Can a Fasting Insulin Level Predict Gestational Diabetes? 

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Introduction

Gestational diabetes mellitus (GDM) is a condition of carbohydrate intolerance that develops in pregnant women who fail to compensate for the insulin resistance associated with the pregnancy. Women with GDM are at increased risk for co-morbidities including gestational hypertension, pre-eclampsia and caesarean delivery. Risk to the offspring of a mother with GDM include conditions such as macrosomia, neonatal hypoglycemia, shoulder dystocia, and birth trauma.

Detection of patients with GDM followed by maintenance during pregnancy is hence essential for the prevention of the adverse outcomes associated with GDM.

Currently, the two most commonly used screening and diagnostic methods in the United States involve either a one-step approach or a two-step approach. These are performed at 24 to 28 weeks gestation.

One-step Approach:

- One 75-gm, 2-hour oral GTT
- Diagnosis is made if any of the following conditions were met (based on American Diabetes Association recommendations):
  - Fasting glucose ≥92
  - 1-HR Glucose ≥180
  - 2-HR Glucose ≥153

Two-step Approach:

Step 1: Initial screening with a 50-gm, 1-hour oral GTT
- Continue if glucose ≥135

Step 2: Diagnostic 100-gm, 3-hour oral GTT
- Diagnosis is made if any of the following conditions were met (based on the Carpenter-Coustan criteria):
  - Fasting Glucose ≥92
  - 1-HR Glucose ≥180
  - 2-HR Glucose ≥153
  - 3-HR Glucose ≥140

There are multiple reasons why an alternative to the GTT and GDT is worthy of investigation:

- glucose solution used for the GTT can cause gastric irritation, delayed emptying, and gastrointestinal osmotic imbalance, leading to nausea and vomiting
- the oral GTT require extended time commitments from the patients, often at an inconvenience
- an earlier detection method may lead to earlier intervention and halt disease progression

Alternatives to the oral screening and GTT have been proposed but appear to be less sensitive and have not been validated in large studies.

Limited studies exist on using fasting insulin as an alternative predictor of GDM.

The Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), a research tool developed by Dr. Matthews et al, used to predict insulin resistance and β-cell deficiency has also not been studied extensively in relation to predicting GDM.

Objectives

In this study, our objective was to determine if measurements of fasting insulin as well as the use of HOMA-IR could predict abnormal results on a 2-hour or 3-hour OGTT.

Methods

Study Population

For the 2-hour OGTT analysis, data was collected on 104 patients. The study was conducted between November 2016 to June 2017 using cohorts from Kern Medical in Bakersfield, California. In this study, all patients had a gestational age of 24 weeks or greater.

For the 3-hour OGTT analysis, data was collected on 120 patients. This was a prospective cohort study performed with patients from multiple private clinics in Bakersfield, CA between November 2016 thru May 2017.

Ages ranged between 16-43 years of age and BMI ranged between 18.9-45.5.

Procedure

Blood for measuring fasting insulin levels was collected at the same time as blood drawn for fasting glucose measurements.

The 3-hour OGTT was considered diagnostic for GDM if one of the three measured values were greater than the values specified by the ADA.

All patients undergoing the 3-hour, 100-gm OGTT had an abnormal 1-hour, 50-gm OGTT (cut-off = 1 hour glucose ≥130mg/dL) performed as part of their routine prenatal care. The 3-hour OGTT was performed after 8 hours of fasting overnight.

The 3-hour OGTT was considered diagnostic for GDM if two of the four measured values were greater than the values specified by the Carpenter-Coustan Criteria.

In the testing the validity of fasting insulin levels and HOMA-IR to predict gestational diabetes as compared to a 3-hour OGTT, two criteria were used in the analysis. Previous studies and meta-analysis have suggested that one abnormal value in 3-hour OGTT carries the same potential for adverse pregnancy outcome as the standard definition of GDM (3 abnormal values):

- Criteria #1 was defined as an abnormal value in any one of three indicators
- Criteria #2 was defined as any two abnormal values

The approach to the 3-hour analysis was identical to that of the 2-hour analysis but was repeated for both Criteria #1 and #2 using fasting insulin and HOMA-IR as individual predictors of gestational diabetes.

Results

Study findings suggest that a fasting insulin level of 115 mg/dL or greater has a sensitivity of 92% and a specificity of 81%.

Based on an ROC analysis, threshold values were determined for FI and HOMA-IR to predict GDM based on the 2-hour test and Criteria #1 and #2 as outlined above for the 3-hour test.

Of the 104 patients in the 2-hour OGTT study, 23 (22.12%) were diagnosed with GDM.

Table 1. Fasting insulin vs 2-HR OGTT (Figure 1)

<table>
<thead>
<tr>
<th>Fasting insulin (FI)</th>
<th>HOMA-IR</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 2.4 (criteria #1)</td>
<td>0.750</td>
<td>0.673</td>
<td>0.880</td>
</tr>
<tr>
<td>≥ 2.32 (criteria #2)</td>
<td>0.775</td>
<td>0.653</td>
<td>0.890</td>
</tr>
</tbody>
</table>

Fasting insulin (FI) is a condition of carbohydrate intolerance and HOMA-IR is a measure of insulin resistance.

The approach to the 3-hour analysis was identical to that of the 2-hour analysis but was repeated for both Criteria #1 and #2 using fasting insulin and HOMA-IR as individual predictors of gestational diabetes.

Conclusions

In the One-step approach, our ROC analysis has shown that a fasting insulin ≥ 14.25 and a HOMA-IR ≥ 2.32 are statistically significant in predicting gestational diabetes mellitus.

In the Two-step approach, similar ROC analysis showed that fasting insulin ≥ 10.75 (criteria #1) or 11.35 (criteria #2) and HOMA-IR ≥ 2.4 (criteria #1) or 2.44 (criteria #2) are also statistically significant in predicting GDM.

In terms of sensitivities and specificities, using FI and HOMA-IR as a predictor of GDM is not an improvement on the current standards (for reference, the 1-hour OGTT with a cut-off of 130mg/dL has a sensitivity and specificity of 88-99% and 66-77% respectively). Likewise, the false negatives and false positive rates using FI to predict GDM are also very high; based on this data, we would not recommend replacing current standards with FI to diagnose GDM.

Given the risk associated with hyperglycemia in early pregnancy on congenital anomalies and subsequent maternal and fetal complications, use of FI and (HOMA-IR) may prove as a cheaper and more time efficient supplementary test in the diagnosis of both gestational and overt diabetes mellitus in pregnancy.

Although the study was limited by a sample size of 234, our findings show promising results. The use of FI to detect overt diabetes earlier in gestation (the first trimester) may aid in better outcomes for mother and fetus by identifying insulin resistant individuals before the standard testing in the last trimester of pregnancy. Further research is warranted based on these results.

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