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

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OBJECTIVE — Gestational impaired glucose tolerance (GIGT), defined by a single abnormal value on antepartum 3-h oral glucose tolerance test (OGTT), is a metabolically heterogeneous disorder. Indeed, the antepartum metabolic phenotype of women with a single abnormal value at 1 h during the OGTT (1-h GIGT) resembles that of women with gestational diabetes mellitus (GDM), whereas GIGT at 2 or 3 h (2/3-h GIGT) is similar to normal glucose tolerance (NGT). Thus, we hypothesized that 1-h GIGT would be associated with the same adverse outcomes as GDM, i.e., increased infant birth weight and postpartum metabolic dysfunction.

RESEARCH DESIGN AND METHODS — A total of 361 women underwent an antepartum glucose challenge test (GCT) and a 3-h OGTT, assessment of obstetrical outcome at delivery, and metabolic characterization by OGTT at 3 months postpartum. The antepartum GCT/OGTT identified five study groups: GDM ($n = 97$), 1-h GIGT ($n = 28$), 2/3-h GIGT ($n = 34$), abnormal GCT NGT (abnormal GCT with NGT on OGTT) ($n = 128$), and normal GCT NGT (normal GCT with NGT on OGTT) ($n = 74$).

RESULTS — Caesarian section rate was higher in women with 1-h GIGT, but birth weight did not differ significantly between the non-GDM groups ($P = 0.1978$). At 3 months postpartum, glycemia (area under the glucose curve) progressively increased across the groups from normal GCT NGT to abnormal GCT NGT to 2/3-h GIGT to 1-h GIGT to GDM ($P < 0.0001$), while both insulin sensitivity (IS_{OGTT}) and β-cell function (insulinogenic index/homeostasis model assessment of insulin resistance [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-h GIGT ($t = -3.8$, $P = 0.0002$).

CONCLUSIONS — Like GDM, 1-h GIGT is associated with postpartum glycemia, insulin resistance, and β-cell dysfunction.

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G estational diabetes mellitus (GDM) is associated with significant short- 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 birth weight (1,3). The long-term concern is that women with a history of GDM have chronic insulin resistance and underlying β-cell dysfunction, leading to a substantially elevated risk of developing type 2 diabetes 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 treated with glucose-lowering therapy (diet, insulin) to improve obstetrical outcome and advised to undergo testing for type 2 diabetes in the postpartum (3,5).

Whereas GDM (diagnosed by two abnormal glucose values on 3-h 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 h during the OGTT (1-h 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 h during the OGTT (2/3-h GIGT) is more similar to NGT (8). In light of these data, we hypothesized that 1-h GIGT may be associated with the same adverse outcomes as GDM, namely, *1*) increased infant birth weight and *2*) postpartum hyperglycemia, insulin resistance, and β-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-h GIGT to 1-h GIGT to GDM.

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RESEARCH DESIGN AND METHODS

This analysis was conducted in the setting of an ongoing observational study of early events in the natural history of type 2 diabetes, 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 50-g 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 before or just after their GCT. Regardless of the GCT result, all study participants then undergo a 3-h 100-g OGTT for determination of glucose tolerance status in pregnancy. At 3 months postpartum, participants undergo reassessment by 2-h 75-g OGTT. The study protocol was approved by the Mount Sinai Hospital Research Ethics Board, and all participants 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 were 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 five baseline glucose tolerance groups:

1. GDM, defined by National Diabetes Data Group (NDDG) criteria (9), which requires at least two of the following on the OGTT: fasting glucose ≥5.8 mmol/l, 1-h glucose ≥10.6 mmol/l, 2-h glucose ≥9.2 mmol/l, or 3-h glucose ≥8.1 mmol/l
2. 1-h GIGT, defined by meeting only the 1-h criterion above
3. 2/3-h GIGT, defined by meeting either only the 2-h criterion or only the 3-h criterion
4. Abnormal GCT NGT, defined as having an abnormal 50-g GCT (1-h postchallenge plasma glucose ≥7.8 mmol/l) followed by NGT on the

OGTT (defined by meeting none of the NDDG criteria)
5. Normal GCT NGT, defined as having a normal GCT followed by NGT on the OGTT

There was also one woman with GIGT based on her fasting glucose value. Because isolated fasting hyperglycemia is likely metabolically very different from postload GIGT, this individual was excluded from the current analysis.

