WHY SCREEN FOR GESTATIONAL DIABETES MELLITUS?

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Abstract

Gestational diabetes mellitus is a condition associated with complications to both the mother and the child. While treatment is imperative, over-aggressive management causes problems as well. The diagnosis of overt diabetes in pregnancy and the necessity of treatment is obvious but the question arises whether women with milder elevations of blood glucose levels should be treated. Two large randomized control trials have shown that there is moderate improvement in neonatal outcomes in women who belong to this group. The International Association of Diabetes and Pregnancy Study Group (IADPSG) provided an internationally endorsed criterion for diagnosis and classification of diabetes in pregnancy. The consensus was that the association between maternal glycemia and adverse outcomes are continuous across the range of glucose concentrations. The evidence therefore recommends that treating milder degrees of diabetes in pregnancy improves neonatal outcomes.

Introduction

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance of varying severity, detected for the first time in pregnancy. Diabetes in pregnancy can be classified practically as gestational diabetes and pre-gestational diabetes which includes Type 1 and Type 2 diabetes. There is usually an overlap between GDM and Type 2 diabetes which is identified for the first time in pregnancy during routine analysis.

Even though the definition of GDM has remained the same over several years, opinion regarding the detection and clinical management of GDM varies widely.

There are two aspects in the management of this condition. At one end is the fact that failure to recognize GDM leads to unnecessary morbidity. At the other end overly aggressive treatment of GDM results in unnecessary intervention including small for gestational age babies.

Complications of gestational diabetes mellitus

The complications associated with GDM include macrosomia, shoulder dystocia, neonatal metabolic abnormalities (hypoglycemia, hyperbilirubinemia), birth trauma, risk of obesity and diabetes (in the child) later in life. The mother has a strong risk of developing diabetes later (50% of mothers with GDM, in a study done by O’Sullivan et al. with a 28 year follow-up). On the other hand, over diagnosis of GDM results in increased antenatal visits, increased induction rates and caesarean section rates.

The treatment dilemma

Treatment of overt diabetes with fasting plasma glucose values more than 126mg/dl and postprandial glucose value of more than 200mg/dl is obvious. But should pregnant women with milder elevations of blood glucose levels be treated?

In an attempt to answer this question, a study was conducted in Australia by Crowther et al, to assess the effect of treatment of pregnant women with mild degree diabetes (1). He conducted a large randomized trial over a period of 10 years on 1000 women at 24-34 weeks of gestation with fasting glucose levels less than 130mg/dl and 2 hour postprandial glucose measurement less than 200mg/dl. The women were
assigned to two groups - the routine obstetric care group or to the intervention group. The intervention group had a diet with or without insulin therapy to achieve fasting glucose level of 63-99mg/dl and 2 hour post prandial glucose levels less than 126mg/dl. The serious complications including perinatal death, shoulder dystocia, bone fracture and nerve palsy were significantly lower in the intervention group than the control group. The numbers needed to treat (NNT) to avoid one adverse outcome was 43. There was however no decrease in caesarean rates with treatment of maternal hyperglycemia.

Another multicenter, randomized trial for the treatment of mild gestational diabetes was done by Landon et al in 2009 on pregnant women at 24 to 30 weeks gestation with glucose challenge test values between 130-200mg/dl \( (2) \). Blinded 3 hour 100g oral glucose tolerance test were done in these women. Mild GDM was defined as fasting glucose levels less than 95mg/dl and two or more timed measurements that exceeded the established thresholds: 1 hour-180mg/dl, 2 hour -155mg/dl, and 3 hour -140mg/dl. The women were then assigned to the control group who received routine obstetric care and treatment group who received nutritional counseling, diet therapy and insulin if required. The major outcomes including macrosomia, large for gestational age, fat mass, caesarean delivery, shoulder dystocia, pre-eclampsia and weight gain in pregnancy were significantly lower in the treatment group. In contrast to the previous study, they found that the caesarean rate was lower in those who had intervention.

So the consensus was that moderate improvement was attained in neonatal outcome even when women were treated for milder degrees of hyperglycemia. Does this mean that there is no doubt regarding whether we need to screen and treat milder degrees of gestational diabetes? Is it cost-effective? The answer is not a straightforward yes.

Currently, according to the U.S. Preventive Services Task Force, the U.K. National Health Service, Canadian Task Forces, there is not sufficient high-level evidence to make a recommendation for, or against, screening for GDM. Meanwhile, a recent study undertaken by U.K. National institute for clinical excellence concluded that “screening, diagnosis, treatment of GDM is cost-effective”

**Screening recommendations**

Screening for GDM can be

- selective based on the risk factors (obesity, previous diabetes etc.) or can be
- universal screening.

**The Indian population is at high risk and we recommend universal screening for Indian women.**

The options available for screening include

1. **Non-challenge blood glucose tests**: Fasting and postprandial test, Random blood sugar level and HbA1C.

Fasting plasma glucose levels of more than 126mg/dl and 2 hour post prandial more than 200mg are diagnostic of diabetes. The advantage of these tests are that it is simple to administer and inexpensive. The disadvantages are low sensitivity, moderate specificity and high false positive rates.

2. **The challenge tests** are glucose challenge test and oral glucose tolerance test.

Glucose challenge test is done with 50 g glucose in a non-fasting state and the blood glucose level measured after 1 hour. The cut off value of 140mg/dl has a specificity of 90% and sensitivity of 80% which improves to 90% if the threshold value is taken as 130mg/dl. This is not confirmatory. This has to be followed by an oral glucose tolerance test before a diagnosis is made.

