Pregnancy and pre-existing diabetes: key concerns

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Women with pre-existing diabetes in pregnancy are at increased risk of fetal loss, fetal congenital anomaly and abnormal fetal growth. Obstetric complications are more likely and good peripartum care is essential. This article also considers preconceptual counselling which may minimize these risks.

Women with pre-existing diabetes are at increased risk of complications, both fetal and maternal. Fetal loss is increased at all stages of gestation, and the major congenital anomaly rate remains 2–8 times higher than in non-diabetics (Farrell et al, 2002) despite improved medical care. Diabetes also increases the rate of macrosomia (birth weight greater than 4 kg) with its associated risk of shoulder dystocia; paradoxically, women with longstanding diabetes or significant diabetic complications such as nephropathy or vasculopathy are more likely to have a growth-restricted infant than non-diabetics (Sibai et al, 2000). Pre-existing diabetes also increases the risk of obstetric complications such as pre-eclampsia, polyhydramnios and premature labour.

Given these wide-ranging and serious risks it is extremely important to provide accessible and comprehensive prepregnancy counselling, as the single best intervention for improving pregnancy outcome is good glycaemic control from conception right through to delivery.

PRECONCEPTUAL CARE

Management of pregnant diabetic women should ideally start before pregnancy. The prepregnancy clinic is an opportunity to establish a relationship between the woman, her partner and the multidisciplinary team members responsible for her care in her subsequent pregnancy. It enables those women with specific diabetic complications to be assessed. Presence of diabetic nephropathy can be assessed preconceptually by performing renal function biochemistry, blood pressure and estimation of proteinuria. This is an important element of prepregnancy care, as nephropathy associated with 3 g of urinary protein in 24 hours, serum creatinine greater than 130 mmol/litre and mean arterial pressure of greater than 107 mmHg are all independent predictors of poor perinatal outcome (Hare, 1994).

Similarly, background proliferative retinopathy can permanently deteriorate in pregnancy, and at booking is a predictor of adverse fetal outcome (Klein et al, 1988). Paradoxically, proliferative retinopathy can also deteriorate if glycaemic control is improved rapidly, which is often the case in early pregnancy. The preconception clinic therefore provides an opportunity for ophthalmic assessment and laser photocoagulation treatment. With improvements in the care received by women with diabetes, successful pregnancy outcome is achieved in those with pre-existing diabetes despite significant diabetic complications.

Many women are unaware that they are pregnant until they have 5–6 weeks' amenorrhoea, by which time organogenesis is well underway and almost complete. The benefits of improving glycaemic control at this point will have little impact on the risk of congenital anomalies. Suevo (1997) demonstrated a significant reduction in congenital anomaly rates in women receiving prepregnancy counselling. Prepregnancy counselling therefore affords an opportunity to discuss general health issues, glycaemic control and folic acid supplementation, which have been shown to reduce congenital anomaly rates.

To conclude, preconceptual counselling does improve pregnancy outcome and is cost effective. Although these benefits are well documented, attendance in UK clinics is around 25–35% (Dunne et al, 1999). This relatively low uptake may reflect social and cultural aspects of diabetic pregnancy but organizational problems with health provision for these women need to be considered.

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FETAL CONCERNS

Fetal loss

Pre-existing diabetes in pregnancy is associated with a perinatal mortality of approximately 2–4% (Reece and Homko, 1994). This has reduced substantially in recent years as a result of improvements in diabetic, obstetric and perinatal care. The perinatal mortality rate has now plateaued because the two major causes of fetal death, congenital anomalies and unexplained fetal distress, remain unchanged despite medical intervention. The incidence of stillbirth is greatest after 36 weeks' gestation, especially in diabetic pregnancies complicated by poor glycaemic control, fetal macrosomia, maternal vascular disease, ketoacidosis or pre-eclampsia. Several factors contribute to poor fetal outcome; these include chronic hypoxia, polycythaemia, lactic acidosis and cardiomyopathy. The fetus does not tolerate chronic hypoxia well if hyperglycaemia is also present. Therefore the macrosomic fetus of a mother with poorly controlled diabetes is at greatest risk and requires the closest antenatal surveillance in the third trimester.

Early pregnancy fetal loss is strongly associated with poor metabolic control. The Diabetes in Early Pregnancy Study (Mills et al, 1988) concluded that the incidence of early pregnancy loss in well-controlled diabetic pregnancies is the same as for non-diabetic controls. However, if poorly controlled (glycosylated haemoglobin (HbA_{1c}) greater than 12%) then a significant increase in the spontaneous miscarriage rate was seen.

