JDI Journal of Diabetes Investigation Open access
Official Journal of the Asian Association for the Study of Diabetes
SHORT REPORT

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

Kazutoshi Sugiyama[1], Yoshifumi Saisho[1]*, Yoshifumi Kasuga[2], Daigo Ochiai[2], Hiroshi Itoh[1]

[1]Division of Endocrinology, Metabolism, and Nephrology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, and [2]Department of Obstetrics and Gynecology, Keio University School of Medicine, Tokyo, Japan

Keywords
Coronavirus disease 2019, Gestational diabetes mellitus, Postpartum glucose intolerance

***Correspondence**
Yoshifumi Saisho
Tel.: +81-3-5363-3797
Fax: +81-3-3359-2745
E-mail address:
ysaisho@keio.jp

J Diabetes Investig 2021; 12: 2242–2246

doi: 10.1111/jdi.13612

ABSTRACT

During the coronavirus disease 2019 pandemic, the Japanese Society of Diabetes and Pregnancy proposed the use of random plasma glucose and glycated hemoglobin measured 1 month after delivery combined with pre-pregnancy body mass index to detect postpartum glucose intolerance instead of carrying out the oral glucose tolerance test in women with gestational diabetes. We retrospectively evaluated the clinical utility of this strategy to detect postpartum glucose intolerance evaluated by the oral glucose tolerance test after delivery. A total of 275 Japanese women with gestational diabetes were included in the present study. The specificity of 1-month postpartum random plasma glucose and glycated hemoglobin combined with pre-pregnancy body mass index to predict postpartum glucose intolerance was 98.0%, with a negative predictive value of 72.6%. However, sensitivity was 6.4%, with a positive predictive value of 55.6%. In conclusion, this Japanese Society of Diabetes and Pregnancy strategy showed high specificity, but low sensitivity, for detecting glucose intolerance postpartum.

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 period[1]. In the long term, women with GDM have a nearly 10-fold higher risk of developing type 2 diabetes mellitus than women with normoglycemic pregnancies[2]. 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 thereafter[3,4].

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/m^2 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.

Received 18 April 2021; revised 6 June 2021; accepted 7 June 2021

MATERIALS AND METHODS

Study patients

Among Japanese women who gave birth at Keio University Hospital (Tokyo, Japan) between July 2012 and September

2020, those with GDM who had random PG and HbA1c measured within 45 days after delivery, and subsequently underwent an OGTT within 180 days after delivery were included in the present retrospective study.

Women underwent two-step screening for GDM with random PG and 1-h 50-g oral glucose challenge test in early and mid-pregnancy, respectively, based on the recommendations of the Japan Society of Obstetrics and Gynecology[5]. Women with a positive screen underwent a diagnostic 75-g OGTT using the International Association of Diabetes and Pregnancy Study Group criteria; that is, fasting PG ≥92 mg/dL, 1-h PG ≥180 mg/dL or 2-h PG ≥153 mg/dL[6]. Those with overt diabetes in pregnancy (fasting PG ≥126 mg/dL or HbA1c ≥6.5%) and pre-pregnancy diabetes were excluded from the present study. In addition, those treated with glucocorticoids or ritodrine hydrochloride at the time of GDM diagnosis, and those with multiple pregnancy were also excluded.

Glucose tolerance status in the postpartum OGTT was defined according to the World Health Organization criteria[7]. Normal glucose tolerance 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/m^2, 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. Specificity 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[8,9].

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[10]. We[11] and others[12,13] have reported 2-h PG 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[11,14,15].

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[16]. 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.

