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CLINICAL ARTICLE

A Korean multicenter study of prenatal risk factors for overt diabetes during the postpartum period after gestational diabetes mellitus

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ABSTRACT

Objective: To identify prenatal risk factors for postpartum diabetes among pregnant women with gestational diabetes mellitus (GDM). *Methods:* In a retrospective study, baseline characteristics and data from a postpartum 75-g glucose tolerance test (GTT) were reviewed for patients with GDM who had delivered in four Korean tertiary institutions from 2006 to 2012. Clinical characteristics were compared between women with and those without postpartum diabetes. Cutoffs to predict postpartum diabetes and diagnostic values were calculated from receiver operating characteristic (ROC) curves. *Results:* Of 1637 patients with GDM, 498 (30.4%) underwent a postpartum 75-g GTT. Postpartum diabetes was diagnosed in 40 (8.0%) patients and impaired glucose intolerance in 157 (31.5%). Women with postpartum diabetes had higher glycated hemoglobin (HbA_{1c}) levels at GDM diagnosis ($P = 0.008$) and higher 100-g GTT values ($P < 0.05$ for all). In ROC curve analysis, optimal cutoffs for predicting postpartum diabetes were 0.058 for HbA_{1c} level and 5.3 mmol/L (fasting), 10.9 mmol/L (1 h), 10.2 mmol/L (2 h), and 8.6 mmol/L (3 h) for 100-g GTT. The highest sensitivity was observed for 3-h 100-g GTT (76.9%) and the highest positive predictive value was for HbA_{1c} at diagnosis (15.2%). *Conclusion:* HbA_{1c} level at GDM diagnosis and 100-g GTT values could be used to identify patients at high risk of postpartum diabetes who should undergo postpartum screening.

1. Introduction

Gestational diabetes mellitus (GDM) is defined as glucose intolerance of variable degree with onset or first recognition during pregnancy [1]. GDM has been reported to affect 5%–10% of pregnant women, and its worldwide prevalence is continually increasing [1–3].

The association between GDM and adverse pregnancy outcomes such as fetal macrosomia, shoulder dystocia, cesarean delivery, and pregnancy-induced hypertension has been well described [1,4]. Although glucose tolerance returns to normal during the postpartum period for most women with GDM, between 3% and 24% develop overt diabetes mellitus in the first year after childbirth [5–7]. Moreover, a long-term follow-up study [8] indicated that up to 50% of women with GDM developed overt diabetes within 20 years of childbirth. These long-term outcomes provide the basis for the routine recommendation of postpartum evaluation 6–12 weeks after delivery among pregnant women with GDM.

Despite the importance of postpartum follow-up and assessment, the rate of postpartum glucose screening has been reported as less than 50% among women with GDM [5,6,9–14]. Because lifestyle modification and/or suitable medication can prevent or delay the occurrence of abnormal glucose metabolism for women with GDM, early identification of prenatal risk factors predicting postpartum diabetes is regarded as essential in clinical practice [15,16]. In addition, such prenatal risk factors can be used to select women at higher risk for diabetes who could be prioritized for postpartum glucose screening.

Against this background, the aim of the present study was to examine the prevalence of overt diabetes in the postpartum period among women with GDM and to identify prenatal risk factors by using a large data set from four Korean tertiary hospitals. A secondary aim was to determine prenatal cutoff values to predict subsequent diagnosis of diabetes in the postpartum period.

2. Materials and methods

In a retrospective multicenter study, data were reviewed from all parturients with GDM who delivered between January 1, 2006, and December 31, 2012, at four tertiary institutions in Seoul, South Korea:

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Samsung Medical Center, Korea University Hospital, Yonsei University Severance Hospital, and Konkuk University School of Medicine. Patients were included when data for a postpartum 75-g glucose tolerance test (GTT) were available. Patients with known pre-existing diabetes were excluded, as were those with a glycated hemoglobin (HbA_{1c}) level of 0.065 or higher, or a fasting glucose level of 7.0 mmol/L or higher on the prenatal 100-g GTT because these women were considered to have had diabetes before pregnancy. The analysis also excluded patients who underwent an HbA_{1c} test without a 75-g GTT test in the postpartum period because lower levels of HbA_{1c} alone do not exclude the presence of diabetes. The retrospective data collection was approved by the institutional review board of Samsung Medical Center, Sungkyunkwan University School of Medicine. Informed consent from the study population was waived because of the retrospective nature.