TABLE 1.
Congenital malformations in offspring of diabetic mothers

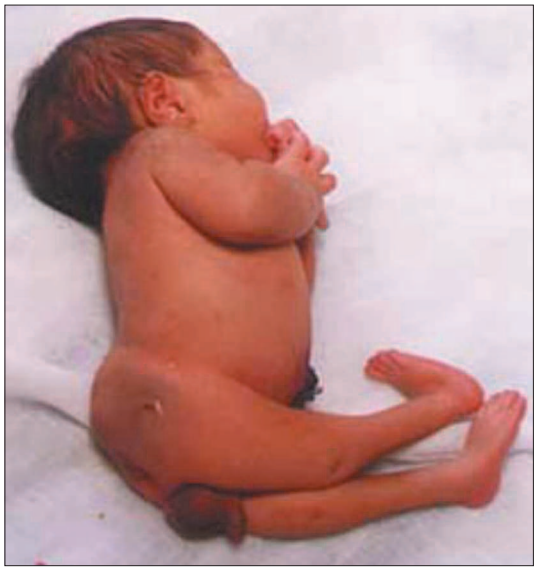
Central nervous system	Anencephaly
	Encephalocoele
	Meningomyelocoele
	Open spina bifida
	Hydrocephaly
	Holoprosencephaly
Cardiovascular	Transposition of the great vessels
	Atrial and ventricular septal defects
	Coarctation
	Hypoplastic left heart
	Two vessel cord
Urogenital	Potter syndrome (renal agenesis)
	Double ureter
	Polycystic kidneys
	Hypospadias
Gastrointestinal	Duodenal atresia
	Imperforate anus
	Tracheo-oesophageal fistula
Skeletal	Caudal regression syndrome

Congenital anomalies

Pregestational diabetes, whether type 1 or type 2, is associated with a 2–8-fold increase in the rate of major congenital defects in the fetus (Farrell et al, 2002). This equates to 5–10% of offspring of women with pre-existing diabetes. The risk factors for a major congenital anomaly include poor periconceptual control, diabetic vasculopathy and the duration of diabetes. The association between pre-existing diabetes and congenital anomalies is thought to be secondary to an insult that affects all organ systems and acts before the 7th week of gestation, i.e. before the completion of organogenesis. The causative insult is likely to be hyperglycaemia, as studies examining glycaemic control and birth defects have shown a dose response effect: the poorer the periconceptual control, the greater the risk of congenital defects (Suhonen et al, 2000).

The infants of diabetic mothers are not prone to any particular pattern of structural defects, which supports a non-specific effect of hyperglycaemia on the development of a wide range of organ systems (*Table 1*). Developmental abnormalities of the fetal heart are the commonest anomalies seen, especially septal defects and more complex lesions such as transposition of the great vessels (Farrell et al, 2002). The congenital anomaly characteristic of diabetic embryopathy is caudal regression syndrome, which is 600 times commoner in diabetic pregnancies (Suevo, 1997) (*Figure 1*).

Figure 1. An example of an infant with caudal regression syndrome.



Fetal growth

Despite improvements in perinatal mortality (Garner, 1995) among infants of diabetic mothers, the incidence of fetuses with excessive size and associated complications remains high. These infants may also be at risk of obesity and cardiovascular morbidity in later life (Plagemann et al, 1997).

Macrosomia can be defined as a birth weight of more than 4 kg or a birth weight greater than the 90th centile using population-specific growth curves (Kolderup et al, 1997). Using these definitions macrosomia can complicate up to 40% of pregestational diabetic pregnancies. Delivery of an infant weighing more than 4.5 kg occurs 10 times more often in diabetic pregnancy than non-diabetic (Spellacy et al, 1985).

Macrosomia is thought to be secondary to fetal hyperinsulinaemia, which results in increased fetal adiposity, muscle mass and organomegaly. The result is a disproportionate increase in trunk size compared with the fetal head (*Figure 2*), which is thought to be responsible for the increase in difficult vaginal delivery. The fetal hyperinsulinaemia is the result of maternal hyperglycaemia: placental transfer of maternal glucose but not maternal insulin results in fetal pancreatic islet cell hyperplasia and subsequent fetal hyperinsulinaemia (Vaughan, 1994). Thus achieving maternal normoglycaemia during pregnancy should reduce the incidence of macrosomia. However, despite good diabetic control, macrosomia rates of up to 40% are still seen. This shows that there are other factors predisposing to fetal macrosomia such as maternal obesity, maternal pregnancy weight gain, parity and genetic factors.

Accurate antenatal diagnosis of fetal macrosomia could permit optimal timing and route of delivery. This is important as shoulder dystocia, with its attendant risk of brachial plexus injury, may complicate up to 50% of vaginal deliveries of pre-existing diabetic pregnancies with birth weights around 4–4.5 kg (Landon, 2000). Brachial plexus injury occurs 18 times more frequently with delivery when maternal diabetes is present (Landon, 2000). With birth trauma in mind, ultrasonographic estimation of fetal size at term is frequently used in the management of diabetic pregnancy. The usually accepted error in the ultrasound fetal weight estimation is approximately 10%; thus an estimated fetal weight of 4000 g in reality may be only 3600 g or an estimated weight of 4500 g may in fact be 4950 g. This may explain why the prediction of significant shoulder dystocia using ultrasound has not been accurate enough to allow confident anticipation of the problem and its avoidance by elective caesarean section.

