Isolated Hyperglycemia at 1-Hour on Oral Glucose Tolerance Test in Pregnancy Resembles Gestational Diabetes in Predicting Postpartum Metabolic Dysfunction

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\textbf{Running Title:} Gestational Impaired Glucose Tolerance

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ABSTRACT

Objective: Gestational impaired glucose tolerance (GI GT), defined by a single abnormal value on antepartum 3-hour OGTT, is a metabolically heterogeneous disorder. Indeed, the antepartum metabolic phenotype of women with a single abnormal value at 1-hour during the OGTT (1-hr GIGT) resembles that of women with gestational diabetes (GDM), whereas GIGT at 2- or 3-hours (2/3-hr GIGT) is similar to normal glucose tolerance (NGT). Thus, we hypothesized that 1-hr GIGT would be associated with the same adverse outcomes as GDM: (i) increased infant birthweight and (ii) postpartum metabolic dysfunction.

Methods: 361 women underwent (i) antepartum glucose challenge test (GCT) and 3-hr OGTT, (ii) assessment of obstetrical outcome at delivery, and (iii) metabolic characterization by OGTT at 3-months postpartum. The antepartum GCT/OGTT identified 5 study groups: (i) GDM (n=97); (ii) 1-hr GIGT (n=28); (iii) 2/3-hr GIGT (n=34); (iv) abnormal GCT with NGT on OGTT (abnormal GCT NGT)(n=128); and (v) normal GCT with NGT on OGTT (normal GCT NGT)(n=74).

Results: Caesarian-section rate was higher in women with 1-hr GIGT but birthweight did not differ significantly between the non-GDM groups (p=0.1978). At 3-months postpartum, glycemia (area-under-glucose-curve) progressively increased across the groups from normal GCT NGT to abnormal GCT NGT to 2/3-hr GIGT to 1-hr GIGT to GDM (p<0.0001), while both insulin sensitivity (ISOGTT) and beta-cell function (insulinogenic index/HOMA-IR) progressively decreased (p=0.002 and p<0.0001, respectively). The strongest independent negative predictors of insulinogenic index/HOMA-IR were GDM (t=-4.1,p<0.0001) and 1-hr GIGT (t=-3.8,p=0.0002).

Conclusions: Like GDM, 1-hr GIGT is associated with postpartum glycemia, insulin resistance, and beta-cell dysfunction.
Gestational diabetes mellitus (GDM) is associated with significant short-term and long-term consequences (1,2). In the short term, the most pressing concern is an increased risk of adverse obstetrical outcomes related to fetal overgrowth and increased birthweight (1,3). The long-term concern is that women with a history of GDM have chronic insulin resistance and underlying beta-cell dysfunction, leading to a substantially elevated risk of developing type 2 diabetes (T2DM) in the years following the index pregnancy (2,4). Thus, given these potential consequences, pregnant women are commonly screened for GDM by oral glucose tolerance test (OGTT) in late 2nd trimester, whereupon affected women are (i) treated with glucose-lowering therapy (diet, insulin) to improve obstetrical outcome and (ii) advised to undergo testing for T2DM in the postpartum (3,5).

Whereas GDM (diagnosed by 2 abnormal glucose values on 3-hour OGTT in pregnancy) leads to these interventions, gestational impaired glucose tolerance (GIGT) (defined by a single abnormal glucose value on the OGTT) generally does not precipitate any specific treatment recommendations. Traditionally, it has been felt that GIGT represents an intermediate phenotype between normal glucose tolerance (NGT) and GDM (6,7). Interestingly, however, it has recently emerged that GIGT is actually a heterogeneous metabolic disorder, as defined by the glycemic response on the OGTT (8). Specifically, the metabolic phenotype in pregnancy of women with a single abnormal glucose value at 1-hour during the OGTT (1-hr GIGT) resembles that of GDM, as both conditions are characterized by increased severity of glycemia, insulin resistance and decreased circulating adiponectin. In contrast, GIGT at 2- or 3-hours during the OGTT (2/3-hr GIGT) is more similar to NGT (8). In light of these data, we hypothesized that 1-hr GIGT may be associated with the same adverse outcomes as GDM, namely (i) increased infant birthweight and (ii) postpartum hyperglycemia, insulin resistance, and beta-cell dysfunction. Thus, our objective in the current study was to systematically evaluate obstetrical outcomes and postpartum metabolic function in a well-characterized cohort of women stratified by glucose tolerance status in pregnancy, ranging from NGT to 2/3-hr GIGT to 1-hr GIGT to GDM.