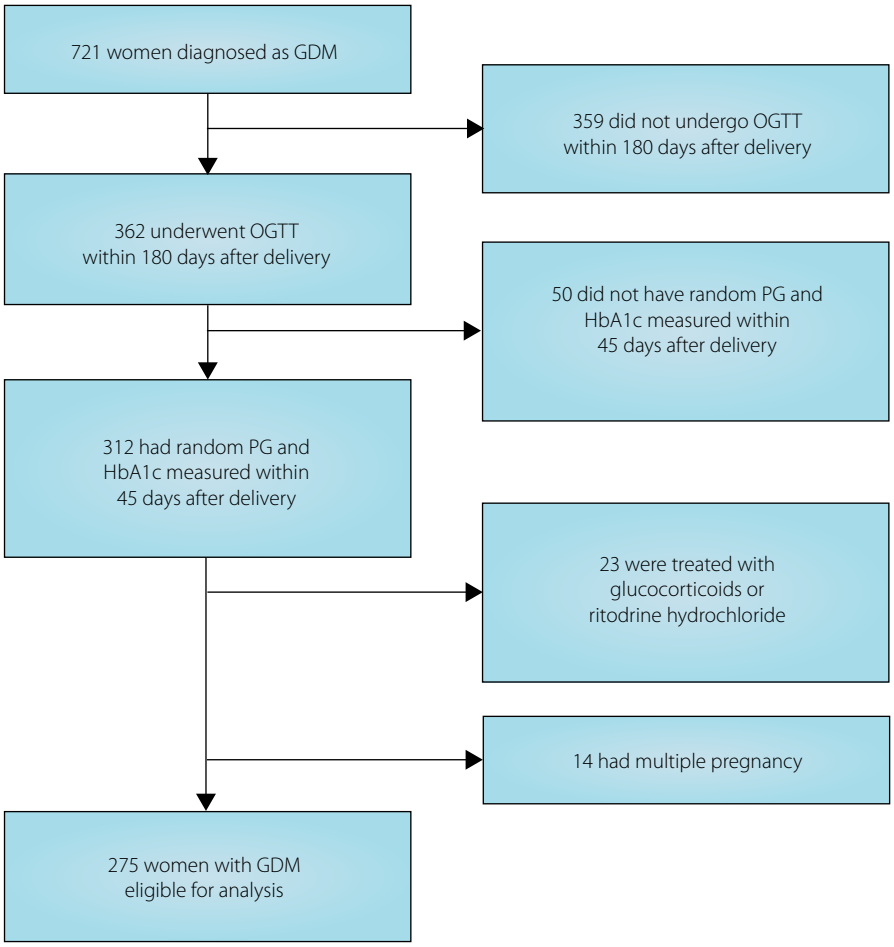

Figure 1 | Flowchart of study participation. GDM, gestational diabetes mellitus; HbA1c, glycated hemoglobin; OGTT, oral glucose tolerance test; PG, plasma glucose.

Table 1 | Characteristics of study patients

Characteristic	*n* = 275
Age at delivery (years)	36.9 (33.5–40.2)
Pre-pregnancy BMI (kg/m^2)	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[7])

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/m^2	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.

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 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

Sensitivity (%)	6.4
Specificity (%)	98.0
Positive predictive value (%)	55.6
Negative predictive value (%)	72.6

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

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)[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[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[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.

ACKNOWLEDGMENTS

The authors thank Wendy Gray, self-employed, for English editing.

DISCLOSURE

The authors declare no conflict of interest.

