

Pregnancy Loss and Neonatal Death in Women with Type 1 or Type 2 Diabetes Mellitus

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ABSTRACT

Background: Diabetes mellitus (DM) is known to be a significant risk factor for pregnancy loss, either through stillbirth or late intrauterine death or as the result of severe congenital malformation. Improved glycemic control and other advances in care substantially reduced the incidence of pregnancy loss in women with type 1 DM in most countries by the 1970s. However, because of a greater prevalence of obesity since the 1980s, the emergence of type 2 DM in pregnancy has become a significant problem. Although more pregnancies now occur in women with type 2 DM than in those with type 1 DM in many locations, relatively little information has been published about pregnancy loss in type 2 DM.

Objectives: This article examines the prevalence and causes of pregnancy loss in type 1 and type 2 DM and identifies factors in addition to glycemic control that may influence pregnancy outcome.

Methods: A MEDLINE search was conducted for recent literature on pregnancy loss in DM. Series reporting >200 pregnancies in type 1 DM and/or >100 pregnancies in type 2 DM were included.

Results: Thirty-four studies were identified (15 in type 1 DM [1997–2007], 19 in type 2 DM [1986–2007]). In type 1 DM, major congenital anomalies now account for ~50% of pregnancy losses, and all-cause perinatal mortality remains higher than in the general population. Several studies have suggested that the perinatal mortality rate is higher in type 2 DM than in type 1 DM. Factors other than glycemic control probably explain this phenomenon: women with type 2 DM typically are older and more obese, and they come from disadvantaged communities—all risk factors for pregnancy loss, particularly late intrauterine death and chorioamnionitis. In some women, type 2 DM may be recognized for the first time during pregnancy; pregnancies in these women carry the same risks of pregnancy loss as those in women with established DM.

Conclusions: Demographic changes in the prevalence of obesity suggest that the prevalence of type 2 DM in pregnancy will almost certainly increase. Although meticulous glycemic control is undoubtedly important in achieving good pregnancy outcomes, clinicians should be aware of the multiple risk factors faced by women with DM. (*Insulin*. 2008;3:167–175) © 2008 Excerpta Medica Inc.

Key words: diabetic pregnancy, congenital malformation, perinatal mortality, type 1 diabetes, type 2 diabetes.

INTRODUCTION

Before the discovery of insulin, a woman with type 1 diabetes mellitus (DM) had almost no chance of successful delivery of a healthy baby, and the maternal mortality rate was as high as 25%.¹ The maternal mortality rate decreased dramatically after the introduction of insulin treatment, but the rate of pregnancy losses remained high for several decades.¹ The predominant cause of pregnancy loss was stillbirth or late intrauterine death, which accounted for ~70% of losses, but congenital malformations, birth trauma, and neonatal complications (eg, severe hypoglycemia and respiratory distress syndrome) also were contributing factors.¹ The dramatic reduction in perinatal loss achieved in the second half of the 20th century (before the introduction of innovations such as glycosylated hemoglobin [A1C] measurement, home blood glucose monitoring, insulin pumps and pens, insulin

analogues, continuous blood glucose monitors, and fetal ultrasonography) is rightly hailed as one of the triumphs of modern medicine.¹

Substantial improvement in perinatal mortality followed the development of units specializing in the management of diabetic pregnancy. Key elements for improving outcomes included close integration of diabetic and obstetric care, strict control of glycemia (both fasting and postprandial), early delivery, and advances in neonatology and obstetric practice.^{1,2} The striking relationship between perinatal mortality and maternal glycemia argues persuasively for the importance of attaining near-normal glycemia for good pregnancy outcomes.³ However, this has promoted a somewhat “glucocentric” view of diabetic pregnancy—that glucose is all that matters. As discussed below, it is probable that other factors also affect pregnancy outcome, particularly in type 2 DM.

