Clinical utility of 1-month postpartum random plasma glucose and glycated hemoglobin combined with pre-pregnancy body mass index for detecting postpartum glucose intolerance in Japanese women with gestational diabetes

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INTRODUCTION

Women with gestational diabetes mellitus (GDM) are at high risk of developing glucose intolerance after delivery. Approximately 20% of women with GDM have impaired glucose tolerance (IGT) during the early postpartum period1. In the long term, women with GDM have a nearly 10-fold higher risk of developing type 2 diabetes mellitus than women with normoglycemic pregnancies2. Therefore, medical societies recommend that women with GDM undergo a 75-g oral glucose tolerance test (OGTT) between 6 and 12 weeks postpartum, and periodically thereafter3,4.

Because of the coronavirus disease 2019 (COVID-19) pandemic, the Japanese Society of Diabetes and Pregnancy (JSDP) proposed a modified postpartum screening method, aiming at reducing the risk of COVID-19 infection by shortening the time spent in the hospital. Specifically, at the 1-month postpartum obstetric checkup, measurement of random plasma glucose (PG) and glycated hemoglobin (HbA1c) was recommended. Patients with random PG ≥200 mg/dL or HbA1c ≥6.5% were treated as having type 2 diabetes mellitus. Patients with HbA1c of 5.7–6.4% and pre-pregnancy body mass index (BMI) ≥25 kg/m² were re-checked with either an OGTT or fasting PG and HbA1c at 6 months. The remainder of the patients were re-checked with either an OGTT or fasting PG and HbA1c at 12 months. However, this modified strategy (hereinafter, referred to as the JSDP criteria) has not been clinically validated. Thus, this current study aimed to evaluate the clinical utility of the JSDP criteria to detect postpartum glucose intolerance based on OGTT carried out within 6 months after delivery.

MATERIALS AND METHODS

Study patients
Among Japanese women who gave birth at Keio University Hospital (Tokyo, Japan) between July 2012 and September...
Glucose intolerance was defined as fasting PG ≥110 mg/dL and 2-h PG <140 mg/dL, impaired fasting glucose was defined as fasting PG 110–125 mg/dL and 2-h PG <140 mg/dL, IGT was defined as fasting PG <126 mg/dL and 2-h PG 140–199 mg/dL, and type 2 diabetes mellitus was defined as fasting PG ≥126 mg/dL or 2-h PG ≥200 mg/dL. Glucose intolerance was defined as impaired fasting glucose, IGT or type 2 diabetes mellitus. The protocol for this research project has been approved by a suitably constituted ethics committee of the institution and it conforms to the provisions of the Declaration of Helsinki. Ethics Committee of Keio University School of Medicine, Approval No. 20110321 (approval date 9 March 2012). A waiver of informed consent was approved because of the retrospective nature of the study.

Statistical analysis
Sensitivity, specificity and predictive value of the JSDP criteria to detect postpartum glucose intolerance based on OGTT after delivery were evaluated. All statistical analyses were carried out using the Statistical Package for the Social Sciences software for Windows version 27.0 (IBM Corp., Armonk, NY, USA).

RESULTS
Patient disposition and characteristics
A total of 721 Japanese women were diagnosed as having GDM during the study period. Among them, 362 (50.2%) underwent OGTT within 180 days after delivery, of whom 312 had random PG and HbA1c measured within 45 days after delivery. Of these women, 37 were excluded as follows: 23 were treated with glucocorticoids or ritodrine hydrochloride at the time of GDM diagnosis, and 14 had multiple pregnancy. As a result, 275 women were included in the final analysis (Figure 1). Table 1 presents the characteristics of the study patients.

Clinical utility of JSDP criteria
At the 1-month postpartum checkup, no patient had random PG ≥200 mg/dL or HbA1c ≥6.5%. Nine (3%) patients had HbA1c of 5.7–6.4% and pre-pregnancy BMI ≥25 kg/m², of whom four (44%) patients were diagnosed as having normal glucose tolerance, and five (56%) as having IGT based on the postpartum OGTT (median 98 days after delivery). A total of 266 (97%) patients did not meet either of the aforementioned criteria, of whom 193 (73%) were diagnosed as having normal glucose tolerance and 73 (27%) as having glucose intolerance based on the postpartum OGTT (Table 2).

Table 3 presents the sensitivity, specificity and predictive value of the JSDP criteria for detecting glucose intolerance based on the postpartum OGTT. Sensitivity was 98.0%, with a negative predictive value of 72.6%. However, sensitivity was 6.4%, with a positive predictive value of 55.6%.

DISCUSSION
In the current study, the JSDP criteria showed high specificity, but low sensitivity, for detecting glucose intolerance. The JSDP states that women negative for these criteria should be rechecked in 12 months during the COVID-19 pandemic. Based on the present results, this strategy is likely to be beneficial in reducing the number of non-urgent postpartum OGTTs and shortening the time spent in hospital. However, the importance of carrying out postpartum OGTT in women with GDM should be noted, because lifestyle intervention for women with glucose intolerance detected by OGTT has been shown to be effective in reducing the progression to type 2 diabetes mellitus.

