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Screening for gestational diabetes mellitus

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Summary The term 'gestational diabetes mellitus' is unsatisfactory as it refers to a heterogeneous group of women, including those with minimal abnormality of carbohydrate metabolism and those with undiagnosed type II diabetes. However, perinatal morbidity is increased even in the group of women who have only impaired glucose tolerance; the mothers are at increased risk of subsequent development of diabetes, and there may also be long-term implications for the offspring. Current research is aiming to define the blood glucose levels at which risks increase so that clinical management can be appropriately directed. When available, the criteria required to justify population screening in pregnancy should be satisfied. The glucose challenge and fasting glucose tests are the leading contenders as appropriate screening tests to determine who should have the diagnostic glucose tolerance test. However, until this is reviewed, the widely used scheme of risk factors as a screening method should continue, as it detects at least 50% of women with gestational diabetes.

Introduction

The subject of gestational diabetes mellitus remains confusing. This is partly because women with abnormal glucose tolerance in pregnancy form a heterogeneous group. Gestational diabetes includes women with:

- undiagnosed type II diabetes;
- mild abnormal glucose tolerance before pregnancy which worsens in pregnancy due to increased insulin resistance;
- normal glucose tolerance before pregnancy which becomes abnormal with advancing gestation and reverts to normal after pregnancy;
- undiagnosed type I diabetes when pregnancy coincides with the prodromal phase of type I diabetes (rare).

Genetic predisposition is clearly of relevance, and in addition some rare specific enzyme mutations have been identified which may affect the

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glucokinase gene. The heterogeneity of the condition is also reflected in the maternal insulin concentrations which range from reduced insulin secretion to hyperinsulinaemia.

Apart from the heterogeneity of the condition and the metabolic changes which occur in pregnancy, there are other areas which cause confusion. There are differences in terminology and definitions, variations in prevalence (particularly among different ethnic groups), and uncertainty about the relevance of the condition. As a result, despite an abundant literature on the subject, many unanswered questions remain. Before discussing screening methods it is necessary to be clear about the definitions which have been used and then review the literature on the relevance of the condition.

Definitions

Following almost 20 years' use of the 75 g oral glucose tolerance test (OGTT) for classifying degrees of abnormality of glucose tolerance, in 1999 the World Health Organization (WHO) revised their previous criteria for diagnosing diabetes in the light of evidence accumulated since 1980.[1] The most significant alteration related to the cut-off values used for fasting blood glucose. These are:

Diabetes (DM)
- a fasting plasma glucose of $\geq$7.0 mmol/L and/or
- a value 2 h after a 75 g OGTT of $\geq$11.1 mmol/L and/or
- a random value of $\geq$11.1 mmol/L

Impaired glucose tolerance (IGT)
- a fasting value of $<$7.0 mmol/L and
- a value 2 h after a 75 g OGTT of $\geq$7.8 but $\leq$ 11.0 mmol/L

Impaired fasting glycaemia (IFG — an addition to the previous classification)
- a fasting value of $\geq$6.1 and $<$7.0 mmol/L

Gestational diabetes

The WHO have now elected to use this term to encompass both gestational impaired glucose tolerance (GIGT) and gestational diabetes mellitus (GDM), which were previously regarded as separate entities. The definitions are as for the non-pregnant state (see above). This is widely regarded as unfortunate, as the physiological changes in normal pregnancy result in an increase in insulin resistance, so that more insulin is required with advancing gestation to produce normoglycaemia. This results in slightly higher postprandial values, so that by the third trimester up to 10% of women in some studies have a 2-h post-75 g OGTT blood glucose value of $\geq$7.8 mmol/L, and are regarded as having GIGT. In view of this, many would regard women with milder degrees of GIGT diagnosed later in pregnancy to be normal.

The European Association for the Study of Diabetes had in 1989 recommended that the lower cut-off for the 2 h value defining GIGT be raised from 7.8 to 9.0 mmol/L in the third trimester on the basis of an epidemiological study.[2] Hopefully, when current research is completed and reviewed this classification may be revisited. In the meantime, from a clinical perspective it is important that the degree of abnormality (i.e. GDM, GIGT, IFG) and the gestation at which it was first noted are considered. As there is a continuum of glucose tolerance, women whose glucose concentrations are at the upper end of the GIGT range may need more careful attention than those at the lower end.

Relevance

The most important prerequisite for a screening test is that the condition which is being screened for must pose a significant health-care problem to the population. With gestational diabetes there are several areas to be considered: the pregnancy risks and long-term risks for the mother, and the fetal, neonatal, childhood and longer-term risks for the baby.

Maternal risks in pregnancy

It has been estimated that about 1 in 10,000 women will become pregnant in the prodromal stages of developing type I diabetes.[3] With the pregnancy changes in glucose tolerance these women may develop ketoacidosis and become seriously unwell; similarly someone with undiagnosed type II diabetes could also develop ketoacidosis. These are rare events which clinicians may see once in a lifetime.

Much more common is the morbidity associated with having a higher caesarean section rate (approximately 60% in population studies) than normal pregnant women. Most studies have shown that