SPECIAL ARTICLE

PREGNANCY AND DIABETES

Y T Tan

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Gestational diabetes is defined as carbohydrate intolerance of variable severity with its onset or first recognition during pregnancy[1]. Some of these gestational women may have no symptoms of the pregestational diabetes which was undetected. Pregnancy itself is a diabetogenic state, whether the woman has pre-existing diabetes or becomes a diabetic for the first time in pregnancy. The demand for insulin increases markedly during pregnancy, especially in the later months. The foetus responds by continually adapting to this abnormal intrauterine environment resulting in structural and functional changes in the foetal islet beta cells. Subsequent inappropriate insulin secretion may result in the appearance of diabetes in the offspring of severe maternal diabetes, as demonstrated in an animal experimental model[2].

Epidemiological evidence supports the "fuel-mediated teratogenesis" hypothesis that foetal development is compromised during a diabetic pregnancy[3]. The offspring of diabetic pregnancies have been noted to be more obese and more glucose intolerant than controls[4]. A number of studies have suggested that the offspring's risk of developing non-insulin dependent-diabetes (NIDDM) is higher if the affected parent is the mother[5].

Because poor maternal nutritional status compromises pregnancy outcome and results in an increased incidence of babies of low birth weight, the pregnant woman with diabetes needs to have adequate nutrition, gain weight appropriately and maintain normoglycaemia throughout pregnancy. Hales observed that offspring with the lowest birth weights and weights at one year, were more likely to develop glucose intolerance or diabetes in middle age, suggesting that foetal adaptation to subnutrition and deprivation is associated with failure of development of pancreatic beta cells[6]. This hypothesis offers an alternative non-genetic explanation of family transmission of diabetes.

To optimise foetal growth and development, pregestational diabetic women are counselled to plan their pregnancies. However, one study revealed that only about one-third of women with established diabetes received pre-conception care[7]. The women with previous pregnancies (and particularly those with previous adverse outcomes) were no more likely to seek pre-conception care during subsequent pregnancies.

A leading cause of perinatal morbidity is the incidence of congenital anomalies occurring in 4% - 12% of infants of diabetic mothers. These anomalies are formed early in pregnancy by 5 to 8 weeks gestation, a time when few women seek antenatal care. The combined risk of congenital anomalies and spontaneous abortions in poorly controlled diabetes in early pregnancy can approach 65%[8]. Most of the congenital anomalies are of cardiac, neural tube, or skeletal origin, and are often multiple, severe and more fatal than in the general population. Ketoacidosis occurring in diabetic pregnancy as a result of severe insulin insufficiency predisposes to a higher risk of foetal loss.

The paper by Chia et al[9] on the obstetric outcome of 23 pregestational diabetic pregnancies revealed a higher incidence of congenital malformations and mortality in infants of diabetic mothers who booked late for antenatal care and whose glycaemic control was suboptimal. This study serves to reemphasise the important role of the prepregnancy clinic and the team approach to provide comprehensive care to women with diabetes and their partners. Public and patient education programmes could be used to encourage the diabetic woman to take a responsible and active role in the team management of her pregnancy.

Foetal macrosomia is a complication of maternal diabetes. Maternal hyperglycaemia increases the risk of macrosomia, both trauma and neonatal hypoglycaemia. Recent evidence indicates that maternal blood glucose levels correlate positively with neonatal weight, independent of other factors including maternal height, BMI and parity. Combs found that macrosomia occurred in 29% of 111 pregnant diabetic women[10]. Macrosomia was associated with higher postprandial glucose levels up to 32 weeks gestation and lower insulin doses from 29 to 36 weeks gestation. Because macrosomia was related to postprandial glucose and not to fasting glucose, the authors concluded that postprandial glucose measurements should be a part of routine care for diabetes in pregnancy. A separate study reported that macrosomia is related to 1-hour postprandial glucose levels in the third trimester and not to fasting glucose levels[11]. Lin et al found that the risk of macrosomia was reduced if intensive glycaemic control was started before 32 weeks gestation but not if it was started after that date[12]. Again the benefits of early glycaemic stabilisation with insulin before conception need to be conveyed to all pregestational diabetic women for a favourable outcome.

Other authors have noted that macrosomia occurs even when normoglycaemia is maintained and have suggested that other non-glucose fuels like amino-acids may be responsible[13]. Schwartz's study noted that 10% to 27% of his diabetic groups had macrosomia not related to maternal mass, but correlated significantly with umbilical total insulin, free insulin and C-peptide, and was mainly independent of glycated haemoglobin (HbA1c)[14]. Excessive foetal growth is secondary to foetal hyperinsulinaemia caused by disturbed metabolic control of the diabetes in the mother, but does not entirely explain its occurrence in the presence of maternal normoglycaemia.

The HbA1c value reflects an intergration of ambient blood glucose levels over a period of 4 to 6 weeks before its measurement. Its level has been directly correlated with the increased incidence of congenital anomalies in infants of diabetic mothers[15]. It has been particularly useful in the assessment of the degree of diabetes control in the critical early weeks of pregnancy. The HbA1c level obtained during the first trimester may be used to counsel diabetic women regarding the risk of congenital anomalies. Miller found 22% malformed infants in 58 patients with elevated HbA1c levels, in contrast to 3.4% in 58 women with HbA1c in the normal range[16].

Department of Endocrinology
Singapore General Hospital
Outram Road
Singapore 169608

Y T Tan, MBBS, MRACP, FAMS
Senior Consultant

The levels of glycated haemoglobin and glycated serum proteins (fructosamine) vary with the different stages of pregnancy and are lower compared to values in the non-pregnant state[17]. Increased erythropoiesis during pregnancy accounts for the lower HbA1c and a fall in the serum albumin and an alteration in the albumin:globulin ratio causes the fall in serum fructosamine.

The second paper by Loke et al attempts to define a reference range for glycated haemoglobin in the local population, and noted ethnic differences. A nadir was noted at 21 to 24 weeks. Morris also found a nadir at 23 to 26 weeks gestation, and that both glycated haemoglobin and fructosamine were elevated in early pregnancy in those women who ultimately developed gestational diabetes[18]. In a study of 99 pregnant women, Thai et al found that fructosamine levels in pregnant women with normal glucose tolerance were not statistically different from those with gestational diabetes[19]. Metabolic changes modulate the glycation process. Fructosamine values decrease with increasing albumin excretion, while HbA1c values remain unchanged. Furthermore, fructosamine concentrations were significantly lower in Type 2 diabetic patients (NIDDM) than in IDDM, while HbA1c concentrations did not differ in the two groups[20]. Because of these variations, both HbA1c and serum fructosamine have not been recommended for the diagnosis of gestational diabetes.

It has been estimated that diabetes complicates 2% to 3% of all pregnancies, and about 90% of these are gestational diabetes. A pilot study of 145 pregnant women who were screened with 75 gm OGTT revealed an incidence 13.1% of gestational diabetes, with an excess of Malay and Indian patients[21]. With the increasing prevalence of diabetes in Singapore, and an increasing number of older women becoming pregnant, both pregestational and gestational diabetes will require early detection and prepregnancy counselling, well-organised antenatal supervision and meticulous glycaemic control throughout the pregnancy.

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