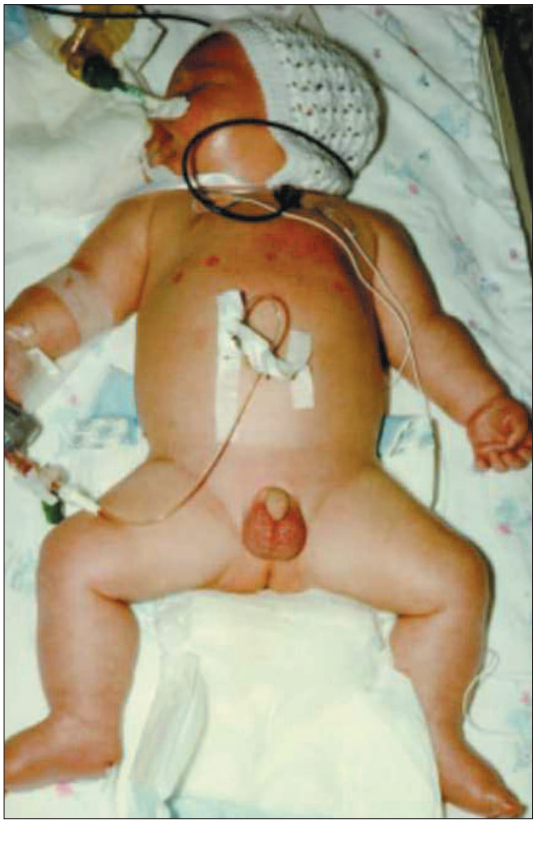
Although there is a great awareness of macrosomia, 20% of infants of diabetic mothers will exhibit growth restriction (Garner, 1995), especially those with prepregnancy nephropathy, vasculopathy and hypertension (Sibai et al, 2000). The mechanism for the restricted growth is unclear in women with pre-existing diabetes but may reflect reduced placental function from uterine vasculopathy and hypertension (Kitzmiller and Combs, 1993). Fetal growth restriction carries an increased risk of fetal death and fetal distress requiring operative intervention, and an associated risk of subsequent development of adult diabetes, coronary heart disease and hypertension (Hattersley and Tooke, 1999).

MATERNAL CONCERNS

Obstetric complications

Pre-eclampsia complicates around 14% of pregnancies of pre-existing diabetics compared with 5% of non-diabetic controls. The risk is directly related to severity and duration of diabetes and whether underlying nephropathy or prepregnancy hypertension exists (Garner, 1995). The risk does not appear to be related to glycaemic control during the pregnancy.

Figure 2. An example of a hyperinsulinaemic infant.



Maternal infections occur more frequently in diabetic pregnancy and are in part a result of poor metabolic control. Eighty per cent of diabetic pregnancies are complicated by at least one episode of infection, compared with 26% of non-diabetic pregnancies (Stamler et al, 1990). Pregnant women with diabetes have higher rates of wound and urogenital infections. The rate of postpartum infection is five times higher than in non-diabetic women, particularly post caesarean section endometritis and wound infection.

Polyhydramnios complicates approximately 18% of diabetic pregnancies. The reason for the excess liquor is unclear but is thought to result from fetal polyuria secondary to fetal hyperglycaemia. The importance of polyhydramnios is its association with preterm ruptured membranes, preterm labour and cord prolapse.

Preterm delivery occurs in up to 20% of diabetic pregnancies. The management of preterm labour is complicated by the potentially severe hyperglycaemic side effects of the beta-agonists used for tocolysis and the corticosteroids used to promote fetal lung maturity. The risk is ketoacidosis, a condition associated with a high perinatal mortality. A sliding insulin scale is usually required to maintain euglycaemia when preterm labour is being treated with beta-agonists and corticosteroids. Other tocolytic agents, particularly oxytocin antagonists like atosiban, do not have significant effects on glucose metabolism and therefore may reduce the risk of ketoacidosis.

Labour and delivery

With good glycaemic control and an otherwise uncomplicated pregnancy it should be possible to reach 39–40 weeks of gestation. Despite this, high rates of elective intervention exist, with high rates of induction of labour and elective caesarean section. Poorly controlled diabetics or those with diabetic complications may require earlier delivery despite the increased problems of prematurity. Choice of route of delivery for the diabetic patient remains controversial. It is dependent upon a number of factors including gestational age, obstetric history, estimated fetal weight, fetal wellbeing and maternal wish. Vaginal delivery is the aim, but despite this caesarean section rates of 50–60% are seen in the authors' department. This is thought to be the result of a higher rate of failed induction, macrosomia causing obstructed labour, and fetal distress. With the current trend of reduced induction rate with the spontaneous onset of labour where safe, a reduction in caesarean section rate may be seen. **HM**

KEY POINTS

- Prepregnancy diabetes is a risk factor for fetal congenital anomaly, especially cardiac defects.
- Both macrosomia and growth restriction are commoner in diabetic pregnancies than non-diabetic.
- Diabetic women are more likely to have polyhydramnios, pre-eclampsia and premature labour.
- Pregnancy loss is commoner at all stages of gestation in diabetics than non-diabetics.
- Optimal diabetic control can reduce the rate of all of these complications.
- Prepregnancy care is vital to optimize control and improve the chances of a successful pregnancy outcome.

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