REFERENCES

1. Kitzmiller JL, Dang-Kilduff L, Taslimi MM. Gestational diabetes after delivery. Short-term management and long-term risks. *Diabetes Care* 2007; 30: S225–235.
2. Vounzoulaki E, Khunti K, Abner SC, *et al*. Progression to type 2 diabetes in women with a known history of gestational diabetes: systematic review and meta-analysis. *BMJ* 2020; 369: m1361.
3. Metzger BE, Buchanan TA, Coustan DR, *et al*. Summary and recommendations of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus. *Diabetes Care* 2007; 30: S251–S260.
4. Araki E, Goto A, Kondo T, *et al*. Japanese clinical practice guideline for diabetes 2019. *Diabetol Int* 2020; 11: 165–223.
5. Minakami H, Maeda T, Fujii T, *et al*. Guidelines for obstetrical practice in Japan: Japan Society of Obstetrics and Gynecology (JSOG). and Japan Association of Obstetricians and Gynecologists (JAOG) 2014 edition. *J Obstet Gynaecol Res* 2014; 40: 1469–1499.
6. Metzger BE, Gabbe SG, Persson B, *et al*. International Association of Diabetes and Pregnancy Study Groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care* 2010; 33: 676–682.
7. World Health Organization. Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia: report of a WHO/IDF consultation 2006. Available from http://apps.who.int/iris/bitstream/handle/10665/43588/9241594934_eng.pdf;jsessionid=933BA5CF8C257DC18840A4017F106857?sequence=1. Accessed June 5, 2021.
8. Ratner RE, Christophi CA, Metzger BE, *et al*. Prevention of diabetes in women with a history of gestational diabetes: effects of metformin and lifestyle interventions. *J Clin Endocrinol Metab* 2008; 93: 4774–4779.
9. Aroda VR, Christophi CA, Edelstein SL, *et al*. The effect of lifestyle intervention and metformin on preventing or delaying diabetes among women with and without gestational diabetes: the Diabetes Prevention Program outcomes study 10-year follow-up. *J Clin Endocrinol Metab* 2015; 100: 1646–1653.
10. Rayanagoudar G, Hashi AA, Zamora J, *et al*. Quantification of the type 2 diabetes risk in women with gestational diabetes: a systematic review and meta-analysis of 95,750 women. *Diabetologia* 2016; 59: 1403–1411.
11. Kasuga Y, Miyakoshi K, Tajima A, *et al*. Clinical and genetic characteristics of abnormal glucose tolerance in Japanese women in the first year after gestational diabetes mellitus. *J Diabetes Investig* 2019; 10: 817–826.
12. Kugishima Y, Yasuhi I, Yamashita H, *et al*. Risk factors associated with the development of postpartum diabetes in Japanese women with gestational diabetes. *BMC Pregnancy Childbirth* 2018; 18: 19.
13. Inoue H, Ishikawa KO, Takeda K, *et al*. Postpartum risk of diabetes and predictive factors for glucose intolerance in East Asian women with gestational diabetes. *Diabetes Res Clin Pract* 2018; 140: 1–8.
14. Kojima N, Tanimura K, Deguchi M, *et al*. Risk factors for postpartum glucose intolerance in women with gestational diabetes mellitus. *Gynecol Endocrinol* 2016; 32: 803–806.
15. Kugishima Y, Yasuhi I, Yamashita H, *et al*. Risk factors associated with abnormal glucose tolerance in the early postpartum period among Japanese women with gestational diabetes. *Int J Gynaecol Obstet* 2015; 129: 42–45.
16. Werner EF, Has P, Rouse D, *et al*. Two-day postpartum compared with 4- to 12-week postpartum glucose

tolerance testing for women with gestational diabetes. *Am J Obstet Gynecol* 2020; 223: e431–439.e437.
17. Cabinet Office, Government of Japan. Annual Report on the Declining Birthrate 2020 (in Japanese). Available from: https://www8.cao.go.jp/shoushi/shoushika/whitepaper/measures/w-2020/r02pdfhonpen/pdf/s1-3.pdf Accessed June 5, 2021.
18. Gunderson EP, Hedderson MM, Chiang V, *et al*. Lactation intensity and postpartum maternal glucose tolerance and insulin resistance in women with recent GDM: the SWIFT cohort. *Diabetes Care* 2012; 35: 50–56.
19. Gunderson EP, Hurston SR, Ning X, *et al*. Lactation and progression to type 2 diabetes mellitus after gestational diabetes mellitus: a prospective cohort study. *Ann Intern Med* 2015; 163: 889–898.
20. Yasuhi I, Soda T, Yamashita H, *et al*. The effect of high-intensity breastfeeding on postpartum glucose tolerance in women with recent gestational diabetes. *Int Breastfeed J* 2017; 12: 32.
21. Pastore I, Chiefari E, Vero R, *et al*. Postpartum glucose intolerance: an updated overview. *Endocrine* 2018; 59: 481–494.