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Original Article

Maternal hyperglycemia and the 100-g oral glucose tolerance test

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ABSTRACT

Objectives: To compare the characteristics of pregnant women with hyperglycemia according to the severity of glucose intolerance using the 100-g oral glucose tolerance test (OGTT) and to demonstrate the need to manage the condition of women with mild hyperglycemia.
Materials and methods: In this retrospective cohort study, a total of 258 women at high risk of gestational diabetes (GDM) based on a positive 50-g oral glucose challenge test (OGCT) were classified into 0+, 1+, 2+, 3+, and 4+ groups according to the number of abnormal plasma glucose values on the 100-g OGTT. The clinical characteristics of the groups were compared.
Results: The rates of advanced maternal age (≥ 35 years), multiparity, prior history of GDM, preterm birth, cesarean delivery, and elevated body mass index were all positively correlated with the number of abnormal plasma glucose values on the OGTT ($p < 0.05$ for all variables). After adjusting for confounding factors, the fasting plasma glucose levels predicted birth weight in 44.4%, 48.4%, and 58.6% of the women in the positive 50-g OGCT group, the 0+ group, and the 1+ group, respectively. Weight gain during pregnancy predicted birth weight in 42%, 44.6%, and 37.6% of the women in the positive 50-g OGCT group, the 0+ group, and the 2+ group, respectively ($p < 0.001$ in each case).
Conclusions: These data demonstrate that the detection and management of mild hyperglycemia below the current diagnostic criteria of GDM as well as GDM diagnosed using the 100-g OGTT are necessary for improving pregnancy outcomes.

Introduction

Gestational diabetes mellitus (GDM) is defined as glucose intolerance of variable severity with onset or first recognition during pregnancy [1]. Fetal hyperinsulinemia secondary to maternal hyperglycemia in diabetic mothers leads to large for gestational age (LGA) and macrosomic infants through the stimulatory action of insulin on fetal growth [2]. A large multicenter, multiethnic group study (the HAPO study) of 25,505 women who underwent a 75-g oral glucose tolerance test (OGTT) revealed a continuous, positive relationship among maternal glucose, fetal insulin, and fetal growth, including LGA infants and neonatal adiposity [3,4]. Therefore, fetal hyperinsulinemia in women with GDM and women with hyperglycemia below the diagnostic criteria for GDM may result in increased birth weight and neonatal adiposity through the stimulatory action of insulin. The data from several studies have supported the results of the HAPO study [5,6].

Maternal hyperglycemia that is below the diagnostic criteria for GDM is associated with an increased risk of various adverse maternal and infant outcomes, such as cesarean delivery, preeclampsia, birth injury, macrosomia, and neonatal hypoglycemia [3,5–7]. Fortunately, several clinicians have reported that managing GDM and hyperglycemia that is below the diagnostic criteria for GDM has improved maternal and infant outcomes [8–10]. Therefore, it is necessary to detect and manage maternal hyperglycemia regardless of severity. However, there is no consensus regarding the criteria for screening and diagnosing GDM. Additionally, the management of hyperglycemia below the diagnostic criteria for GDM is not routinely recommended. It is difficult to identify critical blood glucose values for diagnosing GDM, including hyperglycemia of any severity, and to achieve cost-effective management.

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In this study, we compared the characteristics of pregnant women with hyperglycemia according to the severity of glucose intolerance using the 100-g OGTT, and we aimed to demonstrate the necessity of managing women with hyperglycemia that falls below the diagnostic criteria for GDM.

Materials and methods

The medical records of 300 pregnant women who underwent a 100-g OGTT after a positive 50-g oral glucose challenge test (OGCT) and delivered at Uijeongbu St. Mary's Hospital from January 2006 to August 2012 were retrospectively reviewed. Our hospital uses a two-step (screening followed by diagnostic) approach for GDM, as recommended by the American Diabetes Association [11]. Briefly, we perform a 50-g nonfasting OGCT at 24–28 weeks of gestation. If the 1-hour plasma glucose level is > 140 mg/dL, a 100-g OGTT is performed, and plasma glucose levels are measured in the fasting state and at 1 hour, 2 hours, and 3 hours after ingestion of the glucose load. A diagnosis of GDM is made if two or more plasma glucose levels are above the thresholds established by Carpenter and Coustan [12] in 1982, namely fasting ≥ 95 mg/dL, 1 hour ≥ 180 mg/dL, 2 hours ≥ 155 mg/dL, and 3 hours ≥ 140 mg/dL. Hemoglobin A1c level is not part of the diagnostic criteria. In our hospital, women who are diagnosed with GDM undergo consultations regarding nutrition and are encouraged to exercise. Insulin therapy is typically initiated if a fasting glucose < 95 mg/dL or a 2-hour postprandial plasma glucose < 120 mg/dL is not consistently maintained by dietary management.

