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Original Article

Insulin secretion and tolerance of women with different gestational glucose regulation one year postpartum

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Abstract: Glucose intolerance during pregnancy is defined as gestational diabetes mellitus (GDM). 95 women after 1 year birth were divided into GDM (*n* = 22), GIGT (gestational impaired glucose tolerance, *n* = 41) and NGT (normal, *n* = 32) groups. The GIGT group was subdivided into GIGT1 (abnormal blood glucose in 1 h, *n* = 11), GIGT2 (in 2 h, *n* = 18) and GIGT3 (in 3 h, *n* = 12) after oral glucose tolerance tests (OGTT). Compared with GIGT and NGT groups, GDM group showed higher FBG, 75 g OGTT 2 h BG, HOMA-IR, BMI, TCH, TG and LDL-C levels, while lower IFI. GIGT group had higher 75 g OGTT 2 h BG and BMI than NGT. IFI level was the lowest, while HOMA-IR the highest in GIGT1 subgroup. GDM women are more susceptible to impaired insulin secretion, insulin tolerance and dyslipidemia. Women in GIGT1 subgroup may tend to developing DM.

Keywords: Diabetes mellitus, gestational, oral glucose tolerance test, postpartum, insulin

Introduction

Gestational diabetes mellitus (GDM) is defined as glucose intolerance that is first detected during pregnancy. This simple definition fails to give a true impression of the complexity of this condition with a resulting wide diversity of opinion regarding its clinical management. During early pregnancy, increases in estrogens, progestins, and other pregnancy-related hormones lead to lower glucose levels, promotion of fat deposition, delayed gastric emptying, and increased appetite. As gestation progresses, however, postprandial glucose levels steadily increase as insulin sensitivity progressively decreases (Gabbe, Niebyl & Simpson, 2002). For glucose control to be maintained in pregnancy, it is necessary for maternal insulin secretion to increase sufficiently to counteract the fall in insulin sensitivity (Sullivan, Henderson & Davis, 1998). Thus, GDM occurs when there is insufficient insulin secretion to counteract the pregnancy-related decrease in insulin sensitivity. It derives of physical insulin tolerance, owing to increasing anti-insulin hormones during pregnancy with the increase in gestational weeks. Usually, insulin tolerance does not disappear completely post-partum and even can eventually produce type 2 diabetes mellitus (T2DM). Specific predictive factors for GDM to T2DM include GDM in the early stages of gestation, higher blood glucose during pregnancy, ethnicity, a family history of diabetic mellitus, and advanced maternal age [1-5].

GDM is a growing global health problem, which threatens the safety of pregnant women and the fetus. Many studies have proved that GDM is associated with a significantly higher risk of later development of T2DM. For example, [6] reported that GDM women had an increased risk of developing T2DM compared with those who had a normoglycemic pregnancy (RR 7.43, 95% CI 4.79-11.51). The highest risk period for the development of T2DM is within 5 years after a GDM pregnancy [7]. As many as 50% of Hispanic women develop type 2 diabetes within 5 years of giving birth [8]. A meta-analysis by [7] revealed that 2.6% to 70% of GDM patients suffered from T2DM postnatally for 6 weeks to 28 years, but especially within 5 years. In the present study, women with gestational abnormal

Table 1. Comparison of 1-year follow-up results of postpartum women in the 3 groups (mean ± SD)

Groups	GDM	GIGT	NGT	*P*
n	22	41	32	
FPG (mmol/L)	6.20 ± 1.40	5.10 ± 1.00	5.00 ± 0.60	0.041
75 g OGTT 2 h (mmol/L)	9.70 ± 2.60	7.20 ± 1.90	5.30 ± 0.70	0.038
DBP (mm Hg[1])	66.00 ± 7.00	67.00 ± 6.00	66.00 ± 6.00	0.261
SBP (mm Hg)	108.00 ± 9.00	108.00 ± 9.00	107.00 ± 8.00	0.312
IFI	2.08 ± 0.43	3.52 ± 0.45	3.66 ± 0.66	0.023
HOMA-IR	5.78 ± 1.58	2.62 ± 0.82	2.45 ± 0.53	0.024
BMI (kg/m^2)	22.50 ± 3.50	19.60 ± 3.40	18.10 ± 3.60	0.019
TCH (mmol/L)	5.04 ± 0.92	3.72 ± 0.77	3.70 ± 0.67	0.034
TG (mmol/L)	3.58 ± 1.90	1.77 ± 0.57	1.62 ± 0.30	0.026
LDL-C (mmol/L)	2.81 ± 0.54	2.01 ± 0.35	1.98 ± 0.30	0.027
HDL-C (mmol/L)	1.33 ± 0.28	1.32 ± 0.29	1.34 ± 0.31	0.327

