

MANAGEMENT OF DIABETES MELLITUS IN PREGNANCY

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ABSTRACT

Diabetes is a common problem in pregnancy and the incidence depends on the racial predisposition and geographical distribution where the reports originate.

Despite improvement in perinatal care, many serious clinical problems are still associated with diabetes during pregnancy. The overall strategy of management includes early identification of diabetes during pregnancy, combined management to achieve optimal glucose control with dietary manipulation and insulin, maternal and fetal monitoring during the antenatal period and determination of the delivery time. Intensive intrapartum monitoring and neonatal care at delivery and thereafter are also essential. The outlook for the newborn of the diabetic mother has changed dramatically in recent years and both perinatal mortality and morbidity rate have declined as a result of pre-pregnancy preparation and meticulous control of maternal blood glucose throughout pregnancy.

Successful pregnancy outcome depends on the cooperation of the patient, the obstetrician, the physician, the neonatologist and the health educator.

Keywords: Diabetes in pregnancy, gestational diabetes, dietary manipulation, insulin therapy, infants of diabetic mothers.

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INTRODUCTION

Diabetes in pregnancy continues to represent a therapeutic challenge to obstetricians, physicians, neonatologists, patients and other health care providers in spite of spectacular achievements in the past 40 years. Prior to the discovery of insulin as a therapeutic modality for patients with diabetes mellitus, most insulin dependent diabetic patients did not live to reproductive age. If they did, the result of pregnancy was disastrous with a maternal mortality of as high as 50% and a perinatal mortality of 60% (1-3). With improvement in the management of diabetes and its complications, maternal mortality as a result of diabetes is rare and perinatal mortality in the well controlled patient has fallen to almost identical to that of the non-diabetic population.

The incidence of diabetes complicating pregnancy is reported to range between 0.4 to 29% depending on the population studied. In Singapore, the incidence is reported to be between 1.11% to 13.3% (4). The incidence is increasing and more diabetic women are now prepared to embark on pregnancy as they recognize that it is safe for them to do so and that the outcome is generally a happy one.

EFFECTS OF PREGNANCY ON DIABETES AND DIABETES ON PREGNANCY

Pregnancy alters maternal metabolism by exerting a diabetogenic effect. Insulin antagonist hormones, for example human placental lactogen, progesterone, prolactin and cortisol are believed to be responsible for this effect.(5-8). The diabetogenic effects of pregnancy are exaggerated in the established diabetics and control of diabetes becomes more difficult.

Pregnancy in diabetics is associated with an increase in both diabetic and pregnancy related complications. These complications include an increase incidence of ketoacidosis, progression of vasculopathy, pre-eclampsia, urinary and genital tract infection, intrauterine growth retardation, macrosomia, polyhydramnios and sudden intra-uterine death. The newborns are likely to suffer birth trauma because of the macrosomia, neonatal hypoglycaemia, respiratory distress syndrome, hypocalcemia and congenital abnormalities.

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Two types of diabetes are encountered during pregnancy

1. Pre-existing diabetes
 - both type I and II.
2. Gestational diabetes
 - defined as carbohydrate intolerance of variable severity with onset or first recognition during the present pregnancy. The definition applies irrespective of whether or not insulin is used for treatment or the condition persists after pregnancy. It does not exclude the possibility that the glucose intolerance may have antedated the pregnancy (9).

STRATEGIES TO MANAGEMENT

Optimal management of diabetes in pregnancy involves:

1. Control of diabetes before conception in established diabetics.
2. Early detection of gestational diabetes.
3. Standard team management in stabilization of diabetes as soon as pregnancy is diagnosed and maintenance of euglycemia throughout pregnancy.
4. Detection and early treatment of diabetic related complications.
5. Re-inforce the importance of blood sugar control throughout pregnancy and motivate all patients to actively participate in their own management.
6. Close antenatal maternal and fetal surveillance to detect pregnancy associated complications early.
7. Determine optimal timing of delivery.
8. Intensive labour and postpartum monitoring.
9. Care of the infant of the diabetic mother.
10. Provide pre-conceptional/contraceptive advice to both established and gestational diabetics.