Obstetrical outcomes

Data on obstetrical outcome were obtained from a database that tracks labor and delivery data at Mount Sinai Hospital (Ontario, Canada). Large for gestation age (LGA) was defined as sex-specific birth weight for gestational age above the 90th percentile of Canadian population fetal growth curves (10). Macrosomia was defined as birth weight ≥4,000 g.

Postpartum evaluation

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

Laboratory measurements and physiologic indexes

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 min (and 180 min 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 (AUC_{gluc}) during the OGTT, calculated using the trapezoidal rule. Insulin sensitivity was measured using the insulin sensitivity index (IS_{OGTT}) of Matsuda and DeFronzo (11). In pregnant women, IS_{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 in-

dex (12). β-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 min 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 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 ± SD 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 (Fig. 1) were assessed using ANOVA for continuous variables and either χ^2 or Fisher's exact test for categorical variables. The Tukey-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 β-cell function (log insulinogenic index/HOMA-IR) at 3 months postpartum. Covariates considered included age, prepregnancy BMI, weight gain in pregnancy preceding the OGTT, previous GDM, family history of type 2 diabetes, and glucose tolerance status in pregnancy (with normal GCT NGT as reference group), in addition to months postdelivery 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 the study groups

Table 1 shows the baseline characteristics of the 361 study participants stratified into the five glucose tolerance categories in pregnancy, namely normal GCT NGT ($n = 74$), abnormal GCT NGT ($n = 128$), 2/3-h GIGT ($n = 34$), 1-h GIGT ($n = 28$), and GDM ($n = 97$). There were no significant differences between the groups with

Table 1—*Baseline characteristics of study subjects stratified by glucose tolerance status in pregnancy*

	Normal GCT NGT	Abnormal GCT NGT	2/3-h GIGT	1-h GIGT	GDM	P
n	74	128	34	28	97	
Age (years)	34.4 ± 4.2	33.9 ± 4.3	34.4 ± 4.4	34.6 ± 3.4	34.4 ± 4.3	0.8975
Weeks gestation	32.0 (31.0–34.0)	29.0 (28.0–30.3)	29.0 (28.0–32.0)	29.0 (28.0–31.0)	29.0 (28.0–31.0)	<0.0001
Prepregnancy BMI (kg/m^2)	22.9 (21.5–25.9)	23.8 (21.2–27.7)	23.1 (22.1–26.0)	26.6 (21.9–30.2)	25.2 (22.2–30.1)	0.0148
Weight gain in pregnancy (kg)	12.8 (10.5–16.4)	10.4 (7.7–13.6)	10.0 (8.2–14.6)	9.3 (6.8–13.6)	9.1 (5.7–13.1)	<0.0001
Weight gain per week (kg/week)	0.4 (0.3–0.5)	0.3 (0.28–0.5)	0.3 (0.28–0.5)	0.4 (0.2–0.45)	0.3 (0.2–0.4)	0.2159
Smoking exposure (%)						0.1170
Never	54.1	64.8	76.5	50.0	72.2	
Remote	44.6	34.4	23.5	46.4	25.8	
Current	1.4	0.8	0.0	3.6	2.1	
Parity (%)						0.7271
Nulliparous	62.2	45.3	55.9	50.0	52.6	
1	32.4	40.6	29.4	32.1	39.2	
>1	5.4	14.1	14.7	17.9	8.3	
Previous GDM/macrosomia (%)	0.0	4.7	8.8	14.3	8.3	0.0134
Family history of diabetes (%)	40.5	48.4	50.0	60.7	55.7	0.0382
Glucose challenge test (mmol/l)	5.7 (5.2–6.6)	8.4 (8.1–9.2)	8.4 (7.7–9.0)	8.4 (7.9–9.2)	8.8 (8.2–9.6)	<0.0001
Fasting glucose (mmol/l)	4.2 (4.0–4.5)	4.4 (4.2–4.6)	4.5 (4.2–4.8)	4.8 (4.5–5.1)	4.6 (4.4–5.1)	<0.0001
1-h glucose (mmol/l)	7.9 (6.9–8.6)	8.6 (7.7–9.3)	9.6 (8.9–10.1)	11.1 (10.8–11.3)	11.1 (10.8–11.8)	<0.0001
2-h glucose (mmol/l)	6.6 (5.9–7.5)	7.6 (6.5–8.3)	9.0 (8.1–9.6)	8.3 (7.6–8.7)	10.1 (9.5–10.8)	<0.0001
3-h glucose (mmol/l)	6.0 (5.1–6.7)	5.8 (4.6–6.8)	8.1 (7.0–8.7)	6.4 (5.2–7.1)	8.1 (6.7–9.1)	<0.0001
AUC$_{gluc}$	19.5 ± 2.2	20.8 ± 2.4	24.3 ± 1.4	24.9 ± 1.2	27.7 ± 2.3	<0.0001
IS$_{OGTT}$	5.5 (3.6–7.5)	5.4 (3.7–7.6)	3.6 (2.8–5.2)	3.4 (2.8–4.6)	3.3 (2.3–5.2)	<0.0001
Insulinogenic Index/HOMA-IR	13.2 (9.6–18.4)	12.8 (8.6–18.9)	8.2 (5.8–11.1)	5.9 (4.0–8.8)	6.3 (3.1–10.2)	<0.0001