A meta-analysis of 95,750 women with GDM found that high BMI, family history of type 2 diabetes mellitus, non-white ethnicity, advanced maternal age, early diagnosis of GDM, high PG levels in OGTT, high HbA1c, use of insulin, multiparity, hypertension and preterm delivery were significant risk factors for progression to type 2 diabetes mellitus. We and others have reported that in antepartum OGTT to be a risk factor for postpartum glucose abnormalities in Japanese women with GDM. Lower insulin secretion (i.e., insulinogenic index) and β-cell function (i.e., insulin secretion-sensitivity index 2) have also been shown to be associated with an increased risk of postpartum glucose abnormalities.

Therefore, incorporating the aforementioned risk factors in determining when each individual woman should receive postpartum OGTT might be a reasonable strategy. In addition, a recent study showed that 2-day postpartum OGTT during hospitalization for delivery had similar diagnostic value to 4- to 12-week postpartum OGTT in predicting glucose abnormalities at 1 year after delivery. As testing adherence of nearly 100% can be achieved during hospitalization, and postpartum hospital visits can be minimized, this approach might be especially beneficial during the COVID-19 pandemic.
There were several limitations to the current retrospective study. First, the study was carried out at a single university hospital in Tokyo, and the sample size was small. In

Table 1 | Characteristics of study patients

| Characteristic                              | n = 275 |
|---------------------------------------------|---------|
| Age at delivery (years)                     | 36.9 (33.5–40.2) |
| Pre-pregnancy BMI (kg/m²)                   | 21.2 (19.2–23.0) |
| Nulliparous, n (%)                          | 164 (59.6%) |
| First-degree family history of diabetes, n (%) | 68 (24.7%) |
| GDM in prior pregnancy, n (%)               | 31 (11.3%) |
| Insulin use during pregnancy, n (%)         | 129 (46.9%) |
| GDM diagnosis before 24 weeks of gestation, n (%) | 157 (57.1%) |
| Plasma glucose in antepartum OGTT (mg/dL)   |         |
| Fasting                                     | 89.0 (84.0–93.0) |
| 1-h                                         | 178.0 (151.0–193.0) |
| 2-h                                         | 155.0 (130.0–169.0) |

Data are the median (interquartile range) or n (%). BMI, body mass index; GDM, gestational diabetes mellitus; OGTT, oral glucose tolerance test.

Table 2 | Glucose tolerance status at 1-month postpartum (Japanese Society of Diabetes and Pregnancy criteria) and postpartum oral glucose tolerance test (World Health Organization criteria)

|                          | 1-month postpartum | Postpartum OGTT |
|--------------------------|--------------------|-----------------|
|                          | NGT | IFG | IGT | Type 2 diabetes mellitus | Total |
| (1) Random blood glucose ≥200 mg/dL or HbA1c ≥6.5% | 0   | 0   | 0   | 0   | 0 |
| (2) HbA1c 5.7–6.4% and pre-pregnancy BMI ≥25 kg/m² | 4   | 0   | 5   | 0   | 9 |
| (3) Other than (1) and (2) | 193 | 4   | 61  | 8   | 266 |
| Total no. women          | 197 | 4   | 66  | 8   | 275 |

BMI, body mass index; HbA1c, glycated hemoglobin; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; NGT, normal glucose tolerance; OGTT, oral glucose tolerance test.
Table 3 | Clinical utility of 1-month postpartum random plasma glucose and glycated hemoglobin combined with pre-pregnancy body mass index for detecting glucose intolerance based on postpartum oral glucose tolerance test

| Test         | Sensitivity (%) | Specificity (%) | Positive predictive value (%) | Negative predictive value (%) |
|--------------|-----------------|-----------------|-----------------------------|-------------------------------|
| Glucose intolerance | 6.4             | 98.0            | 55.6                        | 72.6                          |

Glucose intolerance was defined as impaired fasting glucose, impaired glucose tolerance or type 2 diabetes mellitus.

In particular, the median age at delivery of 36.9 years was higher than the general Japanese population (average age at delivery for the first and second baby between 2012–2018 was 30.3–30.7 years and 32.1–32.7 years, respectively)\(^\text{17}\). Second, the rate of postpartum OGTT carried out within 6 months after delivery was 50.2%, which might have caused selection bias. Third, information on breast-feeding, which might have a protective effect on the development of glucose abnormalities\(^\text{18–20}\), was lacking.

In conclusion, the 1-month postpartum random PG and HbA1c combined with pre-pregnancy BMI showed high specificity, but low sensitivity, for detecting glucose intolerance. As women with GDM often discontinue checkups after delivery\(^\text{21}\), it remains important to state that efforts should be focused on preventing missed opportunities for postpartum OGTT during the COVID-19 pandemic. Incorporating risk factors associated with the development of type 2 diabetes mellitus and utilizing postpartum OGTT during hospitalization for delivery might be valuable options, so that women with GDM do not miss the opportunity for early lifestyle intervention, while minimizing the risk of COVID-19 infection.

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DISCLOSURE

The authors declare no conflict of interest.

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