Awareness of type 2 DM as a significant issue in pregnancy began with studies from South Africa, Kuwait, Mexico, and Libya.⁴⁻⁷ Articles from developed countries did not appear until the late 1990s, when the increasing prevalence of obesity was reflected in the rapidly increasing incidence of type 2 DM in younger people. In many locations, the number of pregnancies in women with type 2 DM now exceeds that in women with type 1 DM. Concerns that pregnancy losses may be greater in type 2 DM than in type 1 DM have appeared in the literature.^{8,9}

METHODS

This review examines recent literature on pregnancy loss in DM identified through a MEDLINE search. It includes series reporting >200 pregnancies in type 1 DM and/or >100 pregnancies in type 2 DM. Pregnancy loss is a relatively infrequent, stochastic, and largely unpredictable event that occurs in women with or without diabetes, so there is always statistical uncertainty surrounding published rates. Because the reliability of estimates increases with sample size, smaller studies were excluded from the review. Rates of pregnancy loss are expressed with 95% CIs. A loss rate of zero still has a CI.¹⁰

Pregnancy losses can occur at various times in pregnancy and from a number of causes. Major congenital malformations, for example, can be associated with spontaneous miscarriage (rates of which are almost impossible to determine accurately), elective termination of pregnancy, stillbirth, or neonatal death. Most studies provided data on perinatal mortality rates (usually defined as pregnancy loss after 20 weeks' gestation and up to 1 week post partum), but relatively few studies provided detailed analysis of the causes of pregnancy loss.

RESULTS

The MEDLINE search identified 34 articles. Fifteen articles (published between 1997 and 2007) reported >200 pregnancies in women with type 1 DM; 19 articles (published between 1986 and 2007) reported >100 pregnancies in women with type 2 DM.

Perinatal Mortality in Type 1 Diabetes Mellitus

Numerous studies from different parts of the world addressing perinatal mortality in women with type 1 DM have attested to substantial improvements in perinatal mortality from the 1960s through the 1980s. Since then, the incidence of perinatal mortality seems to have changed little. **Table I** lists the findings from the 15 studies published in the past decade that reported >200 pregnancies in women with type 1 DM.¹¹⁻²⁵ Studies that reported sufficient detail suggested that major congenital malformations accounted for ~54% of pregnancy losses.^{14-18,20,24} The best results reported perinatal mortality rates in women with DM that were comparable to those in women without DM, but these tended to be in the series with the smallest numbers and thus had wide CIs. Most centers reported perinatal mortality rates in

women with type 1 DM that were 2- to 6-fold higher than in the local population. An exception was a study from British Columbia, Canada, in which the background rate was surprisingly high.¹⁵ The 95% CIs for all the studies overlapped, making it difficult to be certain whether true differences existed between the centers or to determine the cause(s) of such differences.

The largest series were compiled either from a single center over many years, which might have missed important secular trends, or from several centers over a short time frame, which might have overlooked important between-site heterogeneity. Unfortunately, a number of reports either had no information on glycemic control or presented it in such a way that comparisons with other series were difficult. Thus, a critical question remained unresolved: how much of the apparent between-center variation in perinatal mortality in type 1 DM could be explained by differences in glycemia? A number of recent papers emphasize that perinatal mortality is lower in women who attend prepregnancy counseling and whose pregnancies are planned,^{17,18,20} although these attributes are likely to be reflected in better social circumstances and other healthy life choices as well as better glycemic control. Factors in addition to glycemia have important influences on perinatal mortality. Pregnancy outcomes in the Diabetes Care and Complications Trial also support this view: women in the conventional and intensive arms who became pregnant had similar perinatal mortality rates, despite significantly higher A1C values early in pregnancy in the conventional group.²⁶

Perinatal mortality is lower in women who attend prepregnancy counseling and whose pregnancies are planned, although these attributes are likely to be reflected in better social circumstances and other healthy life choices as well as better glycemic control.

The background perinatal mortality rate (ie, the rate in the general population) differed between countries and between regions within the same country. These differences reflected factors such as geography and economic development, disparities in wealth, the quality and inclusiveness of the health care system, and the socioeconomic and educational levels of the population. It is likely that additional issues specific to DM were operative, but the published data did not permit detailed analysis.

Successful outcomes in diabetic pregnancy depend on the combined skill and experience of the diabetic and obstetric teams, good communication and cooperation between them, and the resources and technologic support available. Organizational issues are likely to be critical, and it would be interesting to learn from large multicenter studies, such as the recently published data from the United Kingdom,²³

Table I. Studies of perinatal mortality that reported >200 pregnancies in women with type 1 diabetes mellitus.

