Clinical Significance of a False Positive Glucose Challenge Test in Patients with a High Body Mass Index

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Clinical significance of a false positive glucose challenge test in patients with a high body mass index

Anne Borja, Michael Moretti and Nisha Lakhi*

Abstract

Objective: To determine if there is an increased maternal or neonatal morbidity in overweight and obese patients with a false positive glucose challenge test (GCT).

Methods: Patients with a body mass index (BMI) $\geq$ 25.0 at registration were included in this prospective 36-month study. The study cohort consisted of patients with a false positive (FP) GCT, with two comparison cohorts: those with a (1) screen negative (SN) GCT result and (2) true positive (TP) GCT result. Risks were reported as odd ratios with 95% confidence intervals, with a $P < 0.05$ considered as significant.

Results: There were 60 patients in the FP cohort, 106 in the SN cohort, and 64 in the TP cohort. When the BMI of the FP cohort was compared with either the SN cohort or TP cohort, differences were non-significant (SN 32.3 vs. FP 33.3 kg/m$^2$, $P = 0.067$) and (FP 33.3 vs. TP 34.4 kg/m$^2$, $P = 0.303$). When comparing the FP cohort to the SN cohort, patients in the FP group had significantly more gestational hypertension and pre-eclampsia. There was a trend towards delivering large for gestational weight infants and an infant $\geq 4000$ g in the FP cohort, but this fell short of reaching statistical significance. When comparing the FP to TP cohorts, rates of gestational hypertension, pre-eclampsia, and infants $\geq 4000$ g were similar; however, neonatal morbidity was increased in the TP group.

Conclusions: Overweight and obese patients with a FP glucose challenge screen are more likely to have adverse maternal outcomes. Neonatal morbidity was not increased.

Keywords: false positive glucose challenge test; gestational diabetes; obesity.

Introduction

The risk of developing gestational diabetes mellitus (GDM) is increased 1.3–3.8 times in obese women compared to women of normal body mass index (BMI) [1]. GDM has been shown to increase the risk of both maternal and neonatal morbidity [2]. Because of this correlation, the diagnosis of GDM must be both accurate and precise. Thus, a two-step process has been implemented to confirm the presence of GDM: a screening test [glucose challenge test (GCT)] and a glucose tolerance test (GTT). Previous studies demonstrated conflicting data as to whether there is still an increased risk of adverse maternal and neonatal outcomes after a positive screening test, even if confirmatory testing for GDM is negative [3, 4]. In addition, many factors can affect glucose metabolism including advanced maternal age, BMI, or other medical co-morbidities [2]. Because the incidence of obesity is rising in the US, it is important to identify its role in both GDM testing and pregnancy outcomes. We sought to examine the potential effect of adverse maternal and neonatal outcomes associated with a false positive (FP) GCT in overweight and obese women.

Materials and methods

This study was conducted at Richmond University Medical Center, New York, a high-risk tertiary care center for obstetrics and neonates. Patients that had prenatal care in our OB/GYN clinic during the time period from November 2012 to November 2015 were identified from our clinical database and data was prospectively collected. Patients who had a BMI $\geq 25.0$, underwent an antenatal GCT, and subsequently delivered at our institution were included in the study. Patients with non-singleton gestations were excluded from analysis. All patients received a 1 h 50 g GCT between 24 and 28 weeks’
gestation. Serum glucose levels were measured 1 h after a 50 g glucose challenge was administered orally. If the GCT result was <140 mg/dL, then the test was considered a Screen Negative result (SN). If a GCT result ≥140 mg/dL, a confirmatory 3 h 100 g GTT test was administered. For the confirmatory GTT, a 100 g glucose load was administered orally. Serum glucose levels were measured fasting, and at 1 h, 2 h, and 3 h from the time of the 100 g glucose load administration. We utilized the Carpenter-Coustan criteria for diagnosing GDM, and the following cutoffs were used: fasting: 95 mg/dL, 1 h: 180 mg/dL, 2 h: 155 mg/dL, and 3 h: 140 mg/dL. Serum glucose values above these cutoffs were considered abnormal. When two or more abnormal values were present, a diagnosis of gestational diabetes was established and the test was considered a true positive (TP). If less than two values were abnormal, the GCT result was considered to be a FP (Figure 1).

The study cohort consisted of patients with a FP result. Demographic data, antepartum, intrapartum, as well as neonatal outcomes were compared amongst the FP, SN, and TP cohorts.

