Original article

SCREENING FOR GESTATIONAL DIABETES MELLITUS: THE ROLE OF RISK FACTORS.

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ABSTRACT
Background: Gestational diabetes mellitus (GDM) is a metabolic disorder of pregnancy and is associated with poor pregnancy outcomes like pregnancy induced hypertension for the mother and foetal macrosomia for the baby.
Objective: This study aimed to determine the risk factor(s) associated with GDM.
Materials and Methods: A retrospective study was conducted in the antenatal clinic of the Lagos University Teaching Hospital (LUTH), Nigeria among 111 women with risk factors for GDM who were booked from 1st October 2008 to 30th June 2009. The women had selective screening for GDM with the 1-hour 50g glucose challenge test (GCT) at 24-28 weeks gestational age. Ethical approval for the study was obtained from the Health Research Ethics Committee of LUTH.
Results: The incidence of GDM was 9.0% among these women with risk factors for GDM. Only 32.4% of them had an abnormal GCT and 27.8% of those with abnormal GCT were confirmed with GDM. The only risk factors associated with GDM were previous GDM (p=0.017), recurrent glycosuria in index pregnancy (p=0.014), and previous unexplained stillbirth (p<0.001). There was no significant association between booking weight of ≥90kg, family history of diabetes mellitus or previous fetal macrosomia and GDM.
Conclusion: Among all the risk factors for GDM, the risk factors strongly associated with GDM were previous GDM, previous unexplained stillbirth, and recurrent glycosuria in index pregnancy. Clinicians should therefore concentrate more on these strongly associated risk factors while practising selective screening for GDM, especially in low resource settings.
Keywords: Gestational Diabetes Mellitus screening; risk factors; glucose challenge test.

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INTRODUCTION
Gestational diabetes mellitus (GDM) is defined as impaired carbohydrate tolerance leading to hyperglycaemia, and begins or is first recognized during pregnancy.1,2 Pregnancy is a diabetogenic state in which counter-regulatory hormones - human chorionic gonadotropin, human placental lactogen, prolactin, cortisol, oestrogen and progesterone - act against the effect of insulin and thereby contribute to increase in insulin resistance.2-4 The prevalence of GDM in a given population is thought to vary in direct proportion to that of type 2 diabetes mellitus depending on the various demographic characteristics of the specific population, including age and ethnic group, and is generally reported as 2-5%.1,2
Often times, GDM is asymptomatic and can only be detected by screening. It can cause a 4-fold increase in perinatal mortality, and an increase in maternal complications. The use of screening strategies to detect GDM has been largely debated but research has proven the use of risk factors to guide screening. Universal screening involves screening all pregnant women for GDM, and the World Health Organization (WHO) does not advocate this. Selective screening involves screening women at high risk for GDM. Risk factors for GDM include: age >35-40 years, obesity (booking weight >90kg or non-pregnant body mass index >30kg/m²), GDM in a previous pregnancy, strong family history of diabetes, previous delivery of a macrosomic baby, heavy (or recurrent) glycosuria of >2+ on dipstick in the index pregnancy, and previous unexplained stillbirth. However, using the above criteria will include about 90% of the pregnant population. Streamlining and sub-classifying the indications (risk factors) for GDM may ensure a more efficient system for screening and diagnosis of GDM. Risk factors can be sub-classified into ‘risk factors” and “strongly associated factors”. Therefore, in an initially normal result (in the presence of a “strongly associated factor”), an OGTT can be repeated at 34 weeks, as an initially normal result does not mean GDM will not develop later, especially in the presence of strongly associated risk factors.

Whilst the 75g oral glucose tolerance test (OGTT) using WHO criteria is now used almost worldwide as a gold standard test for diagnosing GDM, there is a large number of tests that can be used for screening, but currently it has been widely advocated that a 1-hour 50g oral GCT be administered between 24 and 28 weeks gestation, as screening for GDM. However, a 1-step approach to testing, using only a 2-hour 75-g OGTT is also widely used. It has been proposed that this 1-step approach replace the current screening and diagnostic tests, and it has been recommended that the diagnosis of GDM be made when 1 or more abnormal values occur in the 75-g OGTT.

MATERIALS AND METHODS:

This was a retrospective study of booked pregnant women with one or more risk factors for GDM who were screened for GDM with the 1-hour 50g glucose challenge test in the antenatal clinic of the Lagos University Teaching Hospital from 1st October 2008 to 30th June 2009. A total of 111 booked women had GCT done between 24 and 28 weeks gestational age based on the presence of one or more risk factors for GDM. Risk factors used were: previous fetal macrosomia (birth weight ≥4.0kg); recurrent (>1 episode) glycosuria detected by dipstick in index pregnancy; recurrent (>1) miscarriages; family history of DM; previous unexplained stillbirth; previous early neonatal death; history of neonatal jaundice in previous infants; previous infant with congenital anomaly; maternal booking weight ≥90kg; and previous GDM. Women who had GCT ≥7.8 mmol/L underwent the 75-g OGTT. GDM was diagnosed according to WHO2006 updated criteria (if 1 or more of the following occurred: fasting plasma glucose ≥92mg/dl, 1-hour ≥180mg/dl, 2-hour ≥153mg/dl, following a 75-g OGTT). All the information and test results were obtained from the antenatal case notes. The antenatal case notes were obtained from the labour ward antenatal files unit, during the antenatal period (before the subjects were delivered).