Country, Year of Publication	No. of Pregnancies (Period)	Perinatal Mortality* (95% CI)	Population Perinatal Mortality*	Increment Over General Population	Comment on Glycemic Control
United Kingdom, 1997 ¹¹	462 (1990–1994)	36.1 (17–55)	8.3	4.3x	No data
United States, 2000 ¹²	395 (1978–1993)	12.6 (4–29)	Not stated	–	A1C improved over study period
Finland, 2001 ¹³	954 (1991–1995)	13.6 (7–23)	5.9	2.3x	No data
England, 2002 ¹⁴	547 (1995–1999)	43.0 (26–65)	8.4	5.1x	No data
Canada, 2002 ¹⁵	300 (1989–1999)	6.6 (1–24)	31.0	0.2x	1st Trimester, mean A1C 7.4%
Scotland, 2003 ¹⁶	216 (1997–1999)	27.8 (10–59)	7.6	3.7x	No data
France, 2003 ¹⁷	289 (2000–2001)	45.0 (24–75)	7.0	6.4x	1st Trimester A1C >8.0% in 30%
Netherlands, 2004 ¹⁸	333 (1999–2000)	28.0 (12–51)	8.0	3.5x	1st Trimester A1C <7.0% in 75%
Denmark, 2005 ¹⁹	240 (1996–2001)	16.7 (5–42)	Not stated	–	At presentation, mean A1C 7.0%
Denmark, 2004 ²⁰	1218 (1993–1999)	31.0 (22–42)	7.5	4.1x	1st Trimester, mean A1C 7.4%
United Kingdom, 2005 ²¹	389 (1999–2004)	28.3 (14–50)	Not stated	–	At presentation, mean A1C 7.4%
Spain, 2006 ²²	532 (1984–2004)	16.9 (9–39)	Not stated	–	At presentation, mean A1C 7.2%
United Kingdom, 2006 ²³	1707 (2002–2003)	31.6 (24–41)	8.5	3.7x	1st Trimester A1C <7.0% in 37%
New Zealand, 2007 ²⁴	338 (1986–2005)	11.8 (3–30)	11.2	1.1x	At presentation, mean A1C 7.6%
Spain, 2008 ²⁵	257 (2000–2004)	19.8 (6–46)	Not stated	–	At presentation, mean A1C 7.1%

A1C = glycosylated hemoglobin.

*Expressed per 1000 births.

whether some units consistently perform better than others, and if so, to explore what organizational deficits underlie poorer outcomes in some clinics.

Perinatal Mortality in Type 2 Diabetes Mellitus

Studies of perinatal mortality that reported >100 pregnancies in women with type 2 DM are presented in Table II, together with data (where provided) on perinatal mortality in type 1 DM from the same centers.^{4–7,17,19,21–25,27–34} The studies generally were small (only 7 reported >200 pregnancies) and therefore may not be statistically robust, but they revealed some pertinent findings. First, all the studies showed that, on average, women with type 2 DM were older and more obese than women with type 1 DM. Second, perinatal mortality rates varied widely, but the rate was generally higher in women with type 2 DM than in women with type 1 DM (Figure 1). Third, all the studies that reported comparative data on A1C measurements in early and late pregnancy^{19,21,22,24,25} showed either no difference in glycemic control between pregnancies in type 1 DM and those in

type 2 DM, or that glycemic control was better in the latter group. A recent study of continuous blood glucose monitoring in pregnant women with type 1 or type 2 DM showed that hyperglycemic excursions were less marked in those with type 2 DM.³⁵

Newly Recognized Type 2 Diabetes Mellitus

Type 2 DM is a disorder of insidious onset. Thus, most subjects with type 2 DM will have had it for some time before diagnosis. It follows that a proportion of pregnant women will have unrecognized type 2 DM, and this will be most common in populations with a high background rate of type 2 DM. The American Diabetes Association's 1991 definition of gestational diabetes—"diabetes of onset or first recognition in pregnancy"—thus includes women with unrecognized type 2 DM. This definition is problematic because it groups together women with widely varying degrees of glucose intolerance and risk. Omori and Jovanovic³⁶ suggested that this definition be revised and that women whose glucose tolerance tests during pregnancy clearly fulfill the nonpreg-

Table II. Studies of perinatal mortality that reported >100 pregnancies in women with type 2 diabetes mellitus, together with data (where provided) on perinatal mortality in type 1 diabetes mellitus from the same centers.