1. Control of diabetes before conception in established diabetics.

Clinical and laboratory data suggest that metabolic control in the first trimester of pregnancy, and in particular during the first seven weeks of gestation, is critical to normal embryogenesis. Clinical efforts toward pregnancy management need therefore be directed to the prepregnant period. The role of the physician and the primary health care provider is of utmost importance since they are most likely to be the first doctor that the patients will seek advice from regarding pregnancy. Metabolic control should be achieved using insulin and patients on oral hypoglycaemics should be converted to insulin prior to pregnancy.

There is no convincing evidence that oral hypoglycaemic agents are teratogenic but in general, strict control is difficult to achieve with oral hypoglycaemic drugs and insulin is preferable. The other problem associated with the use of long acting oral hypoglycaemics is its effect on the neonate causing prolonged hypoglycaemia.

2. Early detection of gestational diabetes.

Early detection affects outcome of the pregnancy. Perinatal mortality rate for gestational diabetes is similar to those in the general population provided that the condition is diagnosed early and the patient is treated promptly. Untreated gestational diabetes is associated with similar foetal and neonatal morbidity that are reported with overt diabetics.

All patients with historical and clinical factors traditionally employed to identify patients at high risk of developing gestational diabetes should have an oral glucose tolerance test (OGTT). High risk factors are as follows:

Personal factors:

- a. History of diabetes in first degree relatives.
- b. Maternal obesity, defined as >20% of ideal weight for height.
- c. Elderly (>35 years).
- d. Ingestion of drugs which are known to produce carbohydrate intolerance eg. corticosteroids, beta sympathomimetic drugs etc.
- e. Symptoms of diabetes.

Factors arising from previous pregnancies:

- a. Previous babies with birth weight 4kg or above or 2kg or below.
- b. Previous unexplained perinatal losses.
- c. History of two or more consecutive spontaneous abortions immediately prior to present pregnancy.
- d. History of gestational diabetes in previous pregnancy.
- e. Previous baby with gross congenital malformations.

Factors arising from present pregnancy:

- a. Glycosuria.
- b. Acute polyhydramnios.
- c. Big foetus.
- d. Recurrent genital tract infection.

Universal screening of all pregnant women has been advocated (10). Screening methods include random blood sugar, glucose challenge test, glycosylated haemoglobin and fructosamine (11-14). It is hoped that the ideal screening test which is specific and sensitive as well as simple will be established in the near future.

The diagnosis of diabetes is established by the WHO criteria when using the 75g OGTT. The diagnostic criteria are, a venous fasting plasma glucose of 7.8 mmol/l (140mg%) or more and/or a 2 hours level equal to or more than 11 mmol/l (200mg%). A person is diagnosed to have impaired glucose tolerance if her two hour venous plasma glucose level is between 7.8 mmol/l (140mg%) and 11.1 mmol/l (200mg%).

If the first OGTT is performed before the third trimester and is normal, it is repeated is between 27-31 weeks of gestation (15).

3. Stabilization of diabetes and maintenance of euglycemia throughout pregnancy.

Women with established diabetes and gestational diabetes should be considered at high risk and be referred immediately for specialised care and control of blood sugar. They are usually admitted to the hospital on the first antenatal visit for assessment, initiation of treatment and readjustment of insulin dosage.

A complete physical examination is carried out by the physician including fundoscopy to detect diabetic complications.

Laboratory investigations include a full blood count, serum creatinine, glycosylated haemoglobin (HbA1c), 24 hours blood sugar profile (BSP) which consists of plasma glucose assessment before and after breakfast, lunch and dinner as well as at 10pm. Urine is examined for ketones, microscopy and sent for culture. Creatinine clearance and total urinary protein is carried out in established diabetics and when indicated in gestational

diabetics. Ultrasound scanning for dating should be performed at the first visit and repeated between 18 and 20 weeks gestation to screen for foetal anomaly.