All the women had undergone a 50-g GTT as a GDM screening test at 24–28 weeks of pregnancy or earlier depending on their risk factors for GDM (clinically decided by individual clinicians). Diagnosis of GDM was based on the criteria of Carpenter and Coustan [17], which require the presence of two or more of the following values in the 100-g GTT: fasting serum glucose concentration exceeding 5.3 mmol/L, 1-hour serum glucose concentration of 10 mmol/L or higher, 2-hour serum glucose concentration exceeding 8.6 mmol/L, and 3-hour serum glucose concentration exceeding 7.8 mmol/L. The diagnosis of overt diabetes in the postpartum period was based on the results of a 75-g GTT, which was performed 6–12 weeks after delivery. Overt diabetes was defined as having a fasting plasma glucose level of 7 mmol/L or higher, or a 2-hour plasma glucose level of 11.1 mmol/L or higher, as previously used [11]. Blood glucose concentrations were analyzed enzymatically using a Hitachi 760–210 autoanalyzer (Hitachi, Tokyo, Japan). HbA_{1c} was determined by using high-performance liquid chromatography (HLC-723 G8, Tosoh, Tokyo, Japan).

By reviewing medical records, clinical information was collected on maternal age at delivery, length of pregnancy at delivery, parity, pre-pregnancy body mass index (BMI, calculated as weight in kilograms divided by the square of height in meters), maternal weight at delivery, 50-g GTT result, 100-g GTT result, HbA_{1c} at diagnosis, insulin use, neonatal birth weight, past medical history of GDM, delivery of macrosomic neonate (≥4000 g), family history of diabetes, and complications with pre-eclampsia in index pregnancy.

All statistical analyses were performed via SPSS version 21 (IBM, Armonk, NY, USA). Clinical characteristics and prenatal risk factors for postpartum diabetes were compared between patients with overt diabetes and those without using a Student *t* test for continuous variables and a χ^2 test for categorical variables. Receiver operating characteristic (ROC) curve analysis was used to determine the cutoff values to predict the presence of overt diabetes in the postpartum period, and sensitivity, specificity, and positive and negative predictive values were calculated. $P < 0.05$ was considered statistically significant.

3. Results

During the 7-year study period, 1686 women with GDM delivered neonates. Forty-nine women with an HbA_{1c} level of 0.065 or higher or a fasting glucose level of 7 mmol/L during the 100-g GTT were excluded because these women were considered to have had diabetes before pregnancy. Among the remaining 1637 patients with GDM, 498 (30.4%) underwent a postpartum 75-g GTT and were included in the analysis of prenatal risk factors predicting overt diabetes in the postpartum period. A total of 143 women had undergone an HbA_{1c} test without a 75-g GTT in the postpartum period and so were excluded from the analysis.

Overt postpartum diabetes was diagnosed for 40 (8.0%) of the 498 study women. Impaired glucose tolerance (IGT) was also diagnosed for 157 (31.5%). Thus, 301 (60.4%) of women with GDM were found to have normal glucose metabolism after delivery.

Table 1 shows the differences in clinical characteristics between women with postpartum diabetes and those without. Compared with women without overt diabetes, significantly more women with overt diabetes had a history of GDM ($P = 0.007$) and accompanying pre-eclampsia ($P = 0.001$). As expected, women with overt diabetes tended to have higher pre-pregnancy BMI ($P = 0.089$), a higher frequency of multiparity ($P = 0.060$), and a higher rate of previous macrosomia ($P = 0.081$). They also more frequently required insulin treatment than did those without diabetes ($P = 0.068$). HbA_{1c} at GDM diagnosis and all the glucose parameters for maternal blood in the 100-g GTT were significantly higher among women with overt diabetes than among those without diabetes ($P < 0.05$ for all). Glucose level in the 50-g GTT was also higher among women with diabetes than among non-diabetic women, but the difference was not significant ($P = 0.062$). The two groups did not differ significantly with respect to maternal age, neonatal birth weight, cesarean delivery rate, or family history of diabetes.