**RESEARCH DESIGN AND METHODS**

This analysis was conducted in the setting of an ongoing observational study of early events in the natural history of T2DM, in which a cohort of women recruited at the time of antepartum GDM screening is undergoing longitudinal metabolic characterization in pregnancy and the postpartum period. Standard obstetrical practice at our institution involves universal screening for GDM in all pregnant women at 24-28 weeks’ gestation by 50g glucose challenge test (GCT) followed by, if the GCT is abnormal, referral for a diagnostic OGTT. In the study, healthy pregnant women are recruited in late 2nd trimester, either prior to or just after their GCT. Regardless of the GCT result, all study participants then undergo a 3-hour 100g OGTT for determination of glucose tolerance status in pregnancy. At 3-months postpartum, participants undergo re-assessment by 2-hour 75g OGTT. The study protocol has been approved by the Mount Sinai Hospital Research Ethics Board and all participants have provided written informed consent. The current analysis was restricted to the Caucasian women with singleton pregnancies, who have completed the 3-month postpartum OGTT to date (n=361).

**Baseline Evaluation** - On the morning of the OGTT in pregnancy, data regarding medical, obstetrical, and family history was collected.
by interviewer-administered questionnaire. Anthropometric measurements of height and weight were obtained using a medical scale. Based on the GCT and OGTT, participants were stratified into the following 5 baseline glucose tolerance groups:

(i) **GDM**, defined by National Diabetes Data Group (NDDG) criteria (9) (requires at least 2 of the following on the OGTT:
- fasting glucose $\geq 5.8\text{mmol/L}$,
- 1-hr glucose $\geq 10.6\text{mmol/L}$,
- 2-hr glucose $\geq 9.2\text{mmol/L}$,
- or 3-hr glucose $\geq 8.1\text{mmol/L}$); 

(ii) **1-hr GIGT**, defined by meeting only the 1-hr criterion above

(iii) **2/3-hr GIGT**, defined by meeting either only the 2-hr criterion or only the 3-hr criterion

(iv) **Abnormal GCT NGT**, defined as having an abnormal 50g GCT (1-hour post-challenge)

(v) **Normal GCT NGT**, defined as having a normal GCT followed by NGT on the OGTT.

There was also 1 woman with GIGT based on her fasting glucose value. As isolated fasting hyperglycemia is likely metabolically very different from post-load GIGT, this individual was excluded from the current analysis.

**Obstetrical Outcomes** - Data on obstetrical outcome was obtained from a database that tracks labour and delivery data at Mount Sinai Hospital. LGA was defined as sex-specific birthweight for gestational age above the 90th percentile of Canadian population fetal growth curves (10). Macrosomia was defined as birthweight $\geq 4,000\text{grams}$.

**Postpartum Evaluation** - At 3-months postpartum, participants returned for a 2-hour 75g OGTT. Interviewer-administered questionnaires were completed and physical examination was performed, including measurement of blood pressure (measured twice 5 minutes apart by automatic sphygmomanometer (Dinamap Pro 100-400)), weight and waist circumference.

**Laboratory Measurements and Physiologic Indices** - All OGTTs were performed in the morning after overnight fast. Venous blood samples were drawn for measurement of glucose and insulin at fasting and at 30-, 60- and 120-minutes (and 180-minutes in pregnancy). Specific insulin was measured using the Roche Elecsys 1010 immunoassay analyzer and the electrochemiluminescence immunoassay kit. This assay shows 0.05% cross-reactivity to intact human proinsulin and the primary circulating split form (Des 31,32).