Country, Year of Publication	Diabetes Type	No. of Pregnancies	Mean Age, years	Mean BMI, kg/m ²	Perinatal Mortality* (95% CI)
South Africa, 1986 ⁴	1	76	NR	NR	77 (29–164)
	2	295	NR	NR	72 (45–107)
Kuwait, 1990 ⁵	2	161	NR	NR	81 (44–134)
Mexico, 1991 ⁶	2	118	32	29.7	25 (5–72)
Libya, 1993 ⁷	2†	988†	32	NR	114 (94–134)
United States, 1997 ^{27§}	1	46	27	22.0	0 (0–77)
	2	113	34	32.7	35 (10–88)
Japan, 1997 ²⁸	1	178	30	20.3	11 (1–40)
	2	244	32	22.2	4 (1–22)
France, 2003 ¹⁷	1	280	NR	NR	45 (25–78)
	2	146	NR	NR	41 (15–87)
United Kingdom, 2003 ²⁹	2	182	33	31.1	25 (9–63)
Nigeria, 2004 ³⁰	1	78	~28	NR	145 (73–238)
	2	122	~37	NR	180 (112–249)
Denmark, 2005 ^{19§}	1	240	30	23.0	17 (5–42)
	2	61	33	29.4	67 (18–159)
South Africa, 2005 ³¹	1	172	31	NR	41 (16–82)
	2	213	34	NR	28 (10–60)
United Kingdom, 2005 ³²	1	101	27	NR	40 (11–98)
	2	101	32	NR	130 (63–194)
United Kingdom, 2005 ^{21§}	1	389	30	26.4	28 (14–50)
	2	146	34	34.2	62 (28–114)
Australia, 2005 ³³	1	81	31	NR	12 (1–67)
	2	99	33	NR	40 (11–100)
Spain, 2006 ^{22§}	1	532	29	23.3	17 (8–32)
	2	93	32	28.9	11 (1–60)
United Kingdom, 2006 ²³	1	1707	30	NR	32 (24–42)
	2	652	34	NR	32 (20–49)
South Africa, 2007 ^{34§}	2	379	33	32.8	52 (32–80)
New Zealand, 2007 ^{24§}	1	338	29	25.2	12 (1–30)
	2	862†	33	33.7	33 (22–47)
Spain, 2008 ^{25§}	1	257	29	24.0	20 (6–46)
	2	147	34	33.0	28 (8–69)

BMI = body mass index; NR = not recorded.

*Expressed per 1000 births.

† Type 1 diabetes mellitus present in 1% of this population.

‡ Includes newly recognized diabetes mellitus.

§ Studies that included data on glycosylated hemoglobin.

nant diagnostic criteria (fasting blood glucose: ≥ 7.0 mmol/L; 2-hour postglucose load: ≥ 11.1 mmol/L) be categorized as such and not as having “gestational diabetes.” Our group has argued that women with gestational diabetes who still have diabetes on early (6-week) postpartum testing should be considered as having “newly recognized diabetes” and that in most of these women the diabetes is likely to have antedated the pregnancy. When we examined perinatal mortality rates in women with gestational diabetes and analyzed separately those with “newly recognized diabetes,” we found that the latter have the same risk of perinatal mortality as

women with known type 2 DM (who have similar demographic and anthropometric features).³⁷ In the remainder of the gestational diabetes population, perinatal mortality rates did not differ from the background rate.