Diet manipulation is the mainstay of therapy in gestational diabetes. All patients are put on a caloric restriction diet and the total daily requirement calculated according to ideal body weight and the life style of the patient. This usually amounts to 1,500 kcal in the first trimester and 1,800 kcal in the second and third trimester in our population. The diet should contain at least 60% carbohydrate and 75g protein.

A meal plan is developed for each individual in consultation with the dietitian. The important aspects of this meal plan are that it must be simple to follow and provide the balanced nutrients required in pregnancy in spite of caloric restriction. It should also take into consideration the ethnic and cultural habits of our different races. Inflexibility in the plan is bound to meet with non-compliance.

To avoid sudden swings in blood sugar level, the patient is advised to take small frequent meals and snacks. High fibre carbohydrate dampens the glycaemic swings usually induced by carbohydrate ingestion and is also advocated. The high fibre has also been shown to improve glucose tolerance in gestational diabetic patients (16).

Insulin therapy will be started or adjusted based on the BSP. An arbitrary level of fasting venous plasma glucose level of between 4.5 mmol/l – 5.6 mmol/l (80mg%-100mg%) and a two hours postprandial sugar (2HPPS) level of between 5.5 mmol/l – 6.7 mmol/l (100mg%-120mg%) is considered optimal (17).

This can usually be achieved by using combinations of short-acting and intermediate acting insulin. Continuous subcutaneous insulin infusion has no obvious advantage over the conventional three or four injections a day. Malfunction of the pump may lead to rapid onset of ketoacidosis with a 50% chance of intrauterine death in established diabetics.

The use of prophylactic insulin regardless of satisfactory blood sugar profile in gestational diabetic patients is shown to reduce the incidence of babies over 4,000gm, need for operative delivery and birth trauma (18). There is also the suggestion that there may be a long term preventive benefit from insulin treatment in the high risk subset of women with gestational diabetes (19).

In our practice, prophylactic insulin is given to patients with a 2 hours post oral 75gm glucose load, blood sugar value of 8.9 mmol/l (160mg%) or higher, those with bad obstetric history and those with evidence of complications referable to diabetes in spite of a satisfactory blood sugar profile.

Insulin requirement increases with progress of pregnancy and sugar control must be assessed throughout pregnancy and insulin dosage adjusted when required. The aim of close monitoring is to prevent hyperglycaemia as well as hypoglycaemia.

4. Detection of diabetic complications.

The diabetic woman with established vascular disease is at a substantial risk during pregnancy. Early detection of the complication and appropriate management will result in better outcome.

Approximately 10% of pregnant diabetics demonstrate some evidence of nephropathy. The presence of

nephropathy compounds the risk to mother and foetus. As recently as 1977, prognosis for pregnancies complicated by diabetic nephropathy was so poor that Pederson suggested that these pregnancies be discouraged and terminated. More recent studies have shown better outcome of pregnancy and recommended that pregnancy is not necessarily contraindicated except in the very severe cases (20, 21).

Pregnancy in patients with nephropathy is associated with a progressively worsening of proteinuria, hypertension, anaemia and polyhydramnios. Whether pregnancy worsens long term renal function is controversial. When nephropathy is not detected during early pregnancy, the condition will be difficult to distinguish from pre-eclampsia to which the pregnant diabetic is more prone. Morbidity in the foetus is usually the result of premature delivery and its associated problem.

The influence of pregnancy on the development of retinopathy is unsettled. Many authors believe that there is usually a reversible progression of the condition during pregnancy. The major determinants of the rate of progression of retinopathy are the duration of diabetes and the severity of background retinopathy at the onset of pregnancy. Careful observation and prompt treatment with laser photocoagulation prevents permanent retinal damage as without treatment, the progression is likely to result in severe visual deterioration and blindness.