Data are median (interquartile range), mean ± SD, or % unless otherwise indicated. P values refer to overall differences across the groups.

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 prepregnancy 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-h GIGT and GDM (overall $P < 0.0001$), but weight gain per week gestation did not differ between the groups ($P = 0.2159$).

The five study groups showed marked metabolic differences in pregnancy (Table 1). Indeed, as expected, glycemic parameters (GCT, fasting glucose, and AUC$_{gluc}$) all progressively increased from normal GCT NGT to abnormal GCT NGT to 2/3-h GIGT to 1-h GIGT to GDM (each trend $P < 0.0001$). Furthermore, both IS$_{OGTT}$ (insulin sensitivity) and insulinogenic index/HOMA-IR (β-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-h GIGT resembles GDM in pregnancy.

Obstetrical outcomes of study groups

At delivery, obstetrical outcomes were compared between the four non-GDM study groups (Table 2). (Women with GDM were not included in this comparison because they would have received antepartum dietary therapy with or without

Table 2—*Obstetrical outcomes per glucose tolerance group in pregnancy (excluding GDM)*

	Normal GCT NGT	Abnormal GCT NGT	2/3-h GIGT	1-h GIGT	P
n	74	128	34	28	
Length of gestation (weeks)	39.0 (39–40)	39.0 (38–40)	39.0 (38–40)	39.0 (38–40)	0.4608
Caesarian section (%)	30.6	34.5	45.2	51.9	0.0293
Infant sex (% male/% female)	40/60	54/46	39/61	59/41	0.2319
1 min Apgar <7 (%)	8.3	5.1	3.2	7.4	0.6061
5 min Apgar <7 (%)	0.0	0.0	3.2	0.0	0.2339
Infant birthweight (g)	3,424 ± 480.7	3,472 ± 572.8	3,489 ± 542.4	3,684 ± 501.5	0.1978
Macrosomia (%)	8.1	14.1	17.7	17.9	0.1171
LGA (%)	5.6	14.3	12.9	14.8	0.1719

