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BRIEF ARTICLE

GESTATIONAL DIABETES MELLITUS

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Gestational Diabetes Mellitus (GDM) is the most common medical complication and metabolic disorder of pregnancy. This review provides an overview into the morbidity associated with GDM as well as the current methods of screening, diagnosis and management with the aim of early recognition and prevention of complications to both the mother and foetus.

Key words : *gestational Diabetes mellitus, diagnosis, management*

Introduction

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy (1). This definition applies irrespective of the form of treatment or whether the diabetes persists after the pregnancy. It is the most common medical complication and metabolic disorder of pregnancy (2).

The main purpose of identifying GDM is to detect women at risk of adverse perinatal outcomes. There is evidence to show that women who are intensively treated during pregnancy can achieve near normal rates of macrosomia (3). Correct diagnosis of this condition is important because it requires dietary control and pharmacological intervention as well as close monitoring of the pregnancy and the foetus.

Approximately 4% of all pregnancies are complicated by GDM while the prevalence may range from 1-14% of all pregnancies depending on the population and the method of screening (4).

Pathophysiology of GDM

Pregnancy is a diabetogenic state characterised by hyperinsulinaemia and insulin resistance. This progressive change in the maternal metabolism is due to the body's effort to provide adequate nutrition for the growing foetus. In the early stages of pregnancy maternal hormones promote the release of insulin coupled with increased peripheral utilisation with the end result of a lower maternal blood sugar (5). As pregnancy progresses, the levels of a host of hormones such as cortisol and oestrogen increase and this leads to insulin resistance. The peak effect of these hormones is seen in the 26th to the 33rd week of gestation. Cortisol for example has a very strong diabetogenic effect (2). This peak hormonal effect forms the basis for screening in the 24th to 28th weeks of gestation.

Risk Factors and Screening for GDM

Screening for GDM should be performed between the 24th and 28th weeks of gestation that are of average to high risk of developing diabetes. The aim of the screening procedure is to identify those women who are at sufficient risk to warrant the formal oral glucose tolerance test.

The clinician has to be vigilant to identify those women who develop features of diabetes before the third trimester. All women should be assessed at the first antenatal visit and women should be subjected to screening if the suspicion of GDM arises.

Patients may be categorised into risk category based on the features shown in Table 1, (6).

Table 1: Risk categories for Gestational Diabetes Mellitus (GDM)

High Risk

(One or more of the following)
marked obesity
diabetes in a first-degree relative
history of glucose intolerance
previous infant with macrosomia
current glycosuria

The above category of patients should be subjected to screening as soon as possible after the initial visit and if negative repeat at 24-28 weeks

Low risk patients

Young age < 25 years old
Low risk race
Normal weight gain
No history of macrosomia

Average risk patients

Do not fit into either of the above categories and should have routine screening at 24-28 weeks of gestation

Adapted from Kjos et al, 1999 (6).

Patients who are at high risk should be screened for diabetes as early as the first antenatal booking and if no diagnosis of GDM is made at the time, this should be repeated at 24-28 weeks. Those patients with average risk should be screened at 24-28 weeks gestation.

Women at low risk of developing GDM such as those below the age of 25 years with no family history of diabetes and other features shown in Table 1 do not require formal screening. It is worth noting that the incidence of GDM is low in the absence of risk factors, suggesting that selective screening may be cost effective in situations where health resources are scarce (7).

Method of Screening for GDM

In high-risk patients, a fasting plasma glucose level of more than 7.0 mmol/l or a random glucose level of 11.1 mmol/l meets the American Diabetes Association (ADA) criteria for the diagnosis of **diabetes mellitus** (8). The test should be repeated and if still within the criteria stated above, the diagnosis of diabetes is confirmed and there is no need to perform any further screening tests.

In patients who do not meet the above criteria, the screening test should consist of a 50 g oral glucose load (Glucose challenge test or GCT) followed by a plasma sugar level estimated 1 hour later. A level of more than 7.8 mmol/l indicates the need for a full diagnostic 100 g 3 hour oral glucose tolerance test (OGTT) (9) or further evaluation with the 75 g OGTT. The 7.8 mmol/l cut off will detect approximately 80% of women with GDM (6).

Should one choose to use the 50g GCT, the test should be administered without regard to time of day or of last meal although this test is more sensitive when patients are fasted prior to the test.

In clinical practice, most patients who are at high risk of GDM are subjected to the 75g Oral Glucose Tolerance Test (OGTT) as this will clinch the diagnosis and save the patient from undergoing two procedures.

The diagnosis of GDM

The ADA criteria for diagnosis of GDM (4) are fairly standardised and are based on the recommendations of the Fourth-International Workshop-conference on Gestational Diabetes (1). The epidemiological studies by O'Sullivan (10) and modified by Coustan are the basis for the recommendations. The patient is subjected to a glucose stress of 100 g and plasma glucose levels are drawn at baseline and for a further 3 hours as shown below.

Table 2: The diagnosis of GDM with a 100-g oral glucose load (4)

Time of Measurement	**mg/dl**	**mmol/l**
After overnight fast	95	5.3
Post glucose ingestion		
60 minutes	180	10.0
120 minutes	155	8.6
180 minutes	140	7.8

The diagnosis of GDM requires any two of the four plasma glucose values to be equal or more than the values shown in table 2.