At both baseline and follow-up, glycemia was assessed by the area-under-the-glucose-curve (AUCgluc) during the OGTT, calculated using the trapezoidal rule. Insulin sensitivity was measured using the insulin sensitivity index ($\text{IS}_{\text{OGTT}}$) of Matsuda and DeFronzo (11). In pregnant women, $\text{IS}_{\text{OGTT}}$ exhibits better correlation with insulin sensitivity measured by euglycemic-hyperinsulinemic clamp than either Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) or Quantitative Insulin Sensitivity Check Index (12). Beta-cell function was assessed by the insulinogenic index divided by HOMA-IR (13,14). The insulinogenic index was calculated as the incremental change in insulin concentration during the first 30 minutes of the OGTT divided by the incremental change in glucose during the same time period (15). HOMA-IR was calculated as previously described (16).

**Statistical Analyses** - All analyses were conducted using the Statistical Analysis System (SAS 9.1, SAS Institute, Cary NC). Continuous variables were tested for normality of distribution and natural log transformations of skewed variables were used, where necessary, in subsequent analyses. In Tables 1 and 2, for each study group, continuous variables are presented as median followed by interquartile range if skewed, or mean followed by standard deviation if normally distributed, while
categorical variables are presented as proportions. Univariate differences across the groups in pregnancy (Table 1), at delivery (Table 2), and at 3-months postpartum (Figure 1) were assessed using Analysis of Variance for continuous variables and either $\chi^2$ or Fisher’s exact test for categorical variables. The Turkey-Kramer method was used to account for multiple pairwise comparisons. Multiple linear regression analysis was used to identify the factors at the time of OGTT in pregnancy that independently predicted beta-cell function (log insulinogenic index/HOMA-IR) at 3-months postpartum. Covariates considered included age, pre-pregnancy BMI, weight gain in pregnancy preceding the OGTT, previous GDM, family history of T2DM, and glucose tolerance status in pregnancy (with normal GCT NGT as reference group), in addition to months post-delivery at the time of the postpartum OGTT. A series of models were constructed using these covariates, with the optimal model determined by the adjusted coefficient of multiple determination $R^2_a$ (adjusted R-square) criterion.

RESULTS

Baseline Characteristics of Study Groups - Table 1 shows the baseline characteristics of the 361 study participants stratified into the following 5 glucose tolerance categories in pregnancy: (i) normal GCT NGT (n=74), (ii) abnormal GCT NGT (n=128), (iii) 2/3-hr GIGT group (n=34), (iv) 1-hr GIGT (n=28), and (v) GDM (n=97). There were no significant differences between the groups with respect to mean age, smoking status and parity. Women in the normal GCT NGT group underwent the OGTT in pregnancy slightly later (median 32 weeks’ gestation) than the other four groups (each median 29 weeks)(p<0.0001). As glucose tolerance status worsened, both personal history of previous GDM and family history of diabetes were more prevalent (p=0.0134 and p=0.0382, respectively), and pre-pregnancy BMI increased (p=0.0148). Weight gain in pregnancy preceding the OGTT was greatest in the normal GCT NGT group and lowest in the women with 1-hr GIGT and GDM (overall p<0.0001), but weight gain per week gestation did not differ between the groups (p=0.2159).

The 5 study groups showed marked metabolic differences in pregnancy (Table 1). Indeed, as expected, glycemic parameters (GCT, fasting glucose, AUC$_{gluc}$) all progressively increased from normal GCT NGT to abnormal GCT NGT to 2/3-hr GIGT to 1-hr GIGT to GDM (each trend p<0.0001). Furthermore, both IS$_{OGTT}$ (insulin sensitivity) and insulinogenic index/HOMA-IR (beta-cell function) progressively decreased across the groups in the same manner (both p<0.0001), supporting earlier observations regarding the metabolic heterogeneity of GIGT, wherein 1-hr GIGT resembles GDM in pregnancy.