The magnitude of the problem of previously unrecognized diabetes can be considerable: in our population, about 1 in 7 women with gestational diabetes had newly recognized DM on postpartum testing; from 1986 to 1995, for every 3 women with known type 2 DM, 2 women had newly recognized type 2 DM. However, this ratio has changed, and in the decade 1996 to 2005, the proportion in whom type 2 DM

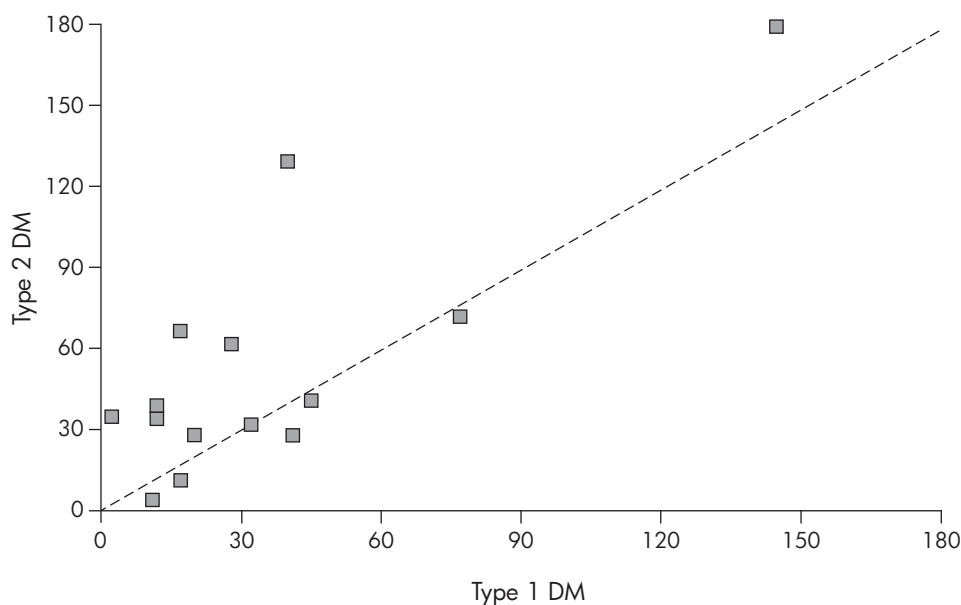


Figure 1. Perinatal mortality rates in type 1 and type 2 diabetes mellitus (DM) reported from individual centers. The broken line indicates the line of identity.

was previously unrecognized had decreased, probably reflecting increased awareness among health care professionals of the importance of diagnosing type 2 DM in young people.²⁴

Studies in women with type 2 DM that reported sufficient detail suggested that major congenital malformations accounted for ~16% of pregnancy losses—a marked contrast to the findings in women with type 1 DM. In our population, we noted significant differences in the causes of pregnancy loss between type 1 and type 2 DM. In a survey of 1200 pregnancies over a 20-year period (1986–2005), we found that late intrauterine deaths and stillbirths were relatively infrequent in women with type 1 DM, in whom the main causes of pregnancy loss were congenital anomalies (therapeutic abortion or early neonatal death) or complications of prematurity. More than 90% of stillbirths occurred in women with known or newly recognized type 2 DM. The stillbirths occurred in 2 clusters, with gestation between 22 and 29 weeks or between 35 and 42 weeks (**Figure 2**). Unexplained stillbirths and chorioamnionitis were strikingly more prevalent in women with type 2 DM than in women with type 1 DM.²⁴

Risk Factors for Perinatal Mortality in Type 2 Diabetes Mellitus

Obesity and type 2 DM do not affect all sections of society equally. For various reasons, the poor and the poorly educated are particularly vulnerable. In urbanized western societies, this often includes marginalized and deracinated indigenous communities and migrants from developing countries. Socioeconomic disadvantage affects pregnancy in

a number of ways. Examples specific to DM include the tendency for women with type 2 DM to present later to specialized pregnancy services than women with type 1 DM and to forego prepregnancy counseling.^{21,24}

Maternal obesity, poverty, and hyperglycemia are risk factors for both late intrauterine death and chorioamnionitis.^{38,39} In the general population, a higher maternal age is closely associated with an increased rate of stillbirths.⁴⁰ As noted previously, the average age of pregnant women with type 2 DM is significantly higher than that of pregnant women with type 1 DM. The trend in developed countries to delay pregnancy also includes women with DM. Over a 20-year period, we noted an increase in mean maternal age in both type 1 and type 2 DM.²⁵ In addition to a higher risk of stillbirth, later pregnancy is associated with higher risks of aneuploidy, multiparous pregnancy, and use of assisted fertility technologies.