Maternal demographic data collected included age and BMI. Antepartum factors included were parity and primigravida status. The intra-partum factors assessed were gestational age at delivery, preterm delivery <34 weeks, preterm delivery 34–36.6 weeks, presence of gestational hypertension (defined as systolic blood pressure of 160 mm Hg or more or a diastolic pressure of 90 mm Hg or more on two occasions at least 4 h apart), preeclampsia (blood pressure according to definition of gestational hypertension with proteinuria: 300 mg of protein or more in a 24-h urine collection or a protein (mg/dL)/creatinine (mg/dL) ratio of 0.3 or higher), presence of maternal fever (temperature ≥100.4°F), mode of delivery, and maternal characteristics of the three groups are summarized in Table 1.

Results

Of the 230 patients who met the inclusion criteria, 106 (46.1%) patients had a negative GCT result and were assigned to the SN cohort. Sixty patients (26.1%) had a positive GCT followed by a negative GTT, and were assigned to the FP cohort. Sixty-four patients (27.8%) had both a positive GCT and GTT, thus were included in the TP cohort. The maternal and neonatal characteristics of the three groups are summarized in Table 1. Significant differences were seen within the three cohorts.
when the patient's age at time of delivery was assessed. Patients in the FP group were older in age when compared to the SN group (SN 26.4 vs. FP 29.8 years, \(P \leq 0.001\)), and patients in the FP group were significantly younger than the TP group (FP 29.8, TP 32.9 years, \(P = 0.001\)). There was a trend towards increasing BMI between cohorts, although it did not reach statistical significance. Patients in the FP cohort had a higher number of births compared to the SN group (SN 1.3 vs. FP 1.9, \(P = 0.043\)), but no significance was seen with the TP group (\(P = 0.372\)). When neonatal and maternal lengths of stay were compared amongst the groups, no differences were seen between the SN and FP group. However, the mean length of neonatal and maternal hospital stay were both longer in the TP group when compared to those with a FP test result (neonatal length of stay FP 3.8 vs. TP 7.6 days, \(P = 0.001\), maternal length of stay FP 3.7 vs. TP 4.2 days, \(P = 0.004\)). There were no differences in gestational age at the time of delivery, fetal weight, and Apgar scores among the three cohorts.

Antepartum, intrapartum, postpartum, and neonatal outcome variables were also compared among the three groups. The data is summarized in Table 2. Significant differences were seen between the SN and FP group. Patients in the FP cohort had significantly higher rates of gestational hypertension (OR 1.14, 95% CI 1.03–1.25, \(P \leq 0.001\)) and pre-eclampsia (OR 3.11, 95% CI 1.98–9.97, \(P = 0.047\)) when compared to the SN group. When the FP cohort was compared to the TP cohort, rates of maternal hypertension, pre-eclampsia, and LGA infants and infants \(\geq 4000\) g were similar. The TP cohort were more likely to have maternal fever (OR 2.45, 95% CI 1.06–5.65, \(P = 0.032\)), cesarean delivery (OR 2.53, 95% CI 1.21–5.28, \(P = 0.019\)), neonatal mechanical ventilation (OR 4.47, 95% CI 1.39–14.38, \(P = 0.007\)), NICU admissions (OR 3.86, 95% CI 1.73–8.64, \(P < 0.001\)), and neonatal hypoglycemia (OR 5.12, 95% CI 1.78–14.74, \(P < 0.001\)), when compared to the FP group.

No differences were seen among the three groups when the following were compared: primigravida status, preterm deliveries, shoulder dystocia, male sex, neonatal seizures/tremors, neonatal hyperbilirubinemia, fetal demise, neonatal death, maternal re-admissions, and maternal wound infections.

**Discussion**

The identification of patients who are at increased risk for adverse maternal or fetal outcomes secondary to impaired glucose tolerance during pregnancy has been an area of longstanding investigation. Many studies have focused...
Table 2: Categorical variables.