Obstetrical Outcomes of Study Groups - At delivery, obstetrical outcomes were compared between the 4 non-GDM study groups (Table 2) (women with GDM were not included in this comparison because they would have received antepartum dietary therapy +/- insulin that can affect infant birthweight). There were no significant differences between the 4 non-GDM groups with respect to length of gestation, infant gender or Apgar scores. The Caesarian-section rate increased across the groups from normal GCT NGT (30.6%) to abnormal GCT NGT (34.5%) to 2/3-hr GIGT (45.2%) to 1-hr GIGT (51.9%) (overall p=0.0293). Nevertheless, although mean infant birthweight was highest in 1-hr GIGT, it did not differ significantly between the 4 groups (overall p=0.1978). Furthermore, while clearly less prevalent in women with normal GCT NGT compared to the other groups, both macrosomia and LGA occurred with comparable frequency in the 1-hr GIGT, 2/3-hr GIGT and abnormal GCT NGT groups. Finally, upon adjustment for factors known or
suspected to influence birthweight (including maternal age, pre-pregnancy BMI, gestational weight gain, smoking status, family history of T2DM, length of gestation and infant gender), mean adjusted birthweight did not differ significantly between the groups (normal GCT NGT: 3372g; abnormal GCT NGT: 3424g; 2/3-hr GIGT: 3507g; 1-hr GIGT: 3580g; overall p=0.2471).

Obstetrical outcomes were also compared between all 5 study groups (ie. including GDM). As shown in the Online Table, infant birthweight was significantly different across the 5 groups (overall p=0.0009) (in contrast to the comparison of the 4 non-GDM groups in Table 2). This result was due to the significantly lower birthweight in women with GDM (mean 3256g, standard deviation 452.2), particularly in comparison to those with 1-hr GIGT (mean 3684, standard deviation 501.5) (pairwise p=0.0002). Rates of Caesarian-section and LGA were also lower in GDM compared to 1-hr GIGT, but these differences did not reach statistical significance (Online Table).

**Postpartum Characteristics of Study Groups**

At the 3-months postpartum OGTT, there were no significant differences between the original 5 study groups with respect to months since delivery, blood pressure, low rates of current smoking and high rates of breastfeeding (data not shown). Waist circumference increased across the groups from normal GCT NGT (median [interquartile range]) (85.5cm [79.8-85.0]) to abnormal GCT NGT (85.4 [79.2-94.2]) to 2/3-hr GIGT (88.5 [84.0-97.0]) to 1-hr GIGT (90.1 [83.7-103.8]) to GDM (89.7 [81.0-98.5]) (p=0.0359). Current BMI showed a similar pattern but did not reach statistical significance: normal GCT NGT (24.4 kg/m$^2$ [22.6-27.9]); abnormal GCT NGT (25.9 [23.5-30.2]); 2/3-hr GIGT (26.1 [22.8-30.2]); 1-hr GIGT (26.9 [25.0-31.5]); GDM (26.9 [23.4-31.1]) (p=0.1203). In total, 54 women had abnormal OGTT results at 3-months postpartum.

Importantly, the metabolic differences between the 5 groups that were observed in pregnancy persisted at 3-months postpartum. Indeed, AUC$_{\text{gluc}}$ progressively increased across the groups from normal GCT NGT to abnormal GCT NGT to 2/3-hr GIGT to 1/hr GIGT to GDM (trend p<0.0001)(Figure 1A). Insulin resistance followed the same progression, with IS$_{\text{OGTT}}$ decreasing across the groups (trend p=0.002)(Figure 1B). Of note, for insulin sensitivity, the only between-group comparisons that reached statistical significance were between (i) GDM and normal GCT NGT (pairwise p=0.0217) and (ii) 1-hr GIGT and normal GCT NGT (pairwise p=0.0212). In contrast to the modest differences in insulin sensitivity, the variation in beta-cell function between the 5 study groups was much more profound. As shown in Figure 1C, insulinogenic index/HOMA-IR progressively decreased from normal GCT NGT to abnormal GCT NGT to 2/3-hr GIGT to 1/hr GIGT to GDM (trend p<0.0001). Furthermore, the GDM and 1-hr GIGT groups, in particular, both exhibited markedly decreased beta-cell function, as evidenced by significant pairwise comparisons with both (i) normal GCT NGT (p<0.0001 for GDM and p=0.0001 for 1-hr GIGT) and (ii) abnormal GCT NGT (p=0.0179 for GDM and p=0.0178 for 1-hr GIGT).