Maternal obesity is strongly linked to pregnancy loss.^{38,41,42} For example, in the study of Kristensen et al,⁴² the risk of stillbirth and neonatal death was doubled in women with a mean prepregnancy body mass index (BMI) >30 kg/m². In our population, in which obesity is prevalent (particularly in the indigenous Maori and migrants from the Pacific Islands), >70% of women with type 2 DM had a prepregnancy BMI >30 kg/m², and a large difference in perinatal mortality was noted between type 1 and type 2 DM.²⁴ In the studies that reported >100 pregnancies in women with type 2 DM and also reported pre- or early-pregnancy maternal BMIs,^{6,21,24,25,27–29,34} a striking relationship was observed between maternal BMI and perinatal mortality rate (**Figure 3**).

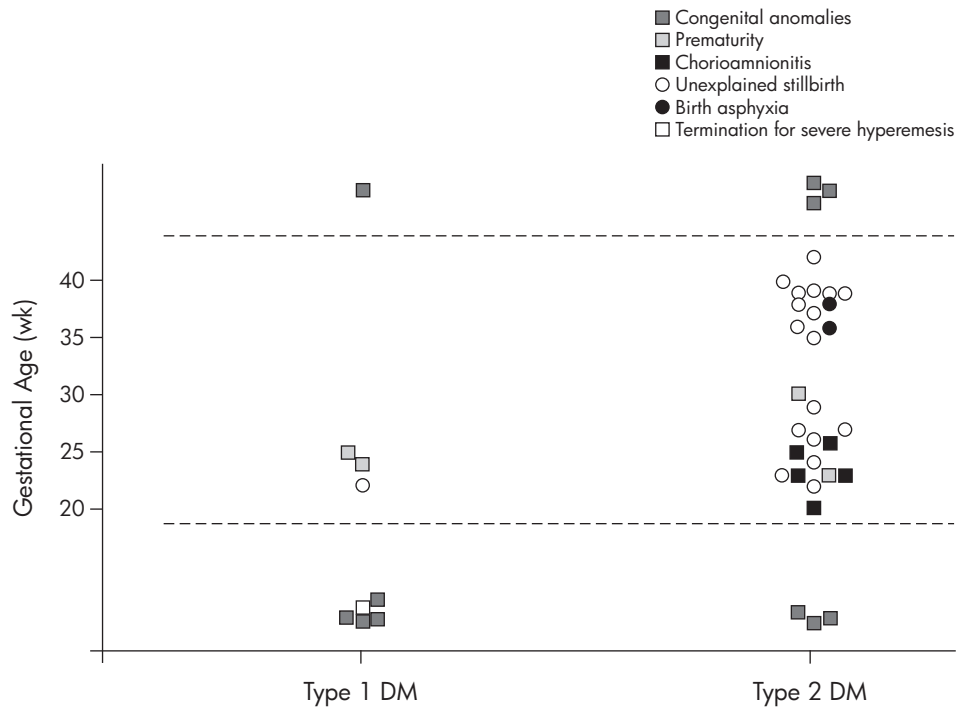


Figure 2. Timing and causes of pregnancy loss in type 1 and type 2 diabetes mellitus (DM), including newly recognized DM. Symbols beneath the lower broken line represent terminations of pregnancy at <24 weeks’ gestation; symbols above the upper broken line represent early neonatal deaths. The major causes of pregnancy loss in women with type 1 DM were major congenital malformations and complications of prematurity. In women with type 2 DM, the major causes were late intrauterine death and chorioamnionitis.²⁴ Copyright © 2007 American Diabetes Association. From *Diabetes Care*®, Vol. 30, 2007; 2603–2607. Modified with permission from The American Diabetes Association.

