

Diabetes in pregnancy

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1 Introduction

Perinatal mortality in pregnancy associated with diabetes has dropped tenfold in the last four decades, compared with a fourfold to fivefold drop in perinatal mortality overall. Nowadays, some specialist centers report perinatal mortality rates close to those of non-diabetic populations but, in general, the risk of perinatal loss for the average diabetic woman remains higher than for non-diabetics, even after adjustment for fetal malformation. Population surveys suggest that the outcome of pregnancy overall is poorer than what would be inferred from the literature.

A number of factors have played a part in this remarkable improvement. These include, among others: increasing acceptance by physicians of the importance of tight control of diabetes; the introduction of programs to achieve this control; the development of home glucose-monitoring to facilitate such programs; gradual trends towards prolongation of pregnancy; and advances in neonatal care.

Although there is general consensus on the adverse impact of overt diabetes in pregnancy, the significance and appropriate management of lesser degrees of hyperglycemia are still widely debated. Diabetes is a disturbance of multiple metabolic pathways rather than of glucose metabolism alone, although the effects on carbohydrate metabolism are the most apparent. Generally accepted criteria for a diagnosis of diabetes in the presence of symptoms (polyuria, poly-

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dipsia, ketoacidosis) are random venous plasma glucose levels greater than 11 mmol/l (200 mg/dl) or fasting levels of greater than 8 mmol/l (140 mg/dl).

Normal values for plasma glucose values are defined as less than 8 mmol/l on a random sample, and less than 6 mmol/l fasting. Values between the normal and those of diabetes are considered to be 'equivocal', and evaluation with a glucose challenge is recommended (e.g. 75 g taken orally after an overnight fast). Values over 11 mmol/l 2 h post-challenge are taken to be diagnostic of diabetes, and those between 8 and 11 mmol/l are termed 'impaired glucose tolerance'.

2 Prepregnancy counseling and assessment

Increasingly, women with diabetes wish to discuss the implications of pregnancy before they conceive, and this should be actively encouraged by all health-care professionals before each pregnancy. While preconception clinics may fulfil an important role, the provision of adequate preconceptional care and advice does not necessarily depend on such specialized clinics. All who care for diabetic women should be aware of, and prepared to discuss, the importance of appropriate contraception and timing of pregnancy, the significance of pregnancy to the diabetic woman, the risks to the fetus and neonate as well as to herself, the importance of tight control of the diabetes just before and during pregnancy, and the need for accurate estimation of the date of conception.

Since diabetes is a chronic and progressive disease, the advice may need to include a discussion of the fact that postponement of pregnancy until a later age may worsen the prognosis.

The risks to the fetus are significant. Diabetes is associated with an increased incidence of congenital anomalies, up to three times as great as for the infants of non-diabetic mothers. Although no information is available from randomized trials, cohort studies suggest that tight control of the diabetes immediately before conception can reduce this risk significantly.

Macrosomia is still more common in the infants of diabetic mothers than in those of non-diabetic mothers, even with the best diabetic control currently available. Diabetes is not typically associated with intra-uterine growth restriction, unless the diabetes is complicated by microvascular disease. Women with vascular complications of diabetes will need particularly careful counseling.

Nephropathy without significant hypertension and a normal serum creatinine is not associated with a poor fetal outcome. The prognosis worsens in the presence of hypertension or impaired renal function. Renal disease that does not cause symptoms in non-pregnant individuals can jeopardize pregnancy outcome in some women. Although the majority of women with renal disease do not experience a deterioration of renal function during pregnancy, some women do suffer significant deterioration that does not improve after delivery.

There is also concern about the effect of pregnancy on women with proliferative retinopathy. Pregnancy appears to be associated with a deterioration in the condition. Cohort studies comparing pregnant and non-pregnant women with diabetic retinopathy show, however, that visual acuity can be maintained with intensive laser treatment throughout pregnancy, and the prognosis is no worse than for the non-pregnant woman.

The risk of spontaneous preterm birth is not increased. The apparent excess of preterm births relates either to delivery for complications, especially hypertensive disorders, or to policies advocating elective preterm delivery. Preterm births can be minimized by a reconsideration of such policies.

Diabetic women contemplating pregnancy will be reassured to learn that there is no good evidence of any long-term adverse effects of their diabetes on the development or intelligence of their offspring, and that the risk of their children developing juvenile diabetes is in the order of 2% or less.

Young diabetic women should have easy access to family planning services at all points of contact with the health-care system, both before and between pregnancies.

3 General care during pregnancy

Diabetic pregnant women should be cared for by both obstetricians and physicians with special interest in this field. Ideally this might be carried out at joint clinical sessions but other local arrangements can deliver quality integrated care. Such arrangements facilitate efficient deployment of other health-care professionals, such as dietitians and specialist liaison midwives or nurses.