In countries where the diagnosis of GDM is based on the standard WHO 75 g glucose tolerance test, the World Health Organisation (WHO) criteria for impaired Glucose tolerance (IGT) and diabetes is used to identify those who have GDM (11). Blood for glucose estimation is drawn after an overnight fast (baseline value) and 2 hours after the oral glucose load. A major advantage of the WHO criteria is the fact that the same parameters are used as the non-pregnant state (12).

The diagnosis of GDM is made if the patient satisfies the criteria for Impaired Glucose Tolerance with a 120 minute blood sugar value of $\geq$ 7.8 mmol/l. The 75-g OGTT is the preferred method of diagnosis in Malaysia.

Manifestations and Prognosis of GDM

Maternal

Most patients with GDM may not have any symptoms attributable to the GDM per se. Features such as polyuria and lethargy often associated with diabetes may be related to the pregnancy. Maternal morbidity may be in the form of increased risk of pre-eclampsia, polyhydramnios and increased incidence of Caesarean Section. Women with GDM are at increased risk of developing diabetes mellitus in later life. The Toronto Tri-Hospital Gestational Diabetes Project, a prospective study evaluating both maternal and foetal outcomes with increasing degrees of glucose intolerance has shown significant association between increasing glucose intolerance and increased incidence of caesarean delivery, preeclampsia and length of maternal hospitalisation (13).

Figures vary but the incidence of type 2 diabetes may be as high as 30% in patients with previous GDM (14). Women with GDM are also at increased risk of developing hypertension and Hyperlipidaemia. In the setting of extremely poor control of diabetes stillbirth is an important complication.

Foetal

Infants of mothers with GDM are not at increased risk of congenital deformities unless there is a history of poorly controlled diabetes prior to conception. There is an increased risk of increased perinatal mortality, macrosomia, jaundice, polycythaemia, hypocalcaemia and shoulder dystocia (2,6). Neonatal hypoglycaemia is a common and transient complication of GDM occurring in 50% of infants with macrosomia and 5-15% of infants with optimally controlled GDM (15). The incidence of hypoglycaemia increases with poor control prior to delivery.

In later life these children born to mothers with GDM have been shown to have a higher incidence of obesity (16), impaired glucose tolerance (IGT) (17) and diabetes mellitus (4).

The Management of Gestational Diabetes Mellitus

Management strategies in patients with GDM can be divided into 4 main aspects, which include:

1. Monitoring
2. Non-pharmacological intervention
3. Pharmacological Intervention
4. Obstetric Management

1. Monitoring

Maternal

Monitoring encompasses an important but often neglected part in the management of diabetes in general but GDM specifically. Maternal metabolic surveillance should be encouraged and daily self-monitoring of blood glucose (SMBG) appears to be superior to intermittent glucose checks during the follow up visit (4).

Although there may be initial fears about SMBG most patients can be taught to overcome these fears. Newer lancet devices are virtually painless. Glucometers themselves are easy to use and newer devices require minute amounts of blood for analysis.

The main limiting factor may be the cost of the glucometer and the strips. Patients should be encouraged to join the Persatuan Diabetes Malaysia (PDM) to facilitate the purchase of the device and the strips. Nurses and doctors play an invaluable role in patient education. Patients should be encouraged to keep a diary and record any adverse events such as hypoglycaemia as well as their blood sugar profiles.

Glucose levels should be as near normal and current recommendations are a pre-meal plasma sugar level of not more than 5.3 mmol/l while post-prandial levels at 1 hour and 2 hours should be below

7.8 and 6.7 mmol/l respectively (1). These are plasma levels. One should note that capillary plasma levels are 1 mmol/l higher than plasma values.

Post-meal hyperglycaemia is more closely related to foetal macrosomia than pre-meal hyperglycaemia in pregnancies in patient with established diabetes. This has led to the recommendations that women should monitor pre- and post meal sugars.

Blood pressure and urinary protein monitoring is important to detect pregnancy induced hypertension. Urine ketones should be measured if there is suspicion of inadequate caloric intake. Urine glucose monitoring is not useful in GDM due to the altered renal threshold.

Foetal Monitoring

The dominant antepartum clinical risks are to the foetus. It is therefore important that foetal monitoring be performed routinely particularly with the increased risk of intrauterine death in mothers with severe hyperglycaemia. The presence of fasting hyperglycaemia of more than 5.8 mmol/l may be associated with an increase risk of intrauterine foetal death during the last 4-8 weeks of pregnancy (4). In such cases, vigilant surveillance is important particularly if the pregnancy progresses past term.

Maternal monitoring of foetal movement, cardiotocography and ultrasonography are recommended methods of foetal monitoring. All patients should perform foetal movement counting after 28 weeks of gestation. Foetal surveillance should begin at 40 weeks in diet controlled patients with GDM with good glycaemic control while similar non-stress testing should begin earlier at 32 weeks in GDM mothers on insulin therapy or in pregnancies complicated by hypertension or prior stillbirth (2).