Relevant data extracted from the antenatal case notes included patients’ age, parity, last menstrual period, estimated gestational age at booking, estimated gestational age at GCT, indications for GCT/risk factors for GDM, GCT value, if OGTT was done and value, and whether GDM was confirmed. Data was recorded in a proforma.

Excluded from the study were women who had GCT done before 24 weeks and after 28 weeks gestational age. The latter might have been due to default or late booking. Also excluded were women in whom GDM was diagnosed without presence of risk factors or an initial GCT screening, as well as known diabetics.

Data was entered and analysed using the Epi Info Version 3.5.1 statistical software package. Analysis included simple frequencies,
percentages, and Fisher’s exact test. A Fisher’s exact p value < 0.05 was regarded as significant. Ethical approval for the study was obtained from the Health Research Ethics Committee of the Lagos University Teaching Hospital and due process was followed in retrieving and handling antenatal case notes from which data were extracted.

RESULTS:
Information from the antenatal case notes of 111 booked patients with risk factors for GDM and had the GCT screening for GDM at 24-28 weeks gestational age, was analysed and reported. Subjects were aged between 23 and 43 years (mean age =32.4 ± 4.2 years). Patients’ parity ranged from 0 to 5, (mean of 1.8 ± 1.4). Only 24.3% of the patients booked at less than 13 weeks gestational age, 61.3% at 13-24 weeks and 14.4% at above 24 weeks. The proportion of subjects who had GCT done at 24 weeks gestational age was 17.1%, 2.7% at 25 weeks, 5.4% at 26 weeks, 2.7% at 27 weeks and 72.1% at 28 weeks. The mean gestational age at which GCT was done was 27.1 ± 1.6 weeks. About a third (32.4%) of the women with risk factors had abnormal GCT and therefore had OGTT done. Out of these women who had OGTT, 27.8% were confirmed with GDM. The frequencies of occurrence of risk factors for GDM among all the subjects are shown in Table 1. The risk factors were not mutually exclusive (some subjects had more than one risk factors for GDM). The association between risk factors for GDM and the actual occurrence of GDM among subjects is shown in Table 2. Only recurrent glycosuria in index pregnancy (p=0.014), previous unexplained stillbirth (p<0.001), and previous GDM (p=0.017) were significantly associated with GDM

DISCUSSION
The prevalence of GDM in high risk women in this study was 9.0%. This is higher than the reported prevalence of 6.2% in an earlier study done in the Lagos University Teaching Hospital, Lagos in 2008.\textsuperscript{10} The prevalence rates of GDM in high risk women vary in various previous studies: 20.2% in a hospital in Thailand\textsuperscript{11}; 12.3%, 6.2% and 7.1% in the studies of DiCiann et al\textsuperscript{12}, Sunsameevithayakul et al\textsuperscript{13} and Chanprapaph et al.\textsuperscript{14} The authors suggested that this difference might be due, in part, to the criteria used for screening. This is in contrast to the prevalence rate of GDM in all antenatal patients, in studies done in a Nigerian antenatal population, which was 2.98 per 1000 pregnancies;\textsuperscript{15} and in Ethiopia (rural communities) which was 3.7% and was said to be high as compared to other parts of Africa.\textsuperscript{16}

Selective screening was used in this study of high risk women because of the cost effectiveness and time conservation, more so WHO does not advocate universal screening.\textsuperscript{2,6} The plasma glucose value of 7.8mmol/L was used as threshold value for GCT in this study because of its high sensitivity and higher specificity than the 7.2mmol/L value from various studies that have been done.\textsuperscript{8,10,11} The 24-28 weeks gestational age was chosen because current recommendations are to perform GCT at 24 – 28 weeks due to lack of evidence of any significant difference in maternal and neonatal outcomes if done earlier.\textsuperscript{2,10,11} A normal GCT and OGTT in early pregnancy does not mean that GDM will not develop, therefore OGTT should be repeated at 34 weeks if there are concerns.\textsuperscript{6} However, a study shows that screening and diagnosis of GDM early in pregnancy (before 20 weeks) will help to detect it early and enhance further evaluation and intervention ensuring improved perinatal outcome.\textsuperscript{17} Some authors also recommend that women assessed to be high risk for GDM at booking should be screened as soon as feasible, and if negative should be retested at 24-28 weeks gestational age.\textsuperscript{2}

Each of our patients in the study had at least one risk factor which was the indication for the GCT screening; and was considered a high risk patient for GDM. Maternal age was generally not included as a risk factor for GDM in the centre where this study was conducted, probably due to the current trend towards increasing maternal age for socioeconomic reasons.\textsuperscript{10} However the mean maternal age at diagnosis of GDM for the
Previous study in another Nigerian antenatal population was 31.0 ± 2.4 years. About a third (32.4%) of these high risk women had an abnormal GCT and 27.8% of them were confirmed with GDM after the 75g OGTT.