Having thus established that GDM and 1-hr GIGT are associated with greater postpartum glycemia than the other study groups and that this glycemia is likely attributable to marked differences in beta-cell function (rather than more modest differences in insulin sensitivity), we sought to determine if these two glucose tolerance groups in pregnancy independently predict postpartum beta-cell dysfunction. On multiple linear regression analysis, the strongest independent and negative predictors of dependent variable log insulinogenic index/HOMA-IR at 3-
months postpartum were indeed GDM (t=-4.14, p<0.0001) and 1-hr GIGT (t=-3.79, p=0.0002). Other weaker independent predictors were a history of GDM in a prior pregnancy (t=-2.94, p=0.0035), 2/3-hr GIGT in the current pregnancy (t=-2.22, p=0.0273) and abnormal GCT NGT (t=-1.98, p=0.0483). These predictors were not significantly changed when the regression analysis was re-run with the exclusion of a single extreme observation (insulinogenic index/HOMA-IR 138 at 3-months postpartum in subject from the abnormal GCT NGT group).

DISCUSSION

In this report, we demonstrate that, in women with GIGT, the timing of the single abnormal glucose value on antepartum OGTT has implications for metabolic function both in pregnancy and in the postpartum. Specifically, in contrast to 2/3-hr GIGT, 1-hr GIGT bears metabolic resemblance to GDM in pregnancy. Furthermore, this similarity with GDM extends to the postpartum, where 1-hr GIGT remains associated with increased glycemia, insulin resistance, and beta-cell dysfunction. Indeed, its independent association with beta-cell dysfunction, in particular, suggests that 1-hr GIGT, like GDM, may predict an increased future risk of T2DM, an important possibility that warrants further study.

The concept that GIGT is a metabolically heterogeneous disorder originally arose from our observation that 1-hr GIGT and GDM were both characterized by greater glycemia, higher insulin resistance and lower circulating levels of the insulin-sensitizing protein adiponectin than 2/3-hr GIGT and NGT in pregnancy (8). Di Cianni and colleagues subsequently reported that 1-hr GIGT was also associated poorer beta-cell function in pregnancy (measured by insulin secretion-sensitivity index) than 2/3-hr GIGT (7). In this context, the current study confirms the idea that 1-hr GIGT represents the more severe metabolic perturbation in pregnancy, characterized by greater glycemia, lower insulin sensitivity, and markedly reduced beta-cell function (measured by insulinogenic index/HOMA-IR). From a clinical perspective, however, the key question is really whether 1-hr GIGT is associated with the same adverse outcomes as GDM, specifically increased infant birthweight and postpartum metabolic dysfunction. The current study was thus designed to address these important issues.

Our findings clearly demonstrate that, like GDM, 1-hr GIGT is associated with significant metabolic dysfunction at 3-months postpartum, including increased glycemia (AUC$_{\text{gluc}}$), greater insulin resistance and poorer beta-cell function. Furthermore, while the differences between the study groups in insulin sensitivity were more modest, the variation in beta-cell function at 3-months postpartum was profound, with insulinogenic index/HOMA-IR markedly reduced in women with 1-hr GIGT and GDM compared to their peers (Figure 1C). Indeed, on multiple linear regression analysis, GDM and 1-hr GIGT emerged as the strongest independent negative predictors of postpartum beta cell function. When one considers that beta-cell dysfunction (i) is felt to underlie the considerable risk of T2DM in women with GDM (2,17) and (ii) recently emerged as the strongest metabolic predictor of progression to T2DM in a longitudinal study of 2115 nondiabetic individuals followed over 6 years (18), the current findings raise the important possibility that women with 1-hr GIGT may face an increased future risk of T2DM. If 1-hr GIGT identifies a high-risk patient population, then postpartum screening for T2DM, akin to that which is currently recommended for GDM, would be indicated. Clearly, this issue demands further study, including long-term follow-up to determine the risk of T2DM and appropriate cost-benefit evaluation of postpartum care strategies.
While the current findings clearly demonstrate that 1-hr GIGT resembles GDM in predicting postpartum metabolic dysfunction, the obstetrical implications of this condition are not certain. Several studies have linked GIGT (without distinction between 1-hr vs 2/3-hr) with an increased risk of adverse obstetrical outcomes related to fetal overgrowth (19-24). Considering that 1-hr GIGT and GDM share a similar metabolic phenotype and that hyperglycemia at 1-hour on OGTT has been associated with an increased likelihood of fetal hyperinsulinemia (25,26), it is reasonable to anticipate that 1-hr GIGT, in particular, may predict increased infant birthweight. Nevertheless, in the current study, although the Caesarian-section rate was highest in the 1-hr GIGT group, there were no significant differences between the 4 non-GDM groups in macrosomia or delivery of an LGA infant. Furthermore, while both unadjusted and adjusted birthweight were highest in the women with 1-hr GIGT, neither result reached statistical significance in comparison across the groups. At present, a few potential explanations may be considered in relation to these observations. First, if 1-hr GIGT is truly associated with increased birthweight, then perhaps the current study was under-powered to detect this relationship. Indeed, since several factors are known to impact infant birthweight (including, most notably, maternal overweight/obesity (27,28)), a large sample size may be required for detection of an otherwise modest effect. Alternatively, it is possible that 1-hr GIGT does not mimic GDM in affecting birthweight. In that case, 1-hr GIGT may provide insight into the physiology of GDM complications, by separating the risk of fetal overgrowth (ie. which 1-hr GIGT does not carry) from the risk of postpartum metabolic dysfunction (which GDM and 1-hr GIGT both share). In any event, further study of this issue is warranted.