The first few weeks of pregnancy are a period of readjustment, and many women require re-education about their diabetes and its control. Rotation of insulin injection sites, the interaction of diet and exercise,

and the dietary requirements of pregnancy may be unfamiliar to many women. Specialist care in and for pregnancy should start as early as possible. Local organization should be such as to allow very rapid referral of diabetic women with suspected pregnancies. When the gestational age is in doubt, it should be estimated precisely by early ultrasound.

Hypoglycemia can be troublesome at this stage, and control of the diabetes may be difficult to achieve because of poor motivation, nausea and vomiting, or changes in the hormonal milieu. Considerable education is needed to resist over-treatment of impending hypoglycemic reactions. Glucose or sugar should be avoided; milk or a light snack, which can be repeated if necessary, are more appropriate. All diabetic women should be provided with glucagon for emergency situations.

In addition to routine prenatal assessment, obstetric care at this time should include assessment of renal function in diabetic women who have hypertension or proteinuria, and retinoscopy, particularly in women who have had diabetes for more than 10 years. This should be repeated once every trimester. Urine cultures should be repeated regularly in those with nephropathy. In view of the increased risk of malformation, detailed ultrasound is recommended. Additional expert fetal echocardiography is advisable given the high frequency of cardiac anomalies.

A diabetic woman without nephropathy or retinopathy, and with no other complications of pregnancy, usually experiences an uncomplicated second trimester. The educational and readjustment processes will hopefully be complete as far as possible and, unless there is a risk of compromised fetal growth or early pre-eclampsia, there is little need for intensive obstetric supervision at this time.

Women with associated hypertension may need to be followed closely and, if necessary, treated with hypotensive drugs. Serial assessment of renal function can be particularly useful in following these pregnancies.

4 Diabetic control

In the non-pregnant diabetic, intensive control using continuous subcutaneous insulin, or regimens with three or more injections daily, improves glycaemic control. Randomized trials have demonstrated that such regimens significantly reduce the risk of progression to

nephropathy and the long-term risk of retinopathy. In the short term, retinopathy may worsen and there is a trend towards more frequent severe hypoglycemic episodes. The incidence of diabetic ketoacidosis does not seem to be significantly higher using intermittent rather than continuous subcutaneous insulin regimens.

These findings may be relevant to pregnancy where intensive regimens are commonly used. The aim of diabetic control is to establish normoglycemia, both fasting and before and after meals. Blood glucose levels can be monitored effectively and controlled by the woman at home, provided that she has readily available advice and support, predominantly through telephone contact. The use of home, instead of hospital, glucose monitoring can significantly reduce the time the woman spends in hospital, without affecting pregnancy outcomes.

The dose and type of insulin needed may require careful and frequent adjustment. Insulin may have to be given more frequently than before pregnancy, often requiring three and, occasionally, four injections a day. Pumps for continuous subcutaneous infusion of insulin are expensive and complex to use. Trials have shown no benefits for continuous infusion over conventional insulin administration in terms of metabolic control, use of cesarean section, or adverse pregnancy outcome. Temporary worsening of retinopathy may occur using such regimens. Despite the importance of the subject, to date the benefits and drawbacks of tight control of diabetes in pregnancy have been assessed in only one randomized trial. This trial compared the effects of very tight control (aiming to keep blood sugar levels below 5.6 mmol/l), tight control (blood sugar levels between 5.6 and 6.7 mmol/l) and moderate control (blood sugar levels between 6.7 and 8.9 mmol/l).

Best results were obtained with tight, rather than either very tight or moderate control. Very tight control was associated with episodes of hypoglycemia, and conferred no benefits in other pregnancy outcomes compared to tight control. On the other hand, a policy of only moderate control, in which blood sugar levels were allowed to rise up to 8.9 mmol/l, is associated with a higher incidence of macrosomia, urinary tract infection, and cesarean section, and a trend towards an increase in hypertension, preterm labor, respiratory distress syndrome, and perinatal mortality.

This evidence tends to confirm the conclusion from observational studies that keeping blood sugars within a well-controlled range, between 5.6 and 6.7 mmol/l, is better than either too strict or too lenient a regimen.

5 Obstetric care

As in any antenatal care program, much attention is focused on the early detection of gestational hypertension and in the identification of problems with fetal growth.

The incidence of pregnancy-induced hypertension is increased in pregnancies of diabetic women and it may occur earlier. Particularly at risk are those with pre-existing hypertension, those with nephropathy, and those with microvascular disease. There are currently no good predictors of pregnancy-induced hypertension and preventive therapy is untested in this population.

Problems with fetal growth divide into two groups – growth failure and macrosomia. Women with hypertension, nephropathy, or microvascular disease are at more risk of the complications of fetal growth failure. Women with moderate or poor diabetic control are at most risk of fetal macrosomia. Pregnancies in diabetic women should have additional ultrasound surveillance of growth in the late second and third trimester. Absolute size is not a good predictor of outcome and attention should be paid to growth velocity. As in the non-diabetic population, the precise value of screening for growth problems is not established.