The highest occurring risk factors among the women screened were maternal booking weight ≥ 90kg (45.9%), previous unexplained stillbirth (36.9%) and previous fetal macrosomia (35.1%). Only previous unexplained stillbirth was significantly associated with GDM (p<0.001) among these. Though a study done in Abakaliki and Enugu showed that patients with GDM were at increased risk of fetal macrosomia than controls (28.7% vs. 5.5%). A randomized controlled trial from the United States comparing selective screening for GDM found positive predictive values for: strong family history of type 1 DM (15%), strong family history of type 2 DM (6.7%), previous fetal macrosomia of ≥4.5kg (12.2%), glycosuria (50%), and current suspected fetal macrosomia and polyhydraminos (40%).

The other risk factors strongly associated with GDM in this study were recurrent glycosuria (p=0.014) and previous GDM (p=0.017). The recurrence rate of GDM has been found to be as high as 30-84%, and women managed with insulin in a previous pregnancy have a recurrence risk of 75%. The remaining risk factors in this study were not statistically significantly associated with GDM.

**Conclusion**

The risk factors strongly associated with GDM are: previous unexplained stillbirth, recurrent glycosuria in the index pregnancy and previous GDM, among all other documented risk factors. Therefore, risk assessment for GDM at booking should be streamlined, so that women with these strongly associated risk factors for GDM will be screened as soon as feasible. If results are negative, they can then be re-tested along with women with the other risk factors at 24-28 weeks gestational age. If still negative, an OGTT can be repeated for this group of women at 34 weeks. However larger multicentre studies will be needed to make a more definite conclusion.

**REFERENCES:**


### Table 1: Indications for GCT (risk factors for GDM)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Frequency</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous fetal macrosomia</td>
<td>39</td>
<td>35.1</td>
</tr>
<tr>
<td>Recurrent glycosuria</td>
<td>19</td>
<td>17.1</td>
</tr>
<tr>
<td>Recurrent miscarriages</td>
<td>12</td>
<td>10.8</td>
</tr>
<tr>
<td>Family history of DM</td>
<td>13</td>
<td>11.7</td>
</tr>
<tr>
<td>Previous unexplained stillbirth</td>
<td>41</td>
<td>36.9</td>
</tr>
<tr>
<td>Previous early neonatal death</td>
<td>10</td>
<td>9.0</td>
</tr>
<tr>
<td>History of neonatal jaundice</td>
<td>9</td>
<td>8.1</td>
</tr>
<tr>
<td>Previous congenital anomaly</td>
<td>1</td>
<td>0.9</td>
</tr>
<tr>
<td>Maternal booking weight ≥90kg</td>
<td>51</td>
<td>45.9</td>
</tr>
<tr>
<td>Previous GDM</td>
<td>3</td>
<td>2.7</td>
</tr>
<tr>
<td>Others*</td>
<td>4</td>
<td>3.6</td>
</tr>
</tbody>
</table>

*Others* are occurrence of recurrent and multiple boils and history of treatment for polycystic ovarian syndrome.

### Table 2: Association between risk factors and GDM among subjects with abnormal GCT.

<table>
<thead>
<tr>
<th>Indications/risk factors</th>
<th>No GDM (n, %)</th>
<th>GDM confirmed (n, %)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous fetal macrosomia</td>
<td>7 (63.6%)</td>
<td>4 (36.4%)</td>
<td>0.353 (NS)</td>
</tr>
<tr>
<td>Recurrent glycosuria</td>
<td>4 (40%)</td>
<td>6 (60%)</td>
<td>0.014**</td>
</tr>
<tr>
<td>Recurrent miscarriages</td>
<td>1 (50%)</td>
<td>1 (50%)</td>
<td>0.484(NS)</td>
</tr>
<tr>
<td>Family history of DM</td>
<td>4 (57.1%)</td>
<td>3 (42.9%)</td>
<td>0.291(NS)</td>
</tr>
<tr>
<td>Previous unexplained stillbirth</td>
<td>4 (21.1%)</td>
<td>15 (78.9%)</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Previous early neonatal death</td>
<td>2 (50%)</td>
<td>2 (50%)</td>
<td>0.305(NS)</td>
</tr>
<tr>
<td>History of neonatal jaundice</td>
<td>2 (50%)</td>
<td>2 (50%)</td>
<td>0.305(NS)</td>
</tr>
<tr>
<td>Previous congenital anomaly</td>
<td>1 (100%)</td>
<td>0 (0%)</td>
<td>0.722(NS)</td>
</tr>
<tr>
<td>Maternal booking weight ≥90kg</td>
<td>16 (76.2%)</td>
<td>5 (23.8%)</td>
<td>0.398(NS)</td>
</tr>
<tr>
<td>Previous GDM</td>
<td>1(33.3%)</td>
<td>2 (66.7%)</td>
<td>0.017**</td>
</tr>
</tbody>
</table>

*Fisher’s exact p value, ** Significant, NS= Not significant