Validity of Fasting Blood Glucose Test in Screening for the Pre-Diabetes State Among Pregnant Females

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1. Introduction

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance of varying degrees of severity with onset or first recognition during pregnancy (Metzer & Coustan, 1998). Glucose tolerance deteriorates in human pregnancy, but about 97% to 98% of all pregnant women retain a normal glucose tolerance and only 2% to 3% develops GDM (Kuhl, 1991). However, failure to diagnose and treat GDM will result in increased morbidity in some pregnancies, while an aggressive approach to diagnosis and treatment may result in unnecessary intervention in others (Kjos & Buchanan, 1999).

The prevalence of GDM ranges from 1% to 14% of all pregnancies, depending on the population studied and the diagnostic tests and criteria employed (World Health Organization [WHO], 1985). In a recent study by Al-Rowaily and Abolfotouh in Riyadh, Saudi Arabia, the prevalence of GDM was 12.5% and 3.8% by the WHO and American Diabetes Association criteria respectively (Al-Rowaily & Abolfotouh, 2010). The appropriateness of these different diagnostic criteria has been debated (Gabir et al., 2000); nevertheless women meeting the definition for GDM by either set of criteria are at greater risk of complications than women without the diagnosis.

The 75-g glucose load has been the international standard for the diagnosis of diabetes in nonpregnant adults for several decades. This oral glucose tolerance test (OGTT) identifies pregnant women who are at risk of pre-eclampsia and whose babies are at risk of macrosomia and perinatal mortality (Schmidt et al., 2001). Although the American Diabetes Association (ADA) still recommends a 3-h 100-g OGTT for the diagnosis of GDM, it has recently included in its recommendations the use of a 2-h 75-g OGTT (American Diabetes Association [ADA], 2000; Metzger & Coustan, 1998).

A recent WHO panel, although in general maintaining previous diagnostic recommendations, now characterizes GDM as the joint category of diabetes and impaired glucose tolerance (fasting glucose ≥ 7.0 mmol/L or 2-h glucose ≥ 7.8 mmol/L (WHO, 1999). At present, screening for gestational diabetes appears to be hampered by the lack of a clear definition, agreed diagnostic criteria and evidence to show that intervention and treatment for this condition leads to improved outcomes for the mother and fetus. Although fasting plasma glucose and Glucose Challenge Test (GCT) have the highest reported sensitivities
and specificities in the literature, there also exists considerable debate about which screening test should be used if there is to be screening. A continuum of risk for GDM should be researched and risk of adverse pregnancy outcomes clarified on such a continuum. This would help to form the basis for diagnosis. The most appropriate strategies for screening, diagnosing and managing asymptomatic GDM remain controversial (Moody, 2003).

The pregnant females who attend the antenatal clinic of King Abdulaziz Medical City at the National Guard Health Affairs (usually between 24-28 weeks of gestation) are prepared for the test by fasting for a minimum of 8 hrs. After that, a fasting sample is analyzed for glucose. Then, every pregnant female is subjected to the Glucose Challenge Test (GCT) by being given 75-g Glucose solution [named Glucola which is a chilled glucose syrup with 75-g of glucose with orange flavor], and another blood sample is collected 2 hours after the drink (Berger et al., 2002). The diagnosis of GDM is based upon the results of both the fasting sample and the 2hr-glucose challenge test.

Although GCT showed good sensitivity and specificity in a previous study (79% and 87% respectively), yet it has been observed that with Glucola drink, there is always a tendency for the pregnant female to vomit (O’Sullivan et al., 1973). This usually leads to non-compliance with the glucose challenge test by most of the pregnant females. Thus, the aim of the present study was to determine the threshold value of fasting blood sugar that suggests the pre-diabetes status that needs further investigations including the GCT.

2. Methods

All pregnant females who attended the antenatal clinic of King Fahd Hospital at Riyadh National Guard Health Affairs during the period from July, 2005 to July, 2006 for the first time (n=769) constituted the target of the present study. For all respondents to the GCT (n=408,53.1%), all values of the fasting blood sugar were cross classified according to their status by the GCT, and by various cut-off points along the range of FBS values above which subjects may be considered having Impaired Glucose Tolerance (IGT) by the GCT(≥ 7.8mmol/L) result. From these tabulations, the sensitivity, specificity and positive predictive value were computed for Fasting Blood Sugar (FBS) at each cut of point.