[1]: 1 mm Hg = 0.133 kPa. FPG, 2-h blood glucose, IFI, HOMA-IR, BMI, TCH, TG and LDL-C. 1. The GDM group *vs.* the NGT group: *SNK q* test = 2.134, 2.409, 2.674, 2.781, 2.211, 2.651, 2.719, 2.341; *P* = 0.037, 0.016, 0.010, 0.007, 0.026, 0.011, 0.009, 0.018. 2. The GDM group *vs.* the GIGT group, SNK *q* test = 2.123, 2.271, 2.594, 2.741, 2.204, 2.331, 2.659, 2.201; *P* = 0.038, 0.024, 0.011, 0.008, 0.027, 0.021, 0.010, 0.030. 3. 2-h blood glucose and BMI. The GIGT group *vs.* the NGT group: *SNK q* test = 2.290, 1.999; *P* = 0.028, 0.048.

glucose tolerance were followed up for 1-year postnatal when blood glucose and fat content was monitored. The objective was to investigate insulin secretion and tolerance 1-year postpartum.

Subjects and methods

Subjects

A total of 336 pregnant women were screened and followed up for 1-year postnatal. They received routine prenatal examinations and were referred to the endocrinology department in the Changzhou No. 2 People's Hospital from the November 2009 to August 2012 for treatment of hyperglycemia, confirmed by the common two-step screening method within the 24th to 28th weeks of pregnancy. They were eligible if they had no previous history of diabetes mellitus (DM), abnormal glucose tolerance, hypertension, dyslipidemia, heart disease, hepatic disease, renal disease, autoimmune disease or other endocrine diseases. Those receiving antidiabetic medicine were excluded from the study. Finally, 95 eligible subjects were divided into the GDM group (n = 22), GIGT group (gestational impaired glucose tolerance, n = 41) and NGT group (normal glucose tolerance, n = 32) according to their glucose tolerance during pregnancy. The GIGT group was further subdivided according to the results of oral glucose tolerance tests (OGTT), into GIGT1 (abnormal blood glucose in 1 h, n = 11), GIGT2 (abnormal blood glucose in 2 h, n = 18) and GIGT3 (abnormal blood glucose in 3 h, n = 12). This study was approved by the Ethics Committee of the Medical College of Soochow University. All subjects provided written informed consent.

Methods

Two-step screening method of GDM: This method consisted of two steps, a 50g glucose challenge test (GCT) and a 75 g oral glucose tolerance test (OGTT). In both tests, patients were instructed to fast for 12 h. In GCT, 50 g of glucose dissolved in 200-300 mL of water was ingested by mouth within a 3 to 5 minute period. If the 1-hour postload glucose level was 7.8 mmol/L or higher, a diagnostic OGTT was indicated, with the same protocols, except for the use of 75 g glucose. Blood samples were taken at zero, 1, 2 and 3 h [9]. GDM was diagnosed if two or more values were equal to or exceeded the upper limits of normal: Fasting: 5.6 mmol/L, 1 h: 10.3 mmol/L, 2 h: 8.6 mmol/L, and 3 h: 6.7 mmol/L while GIGT was confirmed in the presence of only 1 higher value [10].

Postnatal impaired glucose regulation (IGR): A 75 g OGTT was employed 1-year postpartum and zero and 2 h venous glucose levels were measured [9]. DM was established if the FPG was 7.0 mmol/L or higher or if the 2 h glucose level was ≥ 11.1 mmol/L. However, patients with a 2 h glucose level between 7.8 mmol/L and 11.1 mmol/L were classified as having IGT,

Table 2. Comparison of 1-year follow-up results of postpartum women with GIGT history among three subgroups (mean ± SD)

Groups	GIGT1	GIGT2	GIGT3	*P*
n	11	18	12	
BMI (kg/m^2)	19.50 ± 3.30	19.60 ± 3.40	19.60 ± 3.30	0.152
SBP (mmHg)	107.00 ± 8.00	108.00 ± 9.00	108.00 ± 8.00	0.234
DBP(mmHg)	66.00 ± 5.00	67.00 ± 5.00	67.00 ± 6.00	0.325
IFI	3.09 ± 0.02	3.94 ± 0.03	3.95 ± 0.02	0.032
HOMA-IR	3.42 ± 0.02	2.95 ± 0.02	2.95 ± 0.03	0.033
TG (mmol/L)	1.77 ± 0.57	1.76 ± 0.52	1.75 ± 0.53	0.254
TCH (mmol/L)	3.70 ± 0.75	3.72 ± 0.77	3.71 ± 0.72	0.315
LDL-C (mmol/L)	2.01 ± 0.35	2.01 ± 0.35	2.02 ± 0.32	0.216
HDL-C (mmol/L)	1.32 ± 0.28	1.31 ± 0.28	1.32 ± 0.29	0.234

Note: 1. GIGT1 *vs.* GIGT2: *SNK q* test = 2.231, 2.228; *P* = 0.031, 0.036; 2. GIGT1 *vs.* GIGT3: *SNK q* test = 2.230, 2.228; *P* = 0.032, 0.036.

and patients with a FPG between 6.1 mmol/L and 7.0 mmol/L as having IFG [10].