<table>
<thead>
<tr>
<th>Variable</th>
<th>SN (n=106)</th>
<th>FP (n=60)</th>
<th>TP (n=64)</th>
<th>P-value comparing SN to FP</th>
<th>OR (95% CI)</th>
<th>P-value comparing FP to TP</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primigravida</td>
<td>24 (22.6)</td>
<td>11 (18.3)</td>
<td>11 (17.2)</td>
<td>0.513</td>
<td>0.900</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preterm delivery &lt; 34 weeks</td>
<td>2 (1.9)</td>
<td>0 (0)</td>
<td>3 (4.7)</td>
<td>0.406</td>
<td>0.131</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preterm delivery 34–36 weeks</td>
<td>6 (5.7)</td>
<td>4 (6.7)</td>
<td>6 (9.4)</td>
<td>0.394</td>
<td>0.506</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational hypertension</td>
<td>0 (0)</td>
<td>7 (11.6)</td>
<td>8 (12.5)</td>
<td>&lt;0.001</td>
<td>1.14 (1.03–1.25)</td>
<td>0.916</td>
<td></td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>5 (4.7)</td>
<td>8 (13.3)</td>
<td>7 (10.9)</td>
<td>0.047</td>
<td>3.11 (1.98–9.97)</td>
<td>0.707</td>
<td></td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>2 (1.9)</td>
<td>0 (0)</td>
<td>1 (1.6)</td>
<td>0.288</td>
<td>0.516</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal fever</td>
<td>18 (17.0)</td>
<td>11 (18.3)</td>
<td>23 (35.9)</td>
<td>0.750</td>
<td></td>
<td>0.032</td>
<td>2.45 (1.06–5.65)</td>
</tr>
<tr>
<td>Cesarean delivery</td>
<td>39 (36.8)</td>
<td>18 (30.0)</td>
<td>34 (53.1)</td>
<td>0.296</td>
<td>0.019</td>
<td>2.53 (1.21–5.28)</td>
<td></td>
</tr>
<tr>
<td>Shoulder dystocia</td>
<td>2 (1.9)</td>
<td>3 (5.0)</td>
<td>0 (0)</td>
<td>0.244</td>
<td>0.110</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>57 (53.8)</td>
<td>30 (50.0)</td>
<td>32 (50.0)</td>
<td>0.596</td>
<td>0.930</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neonatal mechanical ventilation</td>
<td>11 (10.4)</td>
<td>4 (6.7)</td>
<td>15 (23.4)</td>
<td>0.308</td>
<td></td>
<td>0.007</td>
<td>4.47 (1.39–14.38)</td>
</tr>
<tr>
<td>Neonatal seizures/tremors</td>
<td>3 (2.8)</td>
<td>0 (0)</td>
<td>2 (3.1)</td>
<td>0.255</td>
<td></td>
<td>0.256</td>
<td></td>
</tr>
<tr>
<td>Neonatal intensive care unit admission</td>
<td>22 (20.8)</td>
<td>12 (20.0)</td>
<td>31 (48.4)</td>
<td>0.908</td>
<td></td>
<td>&lt;0.001</td>
<td>3.86 (1.73–8.64)</td>
</tr>
<tr>
<td>Low risk for hyperbilirubinemia</td>
<td>72 (67.9)</td>
<td>43 (71.7)</td>
<td>42 (65.6)</td>
<td>0.677</td>
<td></td>
<td>0.637</td>
<td></td>
</tr>
<tr>
<td>Low intermediate risk hyperbilirubinemia</td>
<td>24 (22.6)</td>
<td>9 (15.0)</td>
<td>12 (18.8)</td>
<td>0.225</td>
<td></td>
<td>0.524</td>
<td></td>
</tr>
<tr>
<td>High intermediate risk for hyperbilirubinemia</td>
<td>5 (4.7)</td>
<td>6 (10.0)</td>
<td>7 (10.9)</td>
<td>0.165</td>
<td></td>
<td>0.817</td>
<td></td>
</tr>
<tr>
<td>High risk for hyperbilirubinemia</td>
<td>4 (3.8)</td>
<td>2 (3.3)</td>
<td>1 (1.6)</td>
<td>0.621</td>
<td></td>
<td>0.488</td>
<td></td>
</tr>
<tr>
<td>Neonatal hypoglycemia</td>
<td>5 (4.7)</td>
<td>5 (8.3)</td>
<td>20 (31.3)</td>
<td>0.269</td>
<td></td>
<td>&lt;0.001</td>
<td>5.12 (1.78–14.74)</td>
</tr>
<tr>
<td>Macrosomia ≥4000 g</td>
<td>3 (2.8)</td>
<td>6 (10.0)</td>
<td>10 (15.6)</td>
<td>0.057</td>
<td></td>
<td>0.333</td>
<td></td>
</tr>
<tr>
<td>Macrosomia ≥4500 g</td>
<td>0 (0)</td>
<td>2 (3.3)</td>
<td>4 (6.3)</td>
<td>0.129</td>
<td></td>
<td>0.363</td>
<td></td>
</tr>
<tr>
<td>Large for gestational age</td>
<td>5 (4.7)</td>
<td>7 (11.7)</td>
<td>15 (23.4)</td>
<td>0.086</td>
<td></td>
<td>0.079</td>
<td></td>
</tr>
<tr>
<td>Fetal demise</td>
<td>0 (0)</td>
<td>1 (1.7)</td>
<td>0 (0)</td>
<td>0.361</td>
<td></td>
<td>0.488</td>
<td></td>
</tr>
<tr>
<td>Neonatal death</td>
<td>0 (0)</td>
<td>1 (1.7)</td>
<td>1 (1.6)</td>
<td>0.361</td>
<td></td>
<td>0.736</td>
<td></td>
</tr>
<tr>
<td>Maternal re-admission</td>
<td>3 (2.8)</td>
<td>1 (1.7)</td>
<td>3 (4.8)</td>
<td>0.542</td>
<td></td>
<td>0.328</td>
<td></td>
</tr>
<tr>
<td>Wound infection</td>
<td>3 (2.8)</td>
<td>2 (3.3)</td>
<td>2 (3.1)</td>
<td>0.596</td>
<td></td>
<td>0.666</td>
<td></td>
</tr>
</tbody>
</table>