The sensitivity of FBS diagnosis for the GCT diagnosis "gold standard" was determined by calculating how frequent the correct FBS diagnosis was made in each GCT diagnosis. The specificity of FBS diagnosis was determined by calculating how frequently the FBS diagnosis was not made when the corresponding GCT diagnosis was not present. Positive predictability indicated how frequently the FBS diagnosis was not made when the corresponding GCT diagnosis was not present. Positive predictability indicated how frequently the FBS diagnosis correctly reflected the GCT diagnosis. Also, the level of agreement between these two methods was determined at each cut-off point by the calculation of kappa coefficient ($\kappa$).

The Receiver Operating Characteristic (ROC) curve of a diagnostic test is a graph of the pairs of sensitivity and 1 minus specificity that correspond to each possible cut-off for the diagnostic test result (Richardson et al., 1993). This curve was used to determine the threshold value of FBS that correspond to the value of 7.8mmol/L by the GCT. The Statistical Package for the Social Sciences (SPSS) software program version 17 was used for all statistical analyses.
3. Results

Based on the cut-off values recommended by the American Diabetic Association (ADA, 2010) for diagnosis of GDM, the results of fasting blood sugar for 769 pregnant females showed that 17.2% had Impaired Fasting Tolerance (IFT) and 1.4% had provisional diagnosis of GDM. The corresponding results for those who responded to the GCT, are 15.2% IGT and 1.2% provisional diagnosis of GDM (Table 1), although the results of these two tests were seen to be comparable, yet the agreement level, as tested by kappa, was low. (Table 2)

<table>
<thead>
<tr>
<th>Category</th>
<th>No</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fasting Blood Glucose [N=769]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal [&lt;100mg/dl(&lt;5.6mmol/L)]</td>
<td>626</td>
<td>81.4</td>
</tr>
<tr>
<td>Impaired fasting tolerance [100-125mg/dl(5.6-6.9mmol/L)]</td>
<td>133</td>
<td>17.2</td>
</tr>
<tr>
<td>Provisional diagnosis of GDM [≥126mg/dl(7mmol/L)]</td>
<td>10</td>
<td>1.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Glucose Challenge Test (2 hr after 75-g glucose drink) [N=408]</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal [&lt;140mg/dl(&lt;7.8mmol/L)]</td>
<td>341</td>
<td>83.6</td>
</tr>
<tr>
<td>Impaired glucose tolerance [140-199mg/dl (7.8-11mmol/L)]</td>
<td>62</td>
<td>15.2</td>
</tr>
<tr>
<td>Provisional diagnosis of GDM [≥ 200mg/dl (11.1mmol/L)]</td>
<td>5</td>
<td>1.2</td>
</tr>
</tbody>
</table>

Table 1. Distribution of pregnant females according to their results of fasting blood glucose and glucose challenge tests based on the ADA classification (ADA, 2010).

<table>
<thead>
<tr>
<th>Fasting Blood Glucose</th>
<th>Glucose Challenge Test</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>IGT</td>
<td>Provisional GDM</td>
</tr>
<tr>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Normal</td>
<td>279</td>
<td>84.8</td>
<td>47</td>
</tr>
<tr>
<td>IFT</td>
<td>59</td>
<td>78.7</td>
<td>14</td>
</tr>
<tr>
<td>Provisional GDM</td>
<td>3</td>
<td>75.0</td>
<td>1</td>
</tr>
</tbody>
</table>

\( K = 0.054, p=0.25 \)

Table 2. Association between the results of Fasting blood sugar and Glucose challenge test among pregnant females at the National Guard Hospital.

Figure 1 shows the scatter plot for the values and the correlation between the values obtained by the fasting blood glucose and those obtained by the 2hr-glucose challenge test. The correlation coefficient \( r \) was 0.25 (t-value = 5.24, p<0.0001) indicating a highly significant direct correlation between the values of blood sugar by the two methods. The linear regression equation was: \( y = 0.66 \times + 2.98 \), where \( y \) is the result of the glucose challenge test, and \( x \) is the result of fasting blood sugar testing.
Fig. 1. Correlation between fasting blood glucose and 75g-2hr glucose challenge test. Solid line represents the linear regression line (y = 0.66 x + 2.98)

Table 3 shows an example for the measurements of all terms used in evaluating the fasting blood glucose test based on the studied data. In this example, a measurement of ≥5.1 mmol/L by the fasting blood glucose test was considered a cut-off point at which subjects having that measurement or above was labeled to have pre-diabetes status by the FBS test result. At this particular cut-off level, it is noted that the sensitivity of the test was 0.64, specificity was 0.53 and the false positive rate (1– specificity) was 0.21.