Observation indices

Observation indices included 75 g glucose OGTT results and fasting serum insulin (FINS) levels determined using an electrochemical luminometer (Roche, BIOMED1, Switzerland), *total* cholesterol (TCH), triacylglycerol (TG), *low*-density lipoprotein (LDL-C) and *high*-density lipoprotein (HDL-C) using an automatic biochemical analyzer (AU5431, OLYMPUS, Japan) and fat kits (WAKO, Japan), systolic blood pressure (SBP), diastolic blood pressure (DBP), body mass index (BMI), insulin secretion index (IFI = FINS/FPG) and insulin tolerance (HOMA-IR = FPG × F1NS/22.5).

Statistical analyses

STATA 7.0 was used for the statistical assessment of significance. Abnormal-distributed measurement data (e.g. HOMA-IR) were analyzed after log transformation. Normally distributed measurement data were expressed as the mean ± standard deviation (SD). The averages were compared among groups using variance analysis and between two groups using the SNK q test. $P < 0.05$ was considered to be statistically significant.

Results

Comparison of 1-year follow-up results of postpartum women in the 3 groups

At 1-year postpartum, 9.1% (2/22) and 18.2 (4/22) of GDM women were diagnosed with T2DM and IGT or IFG, respectively, while 9.8% (4/41) of GIGT women had IGT or IFG (**Table 1**).

Comparison of 1-year follow-up results among the 3 subgroups of the GIGT group

The 1-year follow-up results among the 3 subgroups of the GIGT group are compared in **Table 2**.

Discussion

About 25% of GDM women remained glucose intolerant (or became T2DM or IGT) while others finally turned into T2DM after a transient recovery. In the present study, at 1-year postpartum, 9.8% of GIGT patients were diagnosed as IGT or IFG (4/41), 18.2% of GDM as IGT or IFG (4/22) and 9.1% of GDM as T2DM (9.1%). [11] investigated three groups of Chinese women at 5-10 years postpartum, from which DM was diagnosed in 33.3% of patients in the GDM group (15/44), 9.7% in the IGT group (3/31) and 2.6% in the control (normal) group. The results were obtained at 5-10 years postpartum, indicating that the incidence of DM and IGT at 5-10 years postpartum was very high and that the period postpartum 1-4 years is critical. Lee et al. [3] reported that insulin injection during pregnancy was the strongest predictor of postnatal dysglycemia and these women were excluded from the study to avoid the inference of maternal insulin injection on the metabolism of glucose. In the present study, GDM women with abnormal glucose tolerance 1-year postpartum, including T2DM, IGT and IFG, accounted for 27.3% (6/22) of sub-

jects. Similar results were reported by Bian et al. in that at 13 weeks postpartum, women with abnormal postpartum OGTT accounted for 21.8% of cases, in which IFG was 13.6%, T2DM was 5.5% and IGF was 2.8% [11]. These results strongly suggest that GDM mothers have a higher risk of contracting T2DM after delivery and this population should be regularly followed up.

In the present study, the 2h blood glucose level was highest in the GDM group, followed by the GIGT and NGT groups. TCH, TG and LDL-C were statistically higher in the GDM group than the other groups ($P < 0.05$), suggesting that GDM women still suffered from dysglycemia and dyslipidemia at 1-year postpartum. HOMA-IR was statistically higher and IFI was statistically lower in the GDM group than in the other groups ($P < 0.05$), suggesting that compared with the GIGT and NGC women, GDM women were more susceptible to impaired insulin secretion and insulin tolerance.

Following the OGTT results, the GIGT group was further subdivided into GIGT1 (n = 11), GIGT2 (n = 18) and GIGT3 (n = 12) groups to observe if there were any detectable differences in the metabolism of glucose and lipids in the 3 subgroups. We found that HOMA-IR was statistically higher and IFI was statistically lower in the GIGT1 group than in the other 2 subgroups ($P < 0.05$), suggesting that GIGT women with abnormal 1 h blood glucose exhibited more severe insulin tolerance and lower insulin secretion. Therefore, those women should be closely followed in subsequent clinical assessments. However, studies involving many more participants should be conducted to investigate whether this population is more susceptible to IGT and even to T2DM.

Disclosure of conflict of interest

None.

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