Women with multiple pregnancies, pregestational diabetes mellitus, or non-Korean ethnicity, and who received insulin therapy for GDM or registered at our hospital after the first trimester, were excluded from the analysis. Therefore, the medical records of 258 pregnant women who were eligible for this study were reviewed. The eligible pregnant women were classified into the 0+ group (n = 93, 36.0%), the 1+ group (n = 38, 14.7%), the 2+ group (n = 54, 20.9%), the 3+ group (n = 47, 18.2%), or the 4+ group (n = 26, 10.1%) according to the number of abnormal plasma glucose values that met or exceeded the threshold levels of the 100-g OGTT. The maternal baseline characteristics, the glucose values in the 50-g OGCT, the glucose values in the 100-g OGTT (fasting, 1-hour, 2-hour, and 3-hour), prepregnancy body mass index (BMI), BMI at the time of the 50-g OGCT, BMI at delivery, weight gain prior to the 50-g OGCT, weight gain during pregnancy, and birth weight were compared among the groups. In all of the women, weight was measured at each visit throughout the pregnancy, and height was measured at the first antenatal care visit. BMI was calculated as body mass (kg) divided by the square of height (m^2) and classified as < 18.5 kg/m^2, 18.5–24.9 kg/m^2, 25–29.9 kg/m^2, or ≥ 30 kg/m^2. Prepregnancy BMI was calculated using the baseline weight (self-reported prepregnancy weight or weight measured at the first visit during early pregnancy when the prepregnancy weight was unknown) and measured height. Weight gain prior to the 50-g OGCT was calculated as the difference between the baseline weight and the weight at the time of the 50-g OGCT. Weight gain during pregnancy was calculated as the baseline weight subtracted from the weight at admission for delivery. Gestational weight gain was recorded both as absolute weight gain in grams and as weight gain categories, as defined by the 2009 Institute of Medicine (IOM) recommendations based on an individual patient's prepregnancy BMI: 12.5–18.0 kg for underweight women with a BMI < 18.5 kg/m^2, 11.5–16.0 kg for normal weight women with a BMI of 18.5–24.9 kg/m^2, 7.0–11.5 kg for overweight women with a BMI of 25.0–29.9 kg/m^2, and 5.0–9.0 kg for obese women with a BMI ≥ 30 kg/m^2 [13]. Birth weight was recorded both as absolute weight (in grams) and as birth weight categories: small for gestational age (SGA; < 10^{th} percentile), appropriate for gestational age (AGA; 10^{th}–90^{th} percentile), LGA (> 90^{th} percentile), and macrosomia (estimated fetal weight ≥ 4000 g). This study was approved by the Institutional Review Board of Uijeongbu St Mary's Hospital at The Catholic University in Seoul, Korea.

All analyses were performed using the SAS 9.2 software (SAS Institute, Cary, NC, USA). Data are expressed as either the mean ± standard deviation for continuous variables with a normal distribution or the median and interquartile range for variables with non-normal distributions. Categorical variables are expressed as numbers and percentages. For analysis of the differences in continuous variables among the groups, data were analyzed using one-way analysis of variance (ANOVA) followed by the *post hoc* Duncan's test for parametric data and the Kruskal–Wallis test followed by the *post hoc* Dunn's test for nonparametric data. Analysis of trends in categorical variables was performed using the Chi-square test and the Cochran–Mantel–Haenszel test with adjustment for confounding factors. Spearman's correlation coefficient was used to evaluate the correlations between several variables and birth weight. Multiple linear regression modeling with adjustment for confounding variables was used for the birth weight prediction analysis. A p value < 0.05 was used to indicate statistical significance.

Results

The mean age of the women studied was 33.8 ± 4.1 years (Table 1). Women in the 2+ and 4+ groups were similar in age and older than those in the other three groups. Maternal age < 35 years, primiparity, and vaginal delivery were associated with fewer abnormal OGTT results, whereas maternal age ≥ 35 years, multiparity, a prior pregnancy complicated by GDM, preterm birth, and cesarean delivery were associated with a higher number of abnormal OGTT results (Table 1). The gestational age at birth in the 4+ group was 37 weeks (range, 34–39 weeks), which was significantly shorter than that in the other four groups (p = 0.0024). The plasma glucose values on the 50-g OGCT were similar in the 1+, 2+, and 3+ groups, but together they were significantly higher than those in the 0+ group and significantly lower than those in the 4+ group (Table 1).

After adjusting for confounding factors (including maternal age, parity, history of prior GDM, and gestational age at birth), prepregnancy BMI was higher in the 4+ group than in the 0+ and 3+ groups (p = 0.031), and BMI at the time of the 50-g OGCT was higher in the 2+ and 4+ groups than in the 0+ group (p = 0.027). After adjusting for confounding factors, prepregnancy BMI, BMI at the time of the 50-g OGCT, and BMI at delivery were all positively correlated with the number of abnormal plasma glucose values on the OGTT (Table 2).

After adjusting for confounding factors (including maternal age, parity, history of prior GDM, gestational age at birth, and prepregnancy BMI), fasting plasma glucose values were similar in the 1+, 2+, and 3+ groups but were together significantly higher than those in the 0+ group and significantly lower than those in the 4+ group (Table 3). Both the 1-hour and 2-hour OGTT plasma glucose levels were noted to increase significantly with increasing numbers of abnormal OGTT results (i.e., from the 0+ group through the 4+ group). This observation also held for the 3-hour OGTT plasma glucose levels, however, the difference in 3-hour plasma glucose levels between the 2+ and 3+ groups failed to reach statistical significance (Table 3).

Overall, women gained a total of 6.0 kg (median, range 4.4–8.4 kg) of weight prior to their 50-g OGCT and 11.4 kg (8.5–14.4 kg) throughout their pregnancy. Weight gain prior to the 50-g OGCT and gestational weight gain were not significantly