<table>
<thead>
<tr>
<th>True Pre-diabetic by GCT</th>
<th>FBS test result</th>
<th>Row total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥5.1 mmol/L</td>
<td>&lt; 5.1 mmol/L</td>
</tr>
<tr>
<td>Pre-diabetic-yes (≥7.8mmol/L)</td>
<td>43</td>
<td>24</td>
</tr>
<tr>
<td>Pre-diabetic - no (&lt;7.8mmol/L)</td>
<td>161</td>
<td>180</td>
</tr>
<tr>
<td>Column total</td>
<td>204</td>
<td>204</td>
</tr>
</tbody>
</table>

Sensitivity = 43/67 = 0.64  
Specificity = 180/341 = 0.53  
Positive predictive value = 43/204 = 0.21  
False positive rate = 1 - specificity = 1 - 0.53 = 0.47

Table 3. 2x2 classification of 408 pregnant females by "true pre-diabetes" status and by a cut-off point ≥5.1 mmol/L for the fasting blood glucose test as one diagnostic criterion.
Computations for sensitivity and specificity were made for all cut-off levels along the range of values of the fasting blood glucose test. The resulting values for sensitivity were plotted against the corresponding values of (1 - specificity) to obtain the receiver operating characteristic curve as shown in. (Figure 2)

![Receiver operating characteristic curve](https://www.intechopen.com)

**Fig. 2.** Receiver operating characteristic curve of fasting blood glucose measurements at the value of 7.8mmol/L for the glucose challenge test. The optimal threshold value of 5.1mmol/L for fasting blood glucose test is marked with the arrow.

As mentioned earlier, the point on the curve that was closest to the upper left hand corner would be the optimum trade-off level for the test. The figure shows that point corresponding to ≥5.1 mmol/L. At this cut-off level, the test had a sensitivity = 0.64 and a specificity = 0.53. The computed positive predictive value was 0.21. Thus, at this cut-off level, the test correctly diagnosed 64% of the true pre-diabetics, missed 36% of these pre-diabetics, but misclassified 47% of normal (of low risk for GDM) pregnant females as pre-diabetics (false positives). The Area Under the Curve was reasonable (AUC=0.60). At this cut-off level, the level of agreement between the fasting blood glucose levels and those of glucose challenge test, as calculated by kappa coefficient is significant (k=0.093, p=0.011). If the sensitivity is to be increased, the cut-off level should be lowered, but it will be at the expense of specificity. For example, at a cut of 4.7 mmol/L (85mg/dl) only 16% of the true pre-diabetics would be misclassified as normal, but on the other hand, 80% of normal females would be misclassified as pre-diabetics (false positives).

4. Discussion

GDM is an asymptomatic condition most of the time, and effectiveness of its detection has not been adequately tested. Based on the American Diabetic Association criteria for
diagnosis of GDM, 17.2% of the studied pregnant females had impaired fasting tolerance (IFT) and 1.4% had provisional diagnosis of GDM. The corresponding results for those who responded to the GCT are 15.2% IGT and 1.2% provisional diagnosis of GDM. These figures are suggestive of the necessity for screening for GDM in our community. They are comparable with the figures of other nearby countries (Al-Mahroos et al., 2005), but still higher than those of the western countries (Naylor et al., 1996; Tsutomu et al., 2002).

Diagnostic levels for GDM remain uncertain. The guidelines present a confusing picture as regards screening tests for GDM. The use of a 4.7 mmol/L (85mg/dl) cut-off for fasting plasma glucose is suggested by some researchers, but others have suggested higher cut-offs (IDF, 2006). Fasting glucose may not be the most appropriate measure however, and the 75g glucose challenge test advocated by the WHO is increasingly used internationally (IDF, 2006).