An oral glucose tolerance test criterion was established by O’Sullivan and Mahan in 1964:

Fasting 90mg/l;
1 hour 165mg/dl;
OGTT was done in 752 pregnant women and values more than 2 SD were taken to establish criteria. The values only identified women who subsequently developed diabetes and not correlated with perinatal outcome. The diagnostic criteria for GDM vary worldwide. The commonly used tests and criteria are given below.

**Box 1: The commonly used tests and criteria for diagnosis of GDM**

<table>
<thead>
<tr>
<th>Organization</th>
<th>OGTT glucose load</th>
<th>Criteria</th>
<th>Fasting mg%</th>
<th>1 hour mg%</th>
<th>2 hour mg%</th>
<th>3 hour mg%</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADA</td>
<td>100g</td>
<td>Carpenter&amp; Coust</td>
<td>95</td>
<td>180</td>
<td>155</td>
<td>140</td>
</tr>
<tr>
<td></td>
<td>75g</td>
<td></td>
<td>95</td>
<td>180</td>
<td>155</td>
<td></td>
</tr>
<tr>
<td>ACOG</td>
<td>100g</td>
<td>NDDG</td>
<td>105</td>
<td>190</td>
<td>165</td>
<td>145</td>
</tr>
<tr>
<td>WHO</td>
<td>75g</td>
<td>WHO</td>
<td>126</td>
<td></td>
<td></td>
<td>140</td>
</tr>
<tr>
<td>ADIPS</td>
<td>75g</td>
<td>Australia</td>
<td>99</td>
<td></td>
<td></td>
<td>144</td>
</tr>
<tr>
<td></td>
<td>75g</td>
<td>NZ</td>
<td>99</td>
<td></td>
<td></td>
<td>162</td>
</tr>
</tbody>
</table>

Due to the varying ranges for diagnosis in different countries, there was a need for internationally accepted criteria for diagnosing and classifying GDM.

**IADPSG criteria**

In June 2008, International Association of Diabetes and Pregnancy Study Group (IADPSG) organized an international Workshop- Conference on Gestational Diabetes Diagnosis and Classification in Pasadena, California. The objective was to provide an internationally endorsed criterion for diagnosis and classification of diabetes in pregnancy (4). Around 225 conferees from 40 countries reviewed the results of HAPO (Hyperglycemia and Adverse pregnancy Outcomes) study, unpublished data of the HAPO study and other studies that analyzed the effect of maternal glycemia and perinatal & long-term outcomes in offspring.

The consensus obtained after the review was that the association between maternal glycemia and adverse outcomes are continuous across the range of glucose concentrations below levels diagnostic of diabetes. The consensus panel identified the threshold value for diagnosis of GDM and overt diabetes in pregnancy.

**Box 2: IADPSG consensus panel criteria to diagnose GDM and overt diabetes in pregnancy:**

<table>
<thead>
<tr>
<th>Glucose measure</th>
<th>Glucose concentration threshold*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mmol/l</td>
</tr>
<tr>
<td></td>
<td>mg/dl</td>
</tr>
<tr>
<td></td>
<td>Cumulative</td>
</tr>
<tr>
<td>Fasting plasma glucose</td>
<td>5.1</td>
</tr>
<tr>
<td>1-h plasma glucose</td>
<td>10.0</td>
</tr>
<tr>
<td>2-h plasma glucose</td>
<td>8.5</td>
</tr>
</tbody>
</table>

One or more high value is diagnostic of GDM.
Table 3: Diagnosis of overt diabetes in pregnancy

<table>
<thead>
<tr>
<th>Measure of glycemia</th>
<th>Consensus threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>FPG</td>
<td>≥126 mg/dl</td>
</tr>
<tr>
<td>HbA1C</td>
<td>≥6.5%</td>
</tr>
<tr>
<td>RBS</td>
<td>≥200 mg/dl, confirmed with fasting glucose/HbA1C</td>
</tr>
</tbody>
</table>

When should these tests be done?

1) **At first prenatal visit** - measure FPG or random plasma glucose on all or only high-risk women.

   If results indicate overt diabetes, treatment and follow-up are done as per preexisting diabetes.
   Fasting ≥ 92 mg/dl but <126 mg/dl, diagnose as GDM.
   Fasting <92 mg/dl, test for GDM at 24 to 28 weeks' gestation with a 75-g OGTT.

2) **24 to 28 weeks' gestation** – do a 75-g OGTT (2 hours) on those who have not been diagnosed of diabetes in the first visit.

   Diagnose as overt diabetes - if fasting ≥126 mg/dl,
   Diagnose as GDM - if one or more values equals or exceeds thresholds and
   Diagnose as normal - if all values on OGTT less than thresholds.

Conclusions:

1. The evidence certainly recommends that treating even milder degree of diabetes improves neonatal outcome.
2. It is prudent to screen all Indian mothers for diabetes in pregnancy and to follow IADPSG criteria to diagnose GDM.
3. Screening includes - At first prenatal visit - measure FPG or random plasma glucose on all or only high-risk women, at 24 to 28 weeks' gestation – do a 75-g OGTT (2 hours) on those who have not been diagnosed of diabetes in the first visit.

References:


The more intelligent a man is, the more originality he discovers in men. Ordinary men see no difference between men.

Blaise Pascal