Gestational diabetes mellitus: a clinical challenge in Africa

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Introduction

Gestational diabetes mellitus (GDM) is diabetes that occurs primarily during pregnancy. Most cases of GDM start in the second and third trimester of pregnancy.[1,2] The other types of are type 1, type 2 and secondary types. Type 2 diabetes constitutes more than 95% of the cases of diabetes in Nigeria.[3–5] The other types of diabetes, apart from GDM, can occur before, during and after pregnancy. The incidence of diabetes in pregnant women in Nigeria is about 1.7% – out of which, 39% are pregestational (known diabetics before pregnancy) and 61% are GDM.[6] Globally, about 1–14% of pregnancies are complicated by GDM.[7–9] Most cases start in the second and third trimester of pregnancy.[7,8] Since antenatal care starts in the first trimester, cases of GDM may be missed if not looked for after the initial evaluation on presentation. Also, most cases of GDM are asymptomatic and often present with mild hyperglycaemia only. Therefore, all pregnant women with any risk factors for GDM should be screened using fasting blood glucose (FBG), random blood glucose (RBG) and/or oral glucose tolerance test (OGTT); especially between 24 and 28 weeks of pregnancy.[9] The use of the HbA_{1c} test in the diagnosis and management of GDM is being evaluated by ongoing studies. However, this test can be used to assess known diabetic patients who become pregnant, especially in the first trimester, since this will help to assess the preconception glycaemic picture.[10] The HbA_{1c} test is not reliable in haemolytic conditions which are common in Africa and is not readily available or easily affordable.

About 95% of all cases of GDM revert to normal within 6 weeks of delivery, while about 50% develop type 2 diabetes within 10 years of the onset of GDM.[7] GDM is also associated with an increased risk of obesity and abnormal glucose tolerance during childhood and adult life in the offspring. All types of diabetes are associated with increased maternal and foetal morbidity and mortality. Poor diabetic control early in pregnancy is associated with spontaneous abortion and congenital malformation. Uncontrolled diabetes later in pregnancy is associated with polyhydramnios and preterm delivery.

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Blood glucose values greater than 10 mmol/l (180 mg/dl) are associated with foetal hypoxia in the third trimester of pregnancy.[11,12] Respiratory distress syndrome, hyperglycaemia, hyperbilirubinaemia, hypocalcaemia, and poor feeding are more common in siblings from diabetic mothers.[12]

The primary treatment options for GDM are diet and exercise. Drug treatment becomes additionally useful in many cases due to the failure of the primary options to provide adequate glycaemic control.[13] The appropriate monitoring of blood glucose before meals and 2 hours after, as well as keeping records of the amount of carbohydrate ingested, has been said to improve the outcome of GDM.[13,14] The maintenance of blood glucose values at less than 5.3 mmol/l (95 mg/dl) before meals, and less than 7.8 mmol/l (140 mg/dl) and 6.7 mmol/l (120 mg/dl) 1 and 2 hours after meals, respectively, has been recommended by the Fourth International Workshop Conference on Gestational Diabetes Mellitus.[15] This is because of the inverse association between maternal ketoacidosis in the second and third trimester and psychomotor development and intelligence in the offspring at childhood.[16] The daily dietary recommendations for proper glucose control include: energy intake of 30 to 32 kcal/kg body weight for women with normal weight and less, and 28 to 30 kcal/kg in overweight women.[17]

Pharmacological control of blood glucose has been achieved over the years by the use of insulin. Recently, newer insulin analogues such as lispro and aspart may give better glucose control and reduce foetal macrosomia[18,19] and are safe in pregnancy, since like maternal insulin they do not cross the placental barriers.[20] Traditionally, all pregestational diabetes patients should stop all oral or other forms of hypoglycaemic drugs before conception and commence insulin 2 to 4 weeks before planned pregnancy; this is different in practice because of the poor knowledge among diabetic mothers in Nigeria and elsewhere in Africa. Glyburide, a sulphonylurea which enhances insulin secretion has been found to be a suitable alternative to insulin for the treatment of GDM with good perinatal outcome. Glyburide is less expensive than insulin and easier to take orally, but takes up to 1 week to achieve the desired effect.[21] The safety of glyburide in pregnancy may be due to the fact that it does not cross the placenta into the foetus.[22] The main risk of glyburide (like insulin) is hypoglycaemia. There are speculations that the use of metformin in polycystic ovary syndrome (PCOS) may be safe and reduce the risk of miscarriage and the development of GDM if used

throughout pregnancy.[23] Metformin has for a long time been thought to be safe in pregnancy, and may be used alone or in combination with insulin.[24,25]

Pathophysiology

Pregnancy is characterised by major alterations in metabolism and hormonal changes such as progressive insulin resistance that begins near mid pregnancy and continues through the third trimester. Insulin action is enhanced by oestrogen and progesterone in the first trimester of pregnancy which leads to lower blood glucose values during this period. Increased foetal placental glucose utilisation also contributes to the lower blood glucose values in the first trimester of pregnancy. There is increased basal hepatic glucose production and basal insulin secretion by the pancreas. In early pregnancy fat deposition is enhanced, unlike later in pregnancy when lipolysis is enhanced by human chorionic somatomammotropin (HCS), formerly called human placental lactogen (HPL) and insulin desensitising placental hormones contributing to insulin resistance.[26,27]

HCS is an insulin antagonist that increases in proportion to placental mass throughout pregnancy.[28] It inhibits peripheral uptake of glucose in the mother, but stimulates pancreatic insulin secretion in the foetus.[29] Maternal insulin does not cross the placenta and therefore does not cause hypoglycaemia in the foetus. However maternal hypoglycaemia from any cause is of grave danger to the foetus. HCS is a single chain polypeptide hormone similar to growth hormone and prolactin. Serum cortisol is also increased in pregnancy and this contributes to the relative insulin resistance observed in pregnancy. Increased prolactin may also contribute to the insulin resistance in pregnancy.