To determine cutoffs to predict postpartum diabetes using HbA_{1c} at GDM diagnosis and the glucose parameters for maternal blood in the 50-g and 100-g GTTs, ROC curve analysis was performed and the diagnostic capability of each parameter was observed (Fig. 1). The area under the curve (AUC) for HbA_{1c} was 0.676 (95% confidence interval [CI] 0.562–0.789). The AUC for variables in the 100-g GTT was highest for 3-hour glucose levels, followed by 2-hour levels, 1-hour levels, and fasting levels.

The diagnostic performance indices for HbA_{1c} at GDM diagnosis and each parameter in the 50-g and 100-g GTTs were calculated for the prediction of overt diabetes in the postpartum period (Table 2). With an HbA_{1c} cutoff of 0.058, the sensitivity, specificity, positive predictive value, and negative predictive value in predicting overt diabetes in the postpartum period were 63.6%, 72.0%, 15.2%, and 96.2%, respectively. For the 100-g GTT values, a 3-hour glucose level of 8.6 mmol/L as a cutoff showed the highest diagnostic performance indices: the sensitivity, specificity, positive predictive value, and negative predictive value were 76.9%, 65.5%, 13.4%, and 97.6%, respectively. With the selected cutoffs for all values, the negative predictive values were over 95% (Table 2).

Table 1
Clinical characteristics of women with and without postpartum diabetes mellitus.[a]

Clinical characteristic	Diabetic women (n = 40)	Non-diabetic women (n = 458)	*P* value
Maternal age, y	32.9 ± 3.7	33.6 ± 4.1	0.272
Length of pregnancy at delivery, wk	37.2 ± 3.6	38.0 ± 2.2	0.162
Pre-pregnancy BMI	24.3 ± 4.6	23.1 ± 4.2	0.089
Maternal weight at delivery, kg	71.8 ± 12.1	69.6 ± 11.9	0.262
Neonatal birth weight, g	2997 ± 852	3111 ± 609	0.263
Multiparity	24 (60.0)	204 (44.5)	0.060
History of GDM[b]	9/21 (42.9)	36/202 (17.8)	0.007
History of macrosomia[b]	4/23 (17.4)	13/201 (6.5)	0.081
Family history of diabetes[b]	8/39 (20.5)	145/454 (31.9)	0.139
Accompanying pre-eclampsia	5 (12.5)	11 (2.4)	0.001
Cesarean delivery	21 (52.5)	248 (54.1)	0.841
Multiple pregnancy	0	19 (4.1)	0.387
Admission to the neonatal intensive care unit	8 (20.0)	59 (12.9)	0.206
Insulin use	22 (55.0)	184 (40.2)	0.068
HbA_{1c} at GDM diagnosis	0.057 ± 0.004	0.055 ± 0.005	0.008
50-g GTT value, mmol/L	9.8 ± 1.8	9.2 ± 1.5	0.062
100-g GTT value, mmol/L			
Fasting	5.3 ± 0.7	4.9 ± 0.7	0.004
After 1 h	11.4 ± 1.4	10.6 ± 1.6	0.013
After 2 h	11.2 ± 2.0	9.9 ± 1.4	0.002
After 3 h	9.5 ± 1.6	8.1 ± 1.6	<0.001

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); GDM, gestational diabetes mellitus; HbA_{1c}, glycated hemoglobin; GTT, glucose tolerance test.

[a] Values are given as mean ± SD, number (percentage), or number/total number, unless indicated otherwise.

[b] Primiparous patients and those with missing information were omitted from the percentage calculation.