Almost all women with type 2 DM have other features of the metabolic syndrome; thus, it is no surprise that hypertension is common in pregnant women with type 2 DM. In our population, we assessed the prevalence, type, and impact of hypertension during pregnancy in 100 consecutive singleton pregnancies in women with type 2 DM and 100 in women with type 1 DM.⁴³ Nulliparity, poor glycemic control at presentation, higher blood pressure early in pregnancy, and not smoking were risk factors for hypertension of similar magnitude in both types of DM, and the overall incidence of hypertension in pregnancy was similar in both types (41% in type 2 DM vs 45% in type 1 DM). However, the distribution of subtypes of hypertension differed: women with type 2 DM had more chronic hypertension (diagnosed at <20 weeks’ gestation) but less preeclampsia than women with type 1 DM ($P = 0.028$), and of those with chronic hypertension, a higher proportion of women with type 1 DM developed superimposed preeclampsia. Hypertension in pregnancy was strongly associated with a number of adverse outcomes. However, the impact was less severe for women with type 2 DM than for women with type 1 DM for premature delivery ($P < 0.005$)

and admission to neonatal intensive care units ($P < 0.01$) because adverse outcomes were most strongly associated with preeclampsia, which was less prevalent in type 2 DM.⁴³

Congenital Abnormalities

Women with DM have a 2- to 8-fold increase in the rate of major congenital defects in the fetus.^{44,45} This association is thought to be secondary to the teratogenic effect of hyperglycemia in early pregnancy. The metabolic insult that causes malformations impacts most organ systems and has its effect before the 7th week of gestation—often before the women have even realized that they are pregnant.

Infants of mothers with DM are not prone to any particular pattern of structural defects, which supports a nonspecific effect of hyperglycemia on the development of a wide number of organs and systems. The range of major congenital malformations that occur is well documented. Cardiac defects are the most common and occur at approximately 3 to 4 times the rate reported for the general population. Diabetes has been particularly associated with cardiovascular and atrioventricular discordance, outflow-tract anoma-

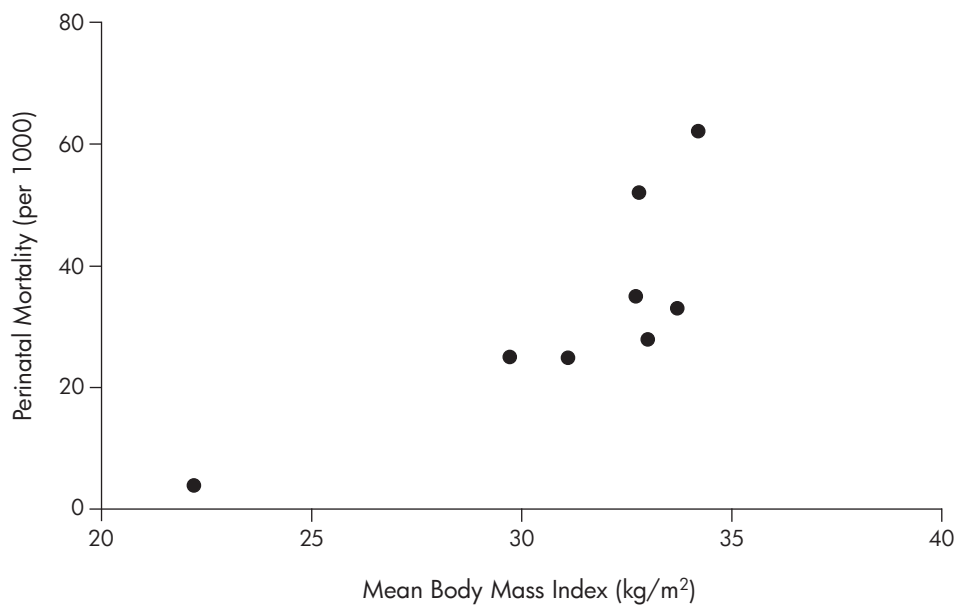


Figure 3. Relationship between maternal body mass index (before pregnancy or early in pregnancy) and perinatal mortality rate in studies that reported >100 pregnancies in women with type 2 diabetes mellitus.