Values in bold represent significant differences, p < 0.05
on the implications of a FP GCT result; however, the data is conflicting. Grotegut et al. compared 165 women with FP GCT diagnosed by the Carpenter-Coustan criteria to a cohort of SN patients, and found no differences in maternal or neonatal outcomes [4]. In contrast, in a cohort comprising of 164 patients with a FP GCT, Stamilio et al. found a higher incidence of adverse perinatal outcomes compared to patients with a negative GCT result [3]. Interestingly, when Stamilio et al. sub-analyzed data based on patient BMI, they found an inverse relationship between BMI and the adverse perinatal outcomes. As the patient’s BMI increased, adverse perinatal outcomes attributed to a FP GCT result diminished linearly, and became statistically non-significant above a BMI of 25 kg/m². They postulated that maternal obesity could have masked the risk attributed to a FP GCT.

Although previous studies have attempted to elucidate the prognostic significance of a FP glucose screening test [3–6], none have exclusively focused on a group of overweight and obese women. The presence of maternal obesity can be a confounding factor in studies, as obese women are at an increased risk for adverse pregnancy outcomes, independent of a FP GCT result [4]. Adverse outcomes attributed to maternal obesity include preeclampsia, gestational hypertension, GDM, LGA infants, thromboembolism, as well as cardiovascular and metabolic disorders later in life [7].

In this study, overweight and obese patients with a FP GCT result had increased risk of adverse pregnancy complications compared to patients of similar BMI with a SN GCT result. Compared to the SN cohort, patients in the FP group were more likely to have gestational hypertension and pre-eclampsia. Interestingly, the incidence of gestational hypertensive disorders in the FP cohort resembled that of the TP cohort. Additionally the incidence of delivering a LGA infant or an infant ≥4000 g was similar between those in the FP cohort and the gestational diabetics (TP cohort). A trend towards increased shoulder dystocia was noted in the FP cohort compared to those who were SN, however, due to the rarity of this complication, it did not reach statistical significance.

In spite of the increased maternal morbidity in the FP cohort, certain neonatal morbidities, including need for mechanical ventilation, neonatal hypoglycemia, and NICU admission remained higher among the gestational diabetics. Gestational diabetics were also at an increased risk for intrapartum fever and cesarean delivery. The presence of intrapartum fever, combined with neonatal hypoglycemia and mechanical ventilation requirements were significantly higher in the TP cohort, and could have contributed to the increased rate of NICU admissions in this group. Thus, patients in the FP cohort represent an intermediate risk group that may benefit from further testing and close monitoring, especially those with an increased BMI, as this could augment risks.