Data are %, median (interquartile range), or means ± SD. P values refer to overall differences across the groups.
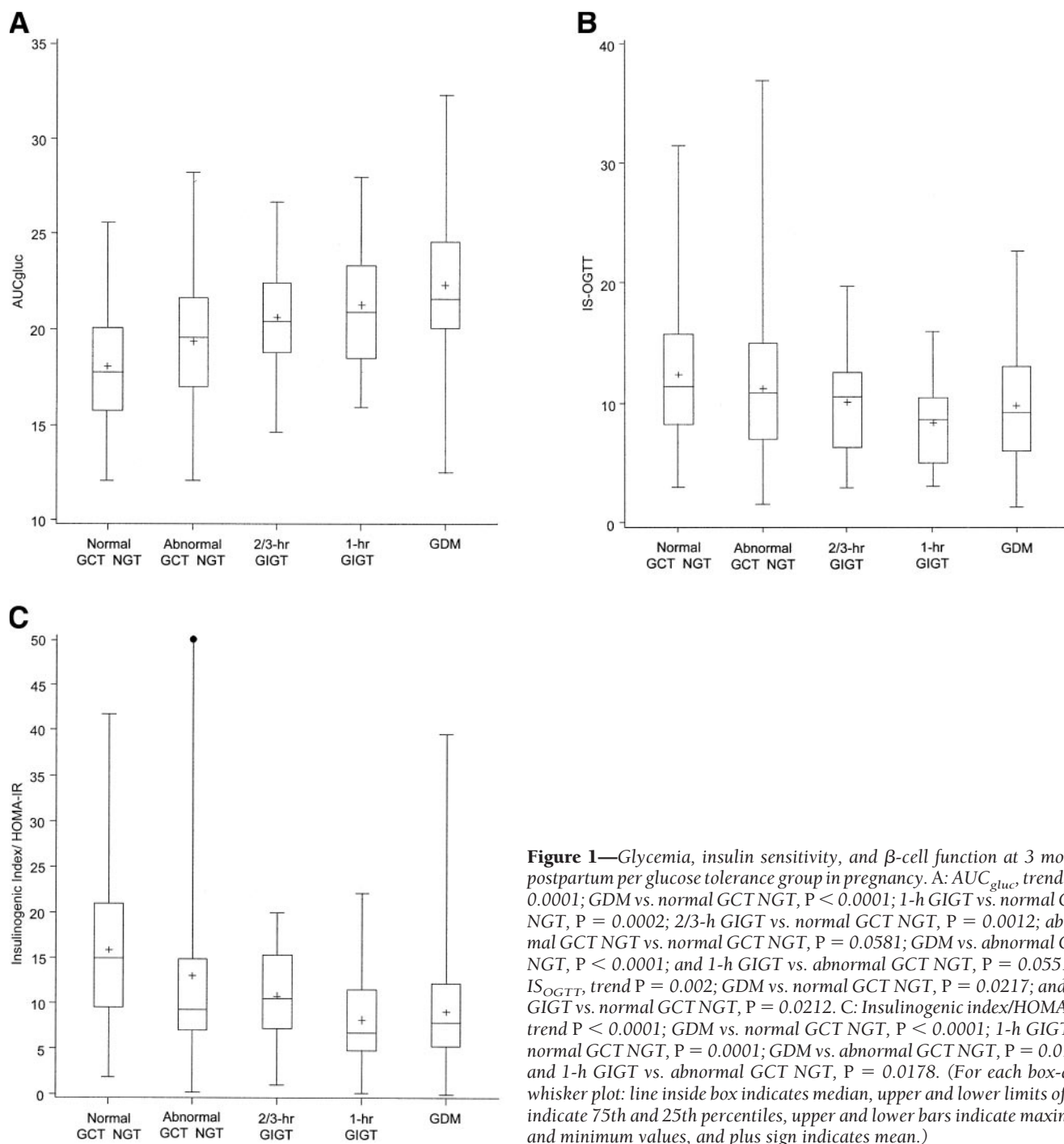
Figure 1—*Glycemia, insulin sensitivity, and β-cell function at 3 months postpartum per glucose tolerance group in pregnancy. A: AUC_{gluc}, trend P < 0.0001; GDM vs. normal GCT NGT, P < 0.0001; 1-h GIGT vs. normal GCT NGT, P = 0.0002; 2/3-h GIGT vs. normal GCT NGT, P = 0.0012; abnormal GCT NGT vs. normal GCT NGT, P = 0.0581; GDM vs. abnormal GCT NGT, P < 0.0001; and 1-h GIGT vs. abnormal GCT NGT, P = 0.0551. B: IS_{OGTT}, trend P = 0.002; GDM vs. normal GCT NGT, P = 0.0217; and 1-h GIGT vs. normal GCT NGT, P = 0.0212. C: Insulinogenic index/HOMA-IR, trend P < 0.0001; GDM vs. normal GCT NGT, P < 0.0001; 1-h GIGT vs. normal GCT NGT, P = 0.0001; GDM vs. abnormal GCT NGT, P = 0.0179; and 1-h 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 75th and 25th percentiles, upper and lower bars indicate maximum and minimum values, and plus sign indicates mean.)*