Retinopathy does not appear per se to represent an increased risk to the foetus. Incidence of respiratory distress syndrome may be increased as a result of early delivery. Prognosis for the foetus is generally good.

There is an increased incidence of myocardial infarction in patients with diabetes. From the little information regarding pregnancy in patients with diabetic cardiomyopathy, the prognosis appears poor. In a review of 12 cases by Silfen, a maternal mortality rate of 67% was noted when myocardial infarction occurred in the pregnant diabetic patient (22).

5. Education.

Health education is an integral part of the management of diabetic pregnancy. Patients must be informed of the short and long term implications of diabetes on their pregnancies, the foetuses and the neonates. They must be motivated to be part of the team managing the disease. The patients and their relatives are taught the technique of self injection of insulin and blood glucose testing using either visual assessment or the glucometer. They should be advised to monitor their blood glucose once or twice a week depending on the severity of the condition.

In the past, frequent hospitalisation had been required to achieve adequate blood sugar control especially during the third trimester. With the introduction of home glucose monitoring, this period has been reduced and patients are now usually admitted only when home glucose monitoring showed unsatisfactory readings or when complications are detected.

6. Detection of complications associated with pregnancy.

Diabetic pregnancies are associated with an increased incidence of pregnancy complications like genital and urinary tract infection, pre-eclampsia, intrauterine growth retardation, macrosomia, polyhydramnios, preterm labour

and sudden intrauterine death. This is especially true in the poorly controlled diabetic. Pregnancy complications should be looked for at frequent antenatal visits in a joint clinic.

At each visit a 2 hour post prandial sugar is assessed and urine is tested for protein and ketones. HbA1c is checked at six weekly intervals or more frequently if the diabetes is not optimally controlled. Ultrasound scanning is repeated at 28 weeks gestation and at four weekly intervals thereafter to assess the growth of the foetus and to detect intrauterine growth retardation, foetal macrosomia and other complications.

Cardiotocographic (CTG) tracing is done during every visit after the thirty-sixth week.

7. Timing of delivery.

The exact timing depends on the type and severity of the diabetes as well as the absence or presence of any associated obstetric complications. For the purpose of timing of delivery, patients are generally divided into three groups.

Group A consists of patients with gestational diabetes, Group B are patients with established diabetes who have no vascular complication and Group C includes established diabetics with vascular complications.

Generally, in patients whose control is satisfactory and without obstetric complication, delivery is carried out at the completion of 38 weeks gestation in group C, completion of 39 weeks gestation in Group B and at completion of 40 weeks gestation in group A.

When diabetic control is poor and/or in the presence of obstetric complication, the labour may be induced earlier. The optimal time of delivery is usually decided on jointly by the obstetrician and the neonatologist.

8. Management of labour and the postnatal period.

Diabetes per se is not an indication for Caesarean section (CS) and vaginal delivery is aimed for. Elective CS is required from time to time for obstetric indications. Occasionally, extenuating factors such as age, and previous subfertility may influence the decision on the mode of delivery.

Cervical assessment is carried out prior to induction of labour and the cervix is scored according to the modified Bishop's scoring system. If the cervical score is less than five, cervical priming will be done.

Spontaneous and induced labours are managed actively. Blood sugar control as well as foetal wellbeing is closely monitored throughout labour. Insulin is given according to blood sugar value. Progress of labour is reviewed at frequent intervals. If the progress of labour is unsatisfactory, CS should be considered.

The insulin requirement falls rapidly after delivery and the dose of insulin should be adjusted according to blood sugar values in established diabetics. They will continue with their diabetic diet with adjustment made now for lactation. They will be referred to their physician for follow-up.

Insulin therapy is stopped and normal diet is resumed in patients with gestational diabetes.

A number of investigators have reported a high incidence of overt diabetes diagnosed immediately after pregnancy complicated by gestational diabetes. This raises the possibility that a significant number of such women had undiagnosed pre-pregnancy diabetes. An OGTT should be done six weeks after delivery for all gestational diabetic patients. If the OGTT is abnormal,

they should be referred to and followed-up at the Medical Out-patient Clinic.