lies associated with normally related great arteries and complete forms of atrioventricular septal defects. The association between DM and cardiovascular malformations is strongest among infants with multisystem anomalies (typically the VACTERL cluster—Vertebral anomalies, Anal atresia, Cardiac defect, Tracheo-Esophageal fistula, Renal abnormalities, and Limb abnormalities).⁴⁶ All-cause mortality of infants with cardiovascular malformations is greater among mothers with DM than among mothers without DM, reflecting their generally greater severity.⁴⁶ Abnormalities of the central nervous system and genitourinary tract are the next most prevalent, occurring at 3 to 4 times the rate in the general population. Limb and spinal defects are less prevalent but more specifically associated with DM. In particular, caudal (sacral) agenesis, which accounts for <5% of major anomalies in diabetic pregnancy, occurs ~50 times more often during pregnancy in women with DM than in women without DM.⁴⁷

Several studies that examined glycemic control and birth defects demonstrated a dose–response effect: the poorer the periconceptional blood glucose control, the greater was the risk of congenital defects. However, considerable uncertainty remains over the exact degree of this risk. A recent review that addressed this issue attempted to calculate the absolute risk of a major congenital anomaly for any given degree of glycemia.⁴⁸ The estimates were based on a total of only 117 major anomalies that occurred in ~2000 pregnancies in women with mainly type 1 DM. The relationship between early-presentation A1C values and the risk of major anomalies was hyperbolic—not linear, and the CIs for risk were wide. Thus, for an individual, it is difficult to quantify precisely the risk associated with any given A1C value.

The definition of major congenital anomalies that was used excluded those identified only by ultrasonography, thus excluding nonfatal but significant renal disorders such as renal dysplasia or unilateral renal agenesis, which are increasingly being recognized as common events in maternal DM.⁴⁹ We need a better understanding of the teratogenic action of hyperglycemia and when and how it should be assessed. In women with type 2 DM, the pattern and prevalence of anomalies is similar to those in women with type 1 DM, indicating that the underlying biologic process is the same in both types of DM.^{50,51}

The incidences of major congenital anomalies in women with newly recognized type 2 DM are the same as those in women with known type 2 DM and women with type 1 DM.^{51,52} In the remainder of the gestational diabetes population, congenital malformation rates are similar to those in the general population. There is a debate in the literature as to whether maternal obesity itself is associated with an increased risk of congenital anomalies.⁵³ This may be an artefact of unrecognized type 2 DM, but additional research on this topic is required.

Pregnancy losses resulting from severe congenital anomalies now account for a large proportion of total pregnancy losses, particularly in women with type 1 DM. The incidence of pregnancy loss due to congenital anomalies has proven hard to reduce. Prepregnancy counseling primarily aimed at improving periconceptional glycemic control has been shown to be effective at reducing the rate of major congenital anomalies, but the success of this approach requires that patients plan their pregnancies and attend counseling. Sadly, for many sociologic reasons, those with the poorest glycemic

control are also the least likely to be adherent to effective contraception and the most likely to have unplanned pregnancies. The problem of major congenital anomalies related to DM, therefore, is not easily solvable.

CONCLUSIONS

In women with type 1 DM, the perinatal mortality rate decreased substantially in most western countries by the early 1980s and has remained stable over the past 25 years. The decrease in perinatal mortality was achieved predominantly by a reduction in the number of late intrauterine deaths and stillbirths. Currently, the major causes of pregnancy loss in type 1 DM are major congenital anomalies and complications of prematurity. Reductions in rates of major congenital anomalies have been harder to achieve and maintain, and it is probably unrealistic, from both biologic and sociologic perspectives, to believe that these anomalies can be eliminated completely.

Pregnancy in type 2 DM has been recognized as a problem in developing countries since the late 1980s, but is now emerging as a significant problem in western countries, particularly in disadvantaged communities. Studies from some centers have suggested that the perinatal mortality rate may be higher in type 2 DM than in type 1 DM and that this excess loss is largely due to a high rate of intrauterine deaths and stillbirths or to chorioamnionitis. Factors other than glycemic control probably explain this phenomenon: in particular, women with type 2 DM tend to be older and more obese, and they come from disadvantaged communities—all risk factors for pregnancy loss. In some women, type 2 DM may be recognized for the first time during pregnancy: such pregnancies carry the same risks of pregnancy loss as those in women with established DM. Demographic changes in the prevalence of obesity indicate that the prevalence of type 2 DM in pregnancy will almost certainly increase.

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