2. Non-Pharmacological Therapy

Patient education is an important part of the management of diabetes. Women should be counselled regularly to reinforce the importance of compliance to the dietary and exercise regimes outlined below. They should also be aware of the implications of poor glycaemic control to the foetus.

Diet

Nutritional counselling is of the utmost importance in patients with GDM. An experienced and qualified dietician should perform counselling. The aim is to provide adequate calories for maternal needs, foetal growth and adequate weight gain while avoiding hyperglycaemia and ketosis (18).

The ADA recommends individualisation of therapy (4). Obese individuals with a BMI > 30 Kg/ m^2 may benefit from a 30% calorie reduction with no untoward effects. A high carbohydrate diet is not helpful for good glycaemic control.

Exercise

Exercise in patients with GDM is not without its controversies. Some studies suggest that exercise may trigger premature labour (19,20). However, a meta-analysis of exercise and pregnancy studies concludes that a pregnant woman can exercise up to 3 times per week for up to approximately 40 minutes with no harm to either herself or the foetus (21). Exercise has been shown to improve glycaemic control in patients with GDM and may be used to improve glycaemic control (22). This exercise regime should be closely monitored. The American College of Obstetricians and Gynaecology (ACOG) (23) advocates exercise in women who have exercised before conception but not in those who previously had no exercise.

3. Pharmacological Therapy

Insulin

If diet and exercise are inadequate to maintain euglycaemia, then therapeutic intervention with insulin should be considered. To identify those women, who will require insulin therapy, frequent monitoring of blood sugar is important. Current recommendations by the ADA include frequent monitoring of both fasting and post -prandial sugar levels at 1-2 week intervals. Alternatively, SMBG can be a useful means of assessing glycaemic control.

The ACOG recommends that insulin therapy should be initiated if the fasting blood sugar is more than 5.3 mmol/l or a two-hour post prandial level is more than 6.7 mmol/l (23). Insulin is the only pharmacological agent that has been shown to reduce foetal morbidity when coupled with dietary control.

Human insulin should be the insulin of choice. Patients understandably will have fear of needles and dread the thought of injections. Pen devices with ultra-fine needles have greatly reduced the stress of self-administration of insulin. These pen devices are

easy to use and portable enough to fit in the handbag without the inconvenience of traditional insulin syringes. The insertion of the insulin cartridge is simple.

Optimal insulin regimes have not been determined and these regimes should be tailored to meet glycaemic goals. It is usual practice in this country to use pre-meal injections of soluble insulin. The dose is titrated to achieve optimal control. Patients should be educated on fundamental issues such as insulin storage, injection techniques and sites of injection as well as on how to use the glucometer properly.

Oral Hypoglycaemic agents (OHAs)

Women with diabetes are rarely treated with oral hypoglycaemic agents. The ADA position statement on GDM categorically states that OHAs are not recommended in pregnancy (4). Older Sulfonylureas, particularly Chlopropramide and Tolbutamide are not recommended in pregnancy because of the potential side effects to the foetus, particularly that of hypoglycaemia and foetal anomalies. Glibenclamide does not cross the placenta and potentially could be an agent for treating GDM (24).

Although there has been a renewed interest in using OHAs in pregnant women, this practice is not universally accepted. In a survey of Obstetrics units in the United Kingdom (25), none of the units surveyed used OHAs for the treatment of GDM. Treatment was either non-pharmacological (diet and exercise) or Insulin. The practice in Malaysia is very much the same as in the United Kingdom.

4. Obstetric Management

The goal of obstetric management is to detect foetal compromise and at the same time deciding on the optimal time and route for delivery (26). Factors such as the size of the baby should be taken into consideration as the risk of birth trauma and shoulder dystocia increases when the birth weight of the infant exceeds 4000 g. This will help the clinician decide on whether to proceed with vaginal delivery or Caesarean Section.

The mother should have her blood sugar monitored regularly through the process of labour to ensure that her sugar levels are kept within the normal range to avoid hypoglycaemia in the newborn. A paediatrician should be on hand at the delivery to assess the child upon birth.

Post Partum Management of Women with GDM

Patients who have been diagnosed to have GDM should be reassessed after at least 6 weeks post delivery (4). If sugar levels are normal post partum, these patients should be monitored at least 3 yearly. All women should receive contraceptive advice should they wish and counseling regarding future pregnancies. They should also be informed of their risk of developing type 2 diabetes and the potential symptoms (2).

The lessons learnt during the days of pregnancy relating to a healthy life style and dietary control should be re-enforced.

Conclusion

GDM is the most common medical and metabolic complication seen in pregnancy. Women who are at high risk of developing GDM should be appropriately screened to reduce maternal and foetal morbidity. The method of screening and diagnosis of GDM has been outlined.

The management of GDM should be based on a team approach involving the diabetologist, obstetrician, dietician and paediatrician with the invaluable support of a diabetic nurse educator.

Patients with GDM are at risk of developing type 2 diabetes in the future and should be monitored regularly. Similarly the offspring of diabetic pregnancies are at risk of developing obesity, IGT and diabetes and should also be periodically followed up.

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