

Diagnosis of more gestational diabetes lead to better pregnancy outcomes: Comparing the International Association of the Diabetes and Pregnancy Study Group criteria, and the Carpenter and Coustan criteria

En-Tzu Wu^{1†}, Feng-Jung Nien^{2†}, Chun-Heng Kuo³, Szu-Chi Chen³, Kuan-Yu Chen⁴, Lee-Ming Chuang⁵, Hung-Yuan Li^{5*‡}, Chien-Nan Lee^{6*‡}

¹Department of Obstetrics and Gynecology, Dianthus MFM Clinic, Departments of ⁵Internal Medicine, and ⁶Obstetrics and Gynecology, National Taiwan University Hospital, Taipei, ²Department of Internal Medicine, National Taiwan University Hospital, Yun-lin Branch, Yun-lin, ³Department of Internal Medicine, New Taipei City Hospital, New Taipei City, and ⁴Department of Internal Medicine, National Taiwan University Hospital, Hsin-Chu Branch, Hsin-Chu, Taiwan

Keywords

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*Correspondence

Chien-Nan Lee

Tel: +886-2-2312-3456 ext. 70919

Fax: +886-2-2351-7459

E-mail address: leecn@ntu.edu.tw

Hung-Yuan Li

Tel: +886-2-23123456 ext. 63540

Fax: +886-2-23123456 ext. 63486

E-mail address: larsli@ntuh.gov.tw

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ABSTRACT

Aims/Introduction: The International Association of the Diabetes and Pregnancy Study Group (IADPSG) criteria for gestational diabetes are associated with increased prevalence. However, it remains unknown if intervention for more women with gestational diabetes mellitus by the IADPSG criteria results in better pregnancy outcomes than adopting the Carpenter and Coustan (C&C) criteria in Asian populations.

Materials and Methods: This was a retrospective cohort study. A total of 1,840 women, 952 subjects by the IADPSG criteria and 888 subjects by the C&C criteria, who delivered singletons in 2011 in a single tertiary center, were included in the study. The same therapeutic interventions were offered to women with gestational diabetes mellitus by the two criteria. Maternal and neonatal outcomes were evaluated.

Results: Adopting the IADPSG criteria increased the prevalence of gestational diabetes mellitus diagnosis to 13.44%, compared with 2.59% by the C&C criteria. The diagnosis was made 3 weeks earlier by the IADPSG criteria (27 vs 30.5 weeks, $P < 0.0001$). Adopting the IADPSG criteria was associated with reduced risk of primary cesarean section (adjusted odds ratio 0.79, 95% confidence interval 0.63–0.998, $P < 0.05$) and having any one of the adverse fetal outcomes (adjusted odds ratio 0.79, 95% confidence interval 0.64–0.998, $P < 0.05$), including birthweight >90th percentile, jaundice, admission to neonatal intensive care unit, birth trauma, neonatal hypoglycemia and fetal death.

Conclusions: Adopting the IADPSG criteria is associated with improved pregnancy outcomes, at the expense of increased prevalence of gestational diabetes mellitus diagnosis.

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined when carbohydrate intolerance is developed or recognized during pregnancy for the first time^{1,2}. Women with GDM have increased risk for

adverse pregnancy outcomes, including macrosomia, birth trauma, jaundice, respiratory distress syndrome, primary cesarean section and maternal hypertensive disorders^{3,4}. After delivery, 15–50% of women with GDM develop type 2 diabetes later in life¹. In addition, children and adolescents with higher birthweight are associated with increased risk of obesity and diabetes, based on reports from our group and others^{5,6}. Therefore, GDM is sometimes called ‘a disease of two generations.’

[†]These two authors contributed equally to this manuscript.

[‡]These two authors contributed equally to this manuscript as co-corresponding authors.