Similar to other published studies, we show that patients with impaired glucose tolerance have an increased risk for pregnancy complications [2, 5, 6]. The hyperglycemia and adverse pregnancy outcome (HAPO) study prospectively examined 25,505 women that underwent a 75 g oral glucose tolerance test (OGTT) between 24 and 32 weeks of gestation [2]. The study showed an association between increasing maternal glucose levels and the following study outcomes: birthweight above 90th percentile, cesarean delivery, elevated cord serum C-peptide level, preterm delivery, shoulder dystocia, neonatal intensive care unit admission, hyperbilirubinemia, and pre-eclampsia [2]. The levels of maternal glycemia at which adverse outcomes occurred were well below the diagnostic threshold for GDM [2].

The presence of both maternal obesity and impaired glucose tolerance is of increasing concern. A link between pregnancy, adiposity, and insulin resistance was first apparent when it was observed that levels of the pro-inflammatory cytokine, tumor necrosis factor alpha (TNF-α) were increased in the adipose tissue of obese individuals [8]. Elevated levels of TNF-α impair glucose metabolism whereas the antagonism of TNF-α increases insulin sensitivity [8]. In addition, weight-loss was found to be associated with a reduction of TNF-α and reversal of insulin resistance [9]. It has been suggested that the increase in TNF-α and other pro-inflammatory cytokines, such as IL-6, observed in diabetic conditions, might result from oxidative stress and inflammatory changes caused by hyperglycemia [10].

Placental inflammation has been observed in pregnancies complicated by obesity [11] and GDM [12]. In normal pregnancy, a highly regulated inflammatory response is necessary to control several processes of placentation and subsequent placental function [13]. Maternal obesity and GDM have been associated with changes in placental nutrient transporter expression and activity [7]. The changes in placental function may be secondary to altered inflammatory cytokine profiles in the maternal, placental and fetal compartments leading to the co-morbidities observed in these pregnancies [7].

With regard to the fetal compartment, Ategbo et al. demonstrated that macroscopic neonates of GDM mothers had lower levels of adiponectin and leptin when compared to aged matched controls [14]. Adiponectin, a physiologically active polypeptide hormone derived from adipose tissue, exhibits insulin-sensitizing
and anti-inflammatory properties. Leptin functions as an appetite suppressant [7, 14]. The pro-inflammatory mediator, TNF-α, as well as IL-6, may be responsible for inhibiting the insulin sensitizing effects of both adiponectin and leptin [14]. As these hormones have roles in glucose and weight regulation and are synergistic with one another, these findings show why neonates born to GDM mothers are more prone to fetal macrosomia and other associated adverse outcomes.

These findings are especially pertinent to our study. Patients with a TP GCT are diagnosed with GDM, and are therefore receiving the appropriate treatment and are monitored more closely. However, those with a FP GCT may also be at similar risk for several of these adverse outcomes, but they are not being monitored. It is clear from this study, as well as other studies, that women with a FP GCT result are at increased risk for adverse outcomes. Maternal obesity adds an additional risk factor. Therefore, large prospective studies that evaluate the effects of surveillance protocols on pregnancy outcomes in obese women with a FP GCT results are needed.

This is the first study to evaluate maternal and neonatal outcomes associated with a FP GCT result in women with increased BMI. We note some limitations in our study. First, this study is underpowered to assess outcomes that have a prevalence of <6%. Therefore definitive conclusions cannot be inferred based on the non-significance of these variables.

Second, when the GCT was positive, we administered a confirmatory 100 g fasting GTT. Although this is standard in the US, diagnostic protocols differ in other parts of the world. This limits direct comparison to other studies that utilize the 2 h 75 mg OGTT. Differences in mean patient age among cohorts may have also influenced outcomes. Finally, the patients that had a TP test result were diagnosed with gestational diabetes. Therefore, it is possible that their outcomes could have been altered due to the increased surveillance and intervention by providers. Management and treatment of patients diagnosed with gestational diabetes was left to the discretion of the treating obstetrician. We did not stratify patients in the TP cohort based on what therapy they received, or whether diet modification alone or medications were used to optimize glucose control.

**Conclusion**

This study reveals the potential risks of overweight and obese women with FP GCT results may encounter during the course of their pregnancies. Patients with FP GCT results are more likely to experience adverse maternal outcomes than those with a SN GCT. Large prospective studies are needed to determine if the current guidelines and cutoff values used for the GCT and GTT require modification for overweight and obese patients. If patients with increased risks for maternal and fetal adverse events can be identified, appropriate surveillance and monitoring can be established in an attempt to optimize outcomes.

**References**


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