9. Care of the infant of the diabetic mother.

All babies of diabetic mothers should be seen by the neonatologist at birth. Complications of infant of diabetic mothers are looked for and treated promptly.

The typical overweight, plethoric infant of the diabetic mother with rounded face, buried eyes, abundant hair and organomegaly is rare. Milder degrees of hypoglycaemia, respiratory distress syndrome, metabolic disturbance, polycythaemia and jaundice however are still frequent.

Intensive antenatal care and good diabetic control during pregnancy reduces the severity of most complications of the newborns of diabetic mothers, but does not solve all the problems. Pre-pregnancy counselling aims to reduce further perinatal morbidity and mortality.

10. Pre-pregnancy counselling and contraception.

As losses from stillbirths, intrauterine deaths and respiratory distress syndrome decrease, it becomes increasingly apparent that there is a large excess of perinatal mortality as a result of congenital abnormality among the infants of diabetic mothers. The abnormalities are severe, multiple and often lethal. Abnormalities associated with diabetes is shown to occur before the seventh week of gestational life (23) and two factors are found to be significantly associated with major congenital malformations, preexisting vasculopathy and poor glycaemic control (24). If we are to prevent diabetes associated abnormalities, pre-conceptual assessment and diabetic control is clearly necessary.

The chances of spontaneous abortion is also increased in poorly controlled diabetics making diabetic control prior to pregnancy beneficial (25).

Patients with retinopathy at the beginning of pregnancy are at risk of visual deterioration and blindness. Their retinopathy should be treated before conception.

Pregnancy should be discouraged in patients with long standing diabetes associated with serious renal impairment and ischaemic heart disease. They have a poor chance of delivering a live baby and in the case of patients with ischaemic heart disease, their life may be placed at unacceptable risk.

There is increasing evidence to show that the occurrence of gestational diabetes herald future development of frank diabetes in later life. Routine check ups are recommended in these women to detect onset of diabetes early. Maintenance of a healthy life style and ideal body weight will delay or prevent the onset of diabetes.

Contraception is required for family spacing, pre-pregnancy preparation and in patients in whom pregnancy should not be undertaken.

Diabetes is not an absolute contraindication to the use of combined oral contraceptive pills although adjustment of insulin dosage may be required in some cases. There are reports of increased risk of ischaemic heart diseases and cerebrovascular accidents in young insulin dependent diabetics. It will be prudent to restrict the combined oral contraceptive pills to patients without serious complication or additional risk factors like smoking, hypertension and strong family history of vascular diseases.

Progestogen-only oral contraceptive and injectables are associated with irregular uterine bleeding and have a high failure rate.

Intra-uterine contraceptive devices do not cause detrimental metabolic effects and the success rate does not depend on patient compliance. The main worry is the risk of infection to which the diabetics are more prone.

Barrier contraceptives are suitable in well motivated couples. Both the diaphragm and sheath are effective when used correctly. They carry neither local nor metabolic side effects.

The Billing's method which is based on the observation of cervical mucus to determine the timing of ovulation and thus, safe or unsafe period, is not acceptable to most as it requires a great deal of motivation and long period of abstinence.

Sterilization should be considered in women who have completed their family. It is a permanent form of contraception.

The choice of contraceptive methods varies from couple to couple. The methods should be discussed with the couple and the choice be individualised.

CONCLUSION

The management of diabetes in pregnancy has improved by leaps and bounds through the years. Maternal mortality as a result of pregnancy in the diabetic is now rare. In neglected cases however, the morbidity associated with these pregnancies is still substantial and results in a disproportionate number of adverse pregnancy outcomes.

Early diagnosis and strict control of diabetes in a setting which offers a combined approach by the physician, obstetrician and neonatologist together with improvement in foetal, maternal and neonatal monitoring has resulted in improved pregnancy outcome. It has made motherhood a reality to many diabetic women.

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