insulin that can affect infant birth weight.) There were no significant differences between the four non-GDM groups with respect to length of gestation, infant sex, 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-h GIGT (45.2%) to 1-h GIGT (51.9%) (overall $P = 0.0293$). Nevertheless, although mean infant birth weight was highest in 1-h GIGT, it did not differ significantly between the four

groups (overall $P = 0.1978$). Furthermore, while clearly less prevalent in women with normal GCT NGT than in the other groups, both macrosomia and LGA occurred with comparable frequency in the 1-h GIGT, 2/3-h GIGT, and abnormal GCT NGT groups. Finally, upon adjustment for factors known or suspected to influence birth weight (including maternal age, prepregnancy BMI, gestational weight gain, smoking status, family history of type 2 diabetes, length of

gestation, and infant sex), mean adjusted birth weight did not differ significantly between the groups (normal GCT NGT 3,372 g, abnormal GCT NGT 3,424 g, 2/3-h GIGT 3,507 g, and 1-h GIGT 3,580 g; overall $P = 0.2471$).

Obstetrical outcomes were also compared between all five study groups (i.e., including GDM). As shown in the supplementary Table (available in an online appendix at http://dx.doi.org/10.2337/dc07-0126), infant birth weight was

significantly different across the five groups (overall $P = 0.0009$) (in contrast to the comparison of the four non-GDM groups in Table 2). This result was due to the significantly lower birth weight in women with GDM (mean $3,256 \pm 452.2$ g), particularly in comparison to those with 1-h GIGT (mean $3,684 \pm 501.5$ g) (pairwise $P = 0.0002$). Rates of Caesarian section and LGA were also lower in the GDM than in the 1-h GIGT group, but these differences did not reach statistical significance (supplementary Table).

Postpartum characteristics of study groups

At the 3-month postpartum OGTT, there were no significant differences between the original five 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]) (85.5 cm [79.8–85.0]) to abnormal GCT NGT (85.4 [79.2–94.2]) to 2/3-h GIGT (88.5 [84.0–97.0]) to 1-h 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 in the normal GCT NGT (24.4 kg/m^2 [22.6–27.9]), abnormal GCT NGT (25.9 [23.5–30.2]), 2/3-h GIGT (26.1 [22.8–30.2]), 1-h GIGT (26.9 [25.0–31.5]), and GDM (26.9 [23.4–31.1]) groups ($P = 0.1203$). In total, 54 women had abnormal OGTT results at 3 months postpartum.

Importantly, the metabolic differences between the five groups that were observed in pregnancy persisted at 3 months postpartum. Indeed, AUC$_{gluc}$ progressively increased across the groups from normal GCT NGT to abnormal GCT NGT to 2/3-h GIGT to 1/h GIGT to GDM (trend $P < 0.0001$) (Fig. 1A). Insulin resistance followed the same progression, with IS$_{OGTT}$ decreasing across the groups (trend $P = 0.002$) (Fig. 1B). Of note, for insulin sensitivity, the only between-group comparisons that reached statistical significance were between *1*) GDM and normal GCT NGT (pairwise $P = 0.0217$) and *2*) 1-h GIGT and normal GCT NGT (pairwise $P = 0.0212$). In contrast to the modest differences in insulin sensitivity, the variation in β-cell function between the five study groups was much more profound. As shown in Fig. 1C, insulinogenic index/HOMA-IR progressively decreased from normal GCT NGT

to abnormal GCT NGT to 2/3-h GIGT to 1/h GIGT to GDM (trend $P < 0.0001$). Furthermore, the GDM and 1-h GIGT groups, in particular, both exhibited markedly decreased β-cell function, as evidenced by significant pairwise comparisons with both normal GCT NGT ($P < 0.0001$ for GDM and $P = 0.0001$ for 1-h GIGT) and abnormal GCT NGT ($P = 0.0179$ for GDM and $P = 0.0178$ for 1-h GIGT).

