with diabetes mellitus. *J Obstet Gynaecol Res* 1997; **23**:555–63.
49. Hawthorne G, Robson S, Ryall EA, Sen D, Roberts SH, Ward MP, *et al*. Prospective population based survey of outcome of pregnancy in diabetic women: results of the Northern Diabetic Pregnancy Audit, 1994. *Br Med J* 1997; **315**:279–81.
50. Garcia-Patterson A, Corcoy R, Rigla R, Caballero A, Adelantado JM, Altirriba O, *et al*. Does preconceptual counseling in diabetic women influence prenatal outcome? *Ann Ist Super Sanita* 1997; **33**:333–6.
51. Reece EA, Sivan E, Francis G, Homko CJ. Pregnancy outcomes among women with and without diabetic microvascular disease (White's classes B to FR) versus nondiabetic controls. *Am J Perinatol* 1998; **15**:549–55.
52. Nordstrom L, Spetz E, Wallstrom K, Walinder O. Metabolic control and pregnancy outcome among women with insulin-dependent diabetes mellitus. A twelve-year follow-up in the country of Jutland, Sweden. *Acta Obstet Gynecol Scand* 1998; **77**:284–9.
53. Carron Brown S, Kyne-Grzebalski D, Mwangi B, Taylor R. Effect of management policy upon 120 Type 1 diabetic pregnancies: policy decisions in practice. *Diabet Med* 1999; **16**:573–8.
54. Dunne FP, Brydon P, Smith T, Essex M, Nicholson H, Dunn J. Pre-conception diabetes care in insulin-dependent diabetes mellitus. *Q J Med* 1999; **92**:175–6.
55. McElvy SS, Miodovnik M, Rosenn B, Khoury JC, Siddiqi T, St. John Dignan P, *et al*. A focused preconceptual and early pregnancy program in women with type 1 diabetes reduces perinatal mortality and malformation rates to general population levels. *J Matern Fetal Med* 2000; **9**:14–20.
56. Raychaudhuri K, Maresh MJ. Glycemic control throughout pregnancy and fetal growth in insulin-dependent diabetes. *Obstet Gynecol* 2000; **95**:190–4.
57. Petitti DB. *Meta-analysis, decision analysis, and cost-effective analysis: methods for quantitative synthesis in medicine*. New York, Oxford University Press, 1994:90–130.
58. Rouse DJ, Owen J. Prophylactic caesarean delivery for fetal macrosomia diagnosed by means of ultrasonography—A Faustian bargain? *Am J Obstet Gynecol* 1999; **181**:332–8.
59. Grobman WA, Peaceman AM, Socol ML. Cost-effectiveness of elective caesarean delivery after one prior low transverse caesarean. *Obstet Gynecol* 2000; **95**:745–51.
60. Towner D, Castro MA, Eby-Wilkens E, Gilbert WM. Effect of mode of delivery in nulliparous women on neonatal intracranial injury. *N Engl J Med* 1999; **341**:1709–14.
61. Woolbright LA. Why is the caesarean delivery rate so high in Alabama? An examination of risk factors, 1991–1993. *Birth* 1996; **23**:20–5.
62. Parry S, Severs CP, Sehdev HM, Macones GA, White LM, Morgan MA. Ultrasonographic prediction of fetal macrosomia. Association with cesarean delivery. *J Reprod Med* 2000; **45**:17–22.
63. Sachs BP, Kobelin C, Castro MA, Frigoletto F. The risks of lowering the caesarean-delivery rate. *N Engl J Med* 1999; **340**:54–7.
64. Kirchengast S, Hartmann B, Schweppe KW, Husslein P. Impact of maternal body build characteristics on newborn size in two different European populations. *Hum Biol* 1998; **70**:761–74.
65. Lewis DF, Edwards MS, Asrat T, Adair CD, Brooks G, London S. Can shoulder dystocia be predicted? Preconceptive and prenatal factors. *J Reprod Med* 1998; **43**:654–8.
66. Page RC, Kirk BA, Fay T, Wilcox M, Hosking DJ, Jeffcoate WJ. Is macrosomia associated with poor glycaemic control in diabetic pregnancy? *Diabet Med* 1996; **13**:170–4.
67. Peck RW, Price DE, Lang GD, MacVicar J, Hearnshaw JR. Birthweight of babies born to mothers with type 1 diabetes: is it related to blood glucose control in the first trimester? *Diabet Med* 1991; **8**:258–62.
68. Rey E, Attie C, Bonin A. The effects of first-trimester diabetes control on the incidence of macrosomia. *Am J Obstet Gynecol* 1999; **181**:202–6.
69. Berkowitz KM. Insulin resistance and preeclampsia. *Clin Perinatol* 1998; **25**:873–85.
70. Feig DS, Naylor CD. Eating for two: are guidelines for weight gain during pregnancy too liberal? *Lancet* 1998; **351**:1054–5.
71. Galtier-Dereure F, Boegner C, Bringer J. Obesity and pregnancy: complications and cost. *Am J Clin Nutr* 2000; **71**:1242–8S.
72. Perlow JH, Morgan MA, Montgomery D, Towers CV, Porto M. Perinatal outcome in pregnancy complicated by massive obesity. *Am J Obstet Gynecol* 1992; **167**:958–62.
73. Marshall PB, Halls HJ, James SL, Grivell AR, Goldstein A, Berry MN. The cost of intensive and special care of the newborn. *Med J Aust* 1989; **150**:568–9, 572–4.
74. Rogowski J. Measuring the cost of neonatal and perinatal care. *Pediatrics* 1999; **103**:329–35S.
75. Ladden M. The impact of preterm birth on the family and society. Part 1: Psychologic sequelae of preterm birth. *Pediatr Nurs* 1990; **16**:515–18.
76. Sibai BM, Caritis S, Hauth J, Lindheimer M, VanDorsten JP, MacPherson C, *et al*. Risks of preeclampsia and adverse neonatal outcomes among women with pregestational diabetes mellitus. National Institute of Child Health and Human Development Network of Maternal-Fetal Medicine Units. *Am J Obstet Gynecol* 2000; **182**:364–9.