A limitation of the current analysis is the relatively modest number of women with GIGT in the study. Nevertheless, it is encouraging that consistent relationships between GIGT subgroups and glycemia, insulin sensitivity and beta-cell function were readily apparent both in pregnancy and at 3-months postpartum, despite the sample size (partly speaking to the strength of these associations). Moreover, this study represents, to our knowledge, the first investigation of the specific effect of 1-hr GIGT on obstetrical outcomes and postpartum metabolic function, and should lead to further studies.

In summary, the metabolic similarity between 1-hr GIGT and GDM extends to the postpartum period. Indeed, both conditions are associated with increased glycemia, insulin resistance and beta-cell dysfunction both in pregnancy and at 3-months postpartum. Furthermore, its independent association with beta-cell dysfunction, in particular, suggests that 1-hr GIGT, like GDM, may predict an increased future risk of T2DM and hence may identify a high-risk patient population that warrants postpartum surveillance.

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Conflicts of Interest. None to declare
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## TABLE 1. Baseline characteristics of study subjects stratified by glucose tolerance status in pregnancy

<table>
<thead>
<tr>
<th></th>
<th>Normal GCT NGT</th>
<th>Abnormal GCT NGT</th>
<th>2/3-hr GIGT</th>
<th>1-hr GIGT</th>
<th>GDM</th>
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<td>n=34</td>
<td>n=28</td>
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<td>34.4 [4.2]</td>
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<td>29.0 [28.0-30.3]</td>
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<td>64.8</td>
<td>76.5</td>
<td>50.0</td>
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<td>23.5</td>
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<td>7.6 [6.5 – 8.3]</td>
<td>9.0 [8.1 – 9.6]</td>
<td>8.3 [7.6 – 8.7]</td>
<td>10.1 [9.5 - 10.8]</td>
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<td>6.0 [5.1 – 6.7]</td>
<td>5.8 [4.6 – 6.8]</td>
<td>8.1 [7.0 – 8.7]</td>
<td>6.4 [5.2 – 7.1]</td>
<td>8.1 [6.7 – 9.1]</td>
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<td>19.5 [2.2]</td>
<td>20.8 [2.4]</td>
<td>24.3 [1.4]</td>
<td>24.9 [1.2]</td>
<td>27.7 [2.3]</td>
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</tr>
<tr>
<td>IS&lt;sub&gt;OGTT&lt;/sub&gt;</td>
<td>5.5 [3.6 - 7.5]</td>
<td>5.4 [3.7 - 7.6]</td>
<td>3.6 [2.8 - 5.2]</td>
<td>3.4 [2.8 - 4.6]</td>
<td>3.3 [2.3 - 5.2]</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Data are presented as median followed by interquartile range, with the exception of (i) age and AUC<sub>gluc</sub> (presented as mean followed by standard deviation) and (ii) family history of diabetes, parity, previous GDM and smoking exposure (presented as percentages).