Having thus established that GDM and 1-h GIGT are associated with greater postpartum glycemia than the other study groups and that this glycemia is likely attributable to marked differences in β-cell function (rather than more modest differences in insulin sensitivity), we sought to determine whether these two glucose tolerance groups in pregnancy independently predict postpartum β-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-h 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-h 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 rerun 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).

CONCLUSIONS — 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 postpartum. Specifically, in contrast to 2/3-h GIGT, 1-h GIGT bears metabolic resemblance to GDM in pregnancy. Furthermore, this similarity with GDM extends to the postpartum, where 1-h GIGT remains associated with increased glycemia, insulin resistance, and β-cell dysfunction. Indeed, its independent association with β-cell dysfunction, in particular, suggests that 1-h GIGT, like GDM, may predict an increased future risk of type 2 diabetes, an important possibility that warrants further study.

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

Our findings clearly demonstrate that, like GDM, 1-h GIGT is associated with significant metabolic dysfunction at 3 months postpartum, including increased glycemia (AUC$_{gluc}$), greater insulin resistance, and poorer β-cell function. Furthermore, while the differences between the study groups in insulin sensitivity were more modest, the variation in β-cell function at 3 months postpartum was profound, with insulinogenic index/HOMA-IR markedly reduced in women with 1-h GIGT and GDM compared with their peers (Fig. 1C). Indeed, on multiple linear regression analysis, GDM and 1-h GIGT emerged as the strongest independent negative predictors of postpartum β-cell function. When one considers that β-cell dysfunction is believed to underlie the considerable risk of type 2 diabetes in women with GDM (2,17) and that it has recently emerged as the strongest metabolic predictor of progression to type 2 diabetes in a longitudinal study of 2,115 nondiabetic individuals followed over 6 years (18), the current findings raise the important possibility that women with 1-h GIGT may face an increased future risk of type 2 diabetes. If 1-h GIGT identifies a high-risk patient population, then postpartum screening for type 2 diabetes, 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 type 2 diabetes and appropriate cost-benefit evaluation of postpartum care strategies.

While the current findings clearly demonstrate that 1-h 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-h vs. 2/3-h) with an increased risk of adverse obstetrical outcomes related to fetal overgrowth (19–24). Considering that 1-h GIGT and GDM share a similar metabolic phenotype and that hyperglycemia at 1-h on OGTT has been associated with an increased likelihood of fetal hyperinsulinemia (25,26), it is reasonable to anticipate that 1-h GIGT, in particular, may predict increased infant birth weight. Nevertheless, in the current study, although the Caesarian section rate was highest in the 1-h GIGT group, there were no significant differences between the four non-GDM groups in macrosomia or delivery of an LGA infant. Furthermore, while both unadjusted and adjusted birth weight were highest in the women with 1-h 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-h GIGT is truly associated with increased birth weight, then perhaps the current study was underpowered to detect this relationship. Indeed, since several factors are known to impact infant birth weight, 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-h GIGT does not mimic GDM in affecting birth weight. In that case, 1-h GIGT may provide insight into the physiology of GDM complications by separating the risk of fetal overgrowth (i.e., which 1-h GIGT does not carry) from the risk of postpartum metabolic dysfunction, which GDM and 1-h 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 β-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-h GIGT on obstetrical outcomes and postpartum metabolic function and should lead to further studies.

In summary, the metabolic similarity between 1-h GIGT and GDM extends to the postpartum period. Indeed, both conditions are associated with increased glycemia, insulin resistance, and β-cell dysfunction both in pregnancy and at 3 months postpartum. Furthermore, its independent association with β-cell dysfunction, in particular, suggests that 1-h GIGT, like GDM, may predict an increased future risk of type 2 diabetes and hence may identify a high-risk patient population that warrants postpartum surveillance.

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