Other types of diabetes apart from GDM may start in pregnancy and continue after pregnancy, and this may form about 5% of cases of GDM that do not revert to normal after delivery of the baby. The 50% of cases of GDM that become type 2 diabetes in the 10 years following onset may be due to people with programmed genetic components of type 2 manifesting earlier as a result of the stress of pregnancy. The recurrence rate of GDM is 33–50% in subsequent pregnancies.[30,31] Post partum, all patients with past GDM should observe dietary regulations and regular exercise. The American Diabetes Association (ADA) recommends yearly fasting blood glucose (FBG), and 75 g 2 hour oral glucose tolerance test (OGTT) at the post-natal visit. Also recommended by ADA, is preconception normoglycaemia 2 to 3 months before conception.[29]

Risk factors

Numerous risk factors are associated with GDM.[32–36] The known risk factors for GDM are shown in Table 1. If blood glucose values do not meet the criteria for the diagnosis of GDM, an OGGT is mandatory at 24–28 weeks of pregnancy to make a diagnosis or otherwise. If a risk factor analysis is done early in pregnancy, an HbA_{1c} test could be done to profile the likely glycaemic control in the past 3 to 6 months.[37] The International Association of Diabetes and Pregnancy Study Groups (IADPSG) advocates testing pregnant women at their first obstetric visit for the presence of overt diabetes using FBG, RBG and HbA_{1c}.[38] However, HbA_{1c} is costly and not commonly available in Africa. In Africa, where most females marry before the age of 20 years and maternal mortality is high in pregnancy, it is advocated that age greater than 25 years should be a risk factor for GDM. Table 2 shows the risk categories for GDM.[33]

Clinical parameter	Clinical features and association
Age	>30 years (>25 years recommended for Africa)
Obesity	BMI >30.0 kg/m²
Ethnicity	African-American, Hispanics, Asian-American, Pacific Islander
Family	Type 2 diabetes in first- or second-degree relation
Insulin resistance	Polycystic ovary syndrome
Large babies	History of babies >4.5 kg at birth
GDM	GDM in previous pregnancies
Glucose tolerance	History of abnormal glucose tolerance
Maternal birth	<2.5 kg or >4.5 kg
Perinatal events	Unexplained perinatal loss
Malformation	Birth of a malformed child

Table 1 Risk factors for gestational diabetes

Most cases of GDM are asymptomatic and present with mild hyperglycaemia. Therefore knowledge of risk factors, screening and a search will help in the diagnosis of GDM. Poor obstetrics history and unexplained still births are common risk factors.[39,40] Pregnant women with an FBG greater than 5.5 mmol/l (100 mg/dl) and less than 6.9 mmol/l (125 mg/dl) should be screened for GDM at 24 to 28 weeks. An FBG greater than 6.9 mmol/l (125 mg/dl) is diabetic, and does not require an OGTT. Various

High risk
- Marked obesity.
- Diabetes in first-degree relative.
- Current glycosuria.
- Previous history of GDM or glucose intolerance.
- Previous infant with macrosomia.

Average risk
- Neither high or low risk.

Low risk
- Age less than 25 years.
- No previous poor obstetrical outcomes.
- Belonging to a low-risk ethnic group.
- No diabetes in first-degree relatives.
- Normal pre-pregnancy weight and weight gain during pregnancy.
- No history of abnormal glucose tolerance.

Table 2 Risk categories for gestational diabetes

Time (hours)	National Diabetes Data Group (NDDG) (100 g glucose)[1]	Carpenter and Coustan (100 g glucose)[34]	WHO (75 g glucose)[35,36]	American Diabetes Association (ADA) (75 g glucose)[2]
0	≥ 5.8 (105)	≥ 5.3 (95)	≥ 7.0 (125)	≥ 5.3 (95)
1	≥ 10.6 (190)	≥ 10.0 (180)	–	≥ 10.0 (180)
2	≥ 9.2 (165)	≥ 8.6 (155)	≥ 7.8 (140)	≥ 8.6 (155)
3	≥ 8.1 (145)	≥ 7.80 (140)	–	–
Note: BG levels are in mmol/L with mg/100 ml in brackets)				

Table 3 Glucose tolerance test criteria for GDM diagnosis

OGTT systems are available, and these are summarised in Table 3. For an OGTT the patient should fast for at least 8 hours before the procedure. There is no carbohydrate restriction indicated before fast. The test is done with the patient seated.

Conclusion

The risk factors for GDM are many and should be assessed in all pregnant women. Placental mass and hormonal changes that occur in pregnancy may contribute to the pathogenesis of GDM. The insidious onset of most cases of GDM necessitate that a diligent search and screening for GDM. RBG, FBG, and OGTT are all used in the diagnosis of GDM. A significant number of cases of GDM in pregnancy require insulin for treatment. There is now increasing evidence, however, that sulphonylureas and metformin are safe in pregnancy. The management and follow-up of GDM is for life.

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