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 pregnant state. Women with GDM are at increased risk for co-morbidities including gestational hypertension, preeclampsia 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 time **75-gram, 2-hour oral GTT**

Diagnosis is made if any one 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-gram, 1-hour oral GCT**
Continue if glucose ≥135

Step 2: Diagnostic **100-gram, 3-hour oral GTT**

Diagnosis is made if any one of the following conditions were met (based on the Carpenter-Coustan criteria):

Fasting Glucose ≥95
1-HR Glucose ≥180
2-HR Glucose ≥155
3-HR Glucose ≥140

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

- the 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. Matthew 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 130 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 ranges fell between 18.9 – 65.5.

Procedure

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

The 2-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-gram OGTT had an abnormal 1-hour, 50-gram OGTT (cut-off was 1-hour glucose ≥ 135mg/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.

The Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) was calculated as:

HOMA-IR = FI (uIU/ml) x FG (mgm/dl) / 405

In testing the viability of fasting insulin and HOMA-IR to predict gestational diabetes as compared to a 3-hour OGTT, two criterions 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 (2 abnormal values):

- Criteria #1 was defined as an abnormal value in any one of these 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 Criteria #2 using fasting Insulin and HOMA-IR as individual predictors of gestational diabetes.

Results

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)
An FI ≥ **14.25** as an indicator of GDM had a sensitivity/specificity of 0.565/0.901, a positive predictive value (PPV) of 0.619 and a negative predicative value (NPV) of 0.880.

Table 2: HOMA-IR vs 2-HR OGTT
A HOMA-IR value ≥ **2.32** as an indicator of GDM had a sensitivity/specificity of 0.739/0.802, PPV of 0.515 and NPV of 0.915.

For the 3-HR OGTT based on Criteria #1 (one abnormal value), 47 of 115 patients (40.88%) were identified as having GDM.

Table 3. Fasting Insulin vs 3-HR OGTT (Criteria 1)
An FI ≥ **10.75** as as an indicator of GDM had a sensitivity/specificity of 0.745/0.647, PPV of 0.593 and NPV of 0.786.

Table 4. HOMA-IR vs 3-HR OGTT (Criteria 1)
A HOMA-IR value ≥ **2.4** as as an indicator of GDM had a sensitivity/specificity of 0.745 and 0.750 respectively, PPV of 0.673 and NPV of 0.810.

For the 3-HR OGTT based on Criteria #2 (two abnormal values), 29 of 115 patient (25.22%) were identified as having gestational diabetes.

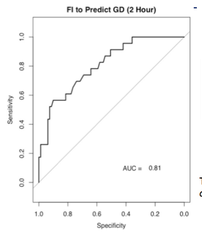
Table 5. Fasting Insulin vs 3-HR OGTT (Criteria 2)
An FI ≥ **13.85** as as an indicator of GDM had a sensitivity/specificity of 0.690/0.733, PPV of 0.465 and NPV of 0.875.

Table 6. HOMA-IR vs 3-HR OGTT (Criteria 2)
A HOMA-IR value ≥ **2.44** as as an indicator of GDM had a sensitivity/specificity of 0.745/0.647, PPV of 0.471 and NPV of 0.922.

All predictors were found to be statistically significant in a logistic regression model (all p-values <= 0.0001).

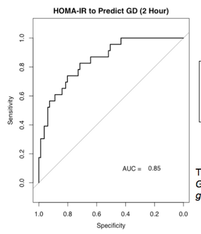
FASTING INSULIN		Gestational Diabetes	
		Yes	No
Predicted Gestational Diabetes	Yes	13	8
	No	10	73

Table 1: *Fasting Insulin as a predictor of Gestational Diabetes compared to a two-hour glucose test.*



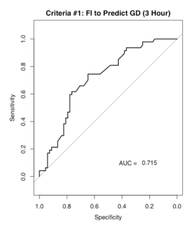
HOMA-IR		Gestational Diabetes	
		Yes	No
Predicted Gestational Diabetes	Yes	17	16
	No	6	65

Table 2: *HOMA-IR as a predictor of Gestational diabetes compared to a two-hour glucose test*



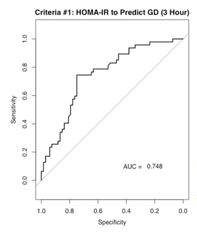
FI Criteria #1		Gestational Diabetes	
		Yes	No
Predicted Gestational Diabetes	Yes	35	24
	No	12	44

Table 3: *Fasting Insulin as a predictor of Gestational Diabetes compared to a three-hour glucose test.*



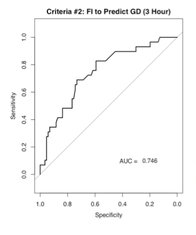
HOMA-IR Criteria #1		Gestational Diabetes	
		Yes	No
Predicted Gestational Diabetes	Yes	35	17
	No	12	51

Table 4: *HOMA-IR as a predictor of Gestational Diabetes compared to a three-hour glucose test.*



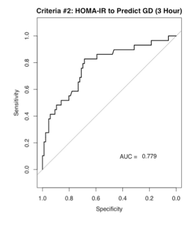
FI Criteria #2		Gestational Diabetes	
		Yes	No
Predicted Gestational Diabetes	Yes	20	23
	No	9	63

Table 5: *Fasting Insulin as a predictor of Gestational Diabetes compared to a three-hour glucose test, criteria #2.*



HOMA-IR Criteria #2		Gestational Diabetes	
		Yes	No
Predicted Gestational Diabetes	Yes	24	27
	No	5	59

Table 6: *HOMA-IR as a predictor of Gestational Diabetes compared to a three-hour glucose test, criteria #2.*



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 **13.85** (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 OGCT 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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