P-values refer to overall differences across the groups.

AUC<sub>gluc</sub> is the area-under-the-glucose-curve. HOMA-IR is the Homeostasis Model of Assessment for insulin resistance.
## TABLE 2. Obstetrical outcomes per glucose tolerance group in pregnancy (excluding GDM)

<table>
<thead>
<tr>
<th></th>
<th>Normal GCT NGT</th>
<th>Abnormal GCT NGT</th>
<th>2/3-hr GIGT</th>
<th>1-hr GIGT</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>n=74</td>
<td>n=128</td>
<td>n=34</td>
<td>n=28</td>
<td></td>
</tr>
<tr>
<td>Length of gestation (wks)</td>
<td>39.0 [39 - 40]</td>
<td>39.0 [38 - 40]</td>
<td>39.0 [38 - 40]</td>
<td>39.0 [38 - 40]</td>
<td>0.4608</td>
</tr>
<tr>
<td>Caesarian-section (%)</td>
<td>30.6</td>
<td>34.5</td>
<td>45.2</td>
<td>51.9</td>
<td>0.0293</td>
</tr>
<tr>
<td>Infant gender (% M/F)</td>
<td>40/60</td>
<td>54/46</td>
<td>39/61</td>
<td>59/41</td>
<td>0.2319</td>
</tr>
<tr>
<td>1 minute Apgar &lt; 7 (%)</td>
<td>8.3</td>
<td>5.1</td>
<td>3.2</td>
<td>7.4</td>
<td>0.6061</td>
</tr>
<tr>
<td>5 minute Apgar &lt; 7 (%)</td>
<td>0.0</td>
<td>0.0</td>
<td>3.2</td>
<td>0.0</td>
<td>0.2339</td>
</tr>
<tr>
<td>Infant birthweight (g)</td>
<td>3424 [480.7]</td>
<td>3472 [572.8]</td>
<td>3489 [542.4]</td>
<td>3684 [501.5]</td>
<td>0.1978</td>
</tr>
<tr>
<td>Macrosomia (%)</td>
<td>8.1</td>
<td>14.1</td>
<td>17.7</td>
<td>17.9</td>
<td>0.1171</td>
</tr>
<tr>
<td>LGA (%)</td>
<td>5.6</td>
<td>14.3</td>
<td>12.9</td>
<td>14.8</td>
<td>0.1719</td>
</tr>
</tbody>
</table>

Data are presented as percentages, with the exception of length of gestation (presented as median followed by interquartile range) and infant birthweight (presented as mean followed by standard deviation).

P-values refer to overall differences across the groups.

Wks is weeks. M/F is male/female. LGA refers to large-for-gestational-age.
**FIGURE 1.** Glycemia, insulin sensitivity and beta-cell function at 3-months postpartum per glucose tolerance group in pregnancy:

**Panel A – AUC\text{gluc}:**
Trend p<0.0001;
GDM vs normal GCT NGT: p<0.0001; 1-hr GIGT vs normal GCT NGT: p=0.0002;
2/3-hr GIGT vs normal GCT NGT: p=0.0012; abnormal GCT NGT vs normal GCT NGT: p=0.0581;
GDM vs abnormal GCT NGT: p<0.0001; 1-hr GIGT vs abnormal GCT NGT: p=0.0551

**Panel B – ISOGTT:**
Trend p=0.002;
GDM vs normal GCT NGT: p=0.0217; 1-hr GIGT vs normal GCT NGT: p=0.0212

**Panel C – insulinogenic index/HOMA-IR:**
Trend p<0.0001;
GDM vs normal GCT NGT: p<0.0001; 1-hr GIGT vs normal GCT NGT: p=0.0001;
GDM vs abnormal GCT NGT: p=0.0179; 1-hr GIGT vs abnormal GCT NGT: p=0.0178

(For each box-and-whisker plot: line inside box indicates median; upper and lower limits of box indicate 75\textsuperscript{th} and 25\textsuperscript{th} percentiles, upper and lower bars indicate maximum and minimum values; plus sign indicates mean)