Macrosomia can be assessed by ultrasound, but most formulae utilized to calculate fetal weight perform poorly in the larger fetus, and such estimates should be interpreted with caution.

Because of the increased perinatal mortality, most pregnancies are subjected to serial antepartum fetal assessment. Various regimens have been described, but to date there are no randomized trials addressing which is the most effective technique. Most studies are of a prospective interventional design and claims of improved outcome for any particular regimen of antepartum fetal surveillance must be interpreted within these limits.

6 Care in labor and delivery

Elective preterm delivery has long been one of the classical management strategies applied in diabetic pregnancy, based on an observation in one influential study that the stillbirth rate rose above the neonatal death rate after 36 weeks of gestation. Other cohort studies have shown, however, that this conclusion was flawed and that pre-emptive delivery

does not result in an improvement in perinatal mortality. There is no valid reason to terminate an otherwise uncomplicated pregnancy in a diabetic woman before the expected date of delivery.

Assessment of pulmonary maturity has, until recently, been considered a prerequisite for planned delivery of the diabetic woman. There is increasing evidence to suggest that in well-controlled diabetics, the lecithin/sphingomyelin ratio reflects the same degree of pulmonary surfactant production and, therefore, the same risk of hyaline membrane disease, as in non-diabetics. The infants of poorly controlled diabetic mothers may have a disturbance in the development of pulmonary maturity. The problem becomes less important as delivery is delayed to a later gestational age, and as elective cesarean section is used less frequently.

Although cesarean section in diabetic women, as in all women, should only be performed for obstetrical indications, cesarean section rates tend to be much higher for diabetic women than for the general population. There seems to be little justification for this, except that the median birthweight for gestation is higher in diabetic pregnancies.

As blood glucose levels can be controlled confidently throughout labor with a glucose infusion with insulin added, the only increased hazard of vaginal delivery in diabetic women is that of birth trauma to the infant, particularly shoulder dystocia and brachial plexus injury secondary to macrosomia. In comparative studies, these risks appear unexpectedly higher in infants of diabetic mothers compared with similarly sized infants of non-diabetic mothers. The management of the second stage of labor in a diabetic pregnancy with suspected macrosomia should reflect this knowledge and appropriately skilled senior staff should be readily available.

7 Care after birth

After birth and delivery of the placenta, insulin requirements should be recalibrated according to blood glucose levels. All women will require significantly less insulin than during pregnancy.

Breastfeeding should be encouraged, although there must be an awareness of the increased caloric intake sometimes needed to support this.

Family planning is an important consideration. There is no contraindication to the use of low-dose oral contraceptives, particularly in

young, non-obese, non-hypertensive, non-smoking diabetics. The development of headaches or hypertension is an indication to change to alternative methods.

Intra-uterine contraceptive devices have, until recently, been a reasonable alternative, but concern over their effectiveness is making it less acceptable; barrier methods provide an acceptable second choice.

For all women, the risk of future pregnancy must be carefully weighed against the risk of the proposed method of contraception. Women with nephropathy or retinopathy should be counseled carefully about limiting family size.

Sterilization, if requested, is better not carried out at the time of cesarean section if this can be avoided, in view of the increased risk of still undiagnosed cardiac malformation in the newborn. The procedure can easily be performed by laparoscopy within the next few months.

8 Conclusions

Diabetic women embarking on pregnancy demonstrate a deep commitment to achieving a normal outcome. This involves much disruption of an already complex lifestyle. Their care must reflect this and should be individualized, so that disruption will be minimized and care tailored to meet the circumstances of each woman.

There is considerable evidence to suggest that pregnancy in diabetic women should be managed with fewer obstetric interventions than are currently practised. Specialized care and collaboration among various disciplines will achieve the best results, but good perinatal outcome is not confined to tertiary-care centers. Many diabetic women can be treated as normal pregnant women, with the one major addition of careful control of blood glucose levels. Tight, rather than either very tight or moderate control is required.

Allowing pregnancy to continue at least until the expected date of delivery, associated with a decreased need to assess pulmonary maturity and more judicious use of cesarean section, may allow pregnant women with diabetes to feel more like their non-diabetic counterparts.

Much has been achieved in improving the care for, and the outcome of, pregnancies in diabetic women without resort to randomized clinical trials. The lack of controlled studies, however, has resulted in a blurring of the contributions made by the various components of care, and in doubts about the utility of some. The need continues for well-designed trials to assess the value both of current treatments and

of suggestions for their improvement. In addition, better survey data on the diabetic population are still needed, as data that refer only to women who attend specialist centers can be seriously misleading. Population based survey data may highlight deficiencies in the system of care and lead to improvements.

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