The aim of the present study was to determine the threshold value of fasting blood glucose for which further testing by the 2hr-glucose challenge test is needed to confirm the pre-diabetic status among pregnant females attending the antenatal clinics of the King Fahd hospital at the National Guard in Riyadh city, Saudi Arabia. Of all pregnant females subjected to the fasting blood glucose testing (n=769), only 408 subjects (53%) complied with the 2hr-glucose challenge test, a finding that may reflect the need for specifying the feasible indication for such GCT, so as not to subject all females for an unnecessary as well as unacceptable test.

The figures of the pre-diabetes by both the fasting blood glucose test (17.2%) and the GCT (15.2%) are nearly comparable, based on the cut-off points recommended by the American Diabetic Association (ADA, 2010). Correlation between the individual values of fasting blood glucose testing and those of 2hr-glucose challenge testing was highly significant (r=0.25,p<0.0001). However, the agreement between the categorical results of both tests (in terms of pre-diabetes, provisional GDM, and normal) was low as calculated by the kappa coefficient (k=0.054,p=0.25). This finding reflect the fact that the cut-off value of 5.6mmol/L for fasting blood glucose test is not the threshold value for the pre-diabetes status, especially when we see that out of those with impaired fasting test, only 18.7 were found with IGT by the GCT. (Table 2)

Thus, this suboptimal accuracy of the cut-off level of 5.6mmol/L will result in the misclassification of subjects. To overcome this problem to a great extent, the receiver operating characteristic curve analysis was used to determine the threshold value of fasting blood glucose. Based on the previously reported high sensitivity and specificity of the GCT (O’Sullivan et al., 1973), it was considered as a gold standard (in detection of the pre-diabetic status) against which to test the validity of different values of fasting blood glucose test. The levels of sensitivity and specificity found in this study for the cut-off value of 5.1mmol/L for fasting blood glucose (64% and 53%) might not suggest the use of this test, especially that in Brazil, examining a range of thresholds, maximum sensitivity (88%) and specificity (78%) was found at 4.9mmol/L (O’Sullivan et al., 1973).

However, in the present study, at this cut-off level of 4.9mmol/L, in spite of the high sensitivity (82%), very low and unacceptable specificity (24%) was attained. Thus, the cut-off level of 5.1mmol/L could be potentially useful. At this level, of all pregnant females subjected to the fasting blood glucose test, only 50% would be tested by the GCT. This may result in better compliance to the GCT. Moreover, if women with clinical characteristics consistent with a high risk of GDM (marked obesity, personal history of GDM, glycosuria, or a strong family history of diabetes) would be considered as the target group for screening (ADA, 2006 &
Dornhorst and Rossi, 1998), this perhaps will increase the validity of the fasting blood glucose threshold value of 5.1mmol/L.

5. Conclusion

From the collective findings of this study, and considering its limitations in terms of testing the validity of fasting blood glucose in defining the pre-diabetics and not the diabetics, it is concluded that the results may be considered preliminary and suggestive for potential validity of advantage of fasting blood glucose test at the specified cut-off point. This strategy allowed 50% of the study population to avoid the glucose challenge test altogether without compromising detection rates. Women with a cut-off value of fasting blood glucose below the threshold of 5.1mmol/L may not need to be subjected to further testing by the GCT. Also, a special consideration to women with high risk for GDM will improve the validity of this threshold, and thus, the unnecessary GCT will be avoided.

6. Acknowledgement

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7. References


Tsutomu, K. et al. (2002). Young men with high normal blood pressure have lower serum adiponectin, smaller LDL, size and higher elevated heart rate than those optimal blood pressure. *Diabetes Care*. Vol. 25, pp. 971, PMID 12032101

Gestational Diabetes mellitus is defined as hyperglycemia with onset or first recognition during pregnancy. The incidence of gestational diabetes is still increasing and this pathological condition has strong association with adverse pregnancy outcomes. Since gestational diabetes can have long-term pathological consequences for both mother and the child, it is important that it is promptly recognized and adequately managed. Treatment of gestational diabetes is aimed to maintain euglycemia and it should involve regular glucose monitoring, dietary modifications, lifestyle changes, appropriate physical activity, and when necessary, pharmacotherapy. Adequate glycemic control throughout the pregnancy can notably reduce the occurrence of specific adverse perinatal and maternal outcomes. In a long-term prospect, in order to prevent development of diabetes later in life, as well to avoid associated complications, an adequate education on lifestyle modifications should start in pregnancy and continue postpartum.

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