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To define carbohydrate intolerance during pregnancy, the term GDM was first used in 1957 by Carrington⁷. In 1964, O'Sullivan⁸ proposed the first diagnosis criteria of GDM, using 100-g, 3-h oral glucose tolerance tests (OGTT) to predict maternal diabetes after delivery using whole blood. These criteria were modified by the National Diabetes Data Group in 1979². In 1982, Carpenter and Coustan (C&C)⁹ revised the cut-offs again, to convert cut-off values from whole blood to plasma. The C&C criteria were adopted by the American Diabetes association (ADA) in 1990¹⁰ and the American College of Obstetrics and Gynecology in 2001¹¹. In clinical practice, the 100-g OGTT is usually preceded by a 50-g glucose challenge test (GCT) as a screening test. In 2008, the Hyperglycemia and Adverse Pregnancy Outcome study found an association of maternal plasma glucose during 2-h, 75-g OGTT and adverse pregnancy outcomes.¹² Based on the findings, the International Association of the Diabetes and Pregnancy Study Group (IADPSG) proposed a new diagnostic strategy using 75-g OGTT¹³, which was adopted by the ADA in 2011¹⁴. The 50-g GCT is not included in the IADPSG strategy. In a randomized controlled study, treatment for women with GDM has been shown to be beneficial⁴. However, in the study, the 75-g OGTT was preceded by 50-g GCT, which was different from the IADPSG strategy. Recently, a report from Spain showed that adopting the IADPSG criteria is associated with increased prevalence and improved pregnancy outcome¹⁵. However, the prevalence of GDM varies significantly among different ethnic groups^{16–19}, which could result in a different impact on pregnancy outcome. To the best of our knowledge, there is no study of Asians that compared the pregnancy outcomes by using the IADPSG criteria and the C&C criteria. Therefore, we compared the prevalence of GDM, maternal adverse outcomes and fetal adverse outcomes by using the IADPSG criteria (75-g OGTT) and the C&C criteria (50-g GCT followed by 100-g OGTT) in the present study.

METHODS

We carried out a retrospective cohort study including all pregnant women who delivered a singleton between January 2011 and December 2011 in the National Taiwan University Hospital, Taipei, Taiwan. During this period, women who had diagnostic tests for GDM before January 2011 received 50-g GCT followed by 100-g OGTT by the C&C criteria; whereas women who had diagnostic tests for GDM after January 2011 received 75-g OGTT by the IADPSG criteria. There was no change in other prenatal care guidelines or indications for cesarean section in our hospital at that time. Each pregnant woman received one test only, either 50-g GCT followed by 100-g OGTT or 75-g OGTT. For 75-g OGTT, women were diagnosed as GDM if they had plasma glucose above one of the following cut-offs, including fasting plasma glucose ≥ 92 mg/dL, plasma glucose 1 h after OGTT ≥ 180 mg/dL and plasma glucose 2 h after OGTT ≥ 153 mg/dL¹³. For 50-g GCT followed by 100-g OGTT, GDM was screened by 50-g GCT first. If plasma glucose 1 h

after 50-g GCT was ≥ 140 mg/dL, the woman received a 100-g OGTT⁹. GDM was diagnosed if two of her plasma glucose were above the following cut-offs, including fasting plasma glucose ≥ 95 mg/dL, plasma glucose 1 h after OGTT ≥ 180 mg/dL, plasma glucose 2 h after OGTT ≥ 155 mg/dL and plasma glucose 3 h after OGTT ≥ 140 mg/dL.⁹ Women with GDM by the two criteria received similar therapeutic interventions, including nutrition counseling and lifestyle modification. All women with GDM were advised to carry out self-monitoring of their blood glucose. If glycemic control was poor by lifestyle modification according to the recommendation from American College of Obstetrics and Gynecology in 2001¹¹; that is, fasting plasma glucose ≥ 95 mg/dL or 2-h postprandial plasma glucose ≥ 120 mg/dL, physicians would consider insulin or oral hypoglycemia agents to treat GDM.

Pregnancy outcomes, including maternal and fetal outcomes, were obtained by reviewing medical records. Maternal outcomes included bodyweight gain between first visit and at delivery, pregnancy-induced hypertension (PIH; systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg for the first time during pregnancy)²⁰, pre-eclampsia (PIH with proteinuria ≥ 300 mg/24 h)²⁰ and cesarean section. Fetal outcomes included birthweight, birth trauma, jaundice, neonatal hypoglycemia, admission to neonatal intensive care unit and fetal death. The 90th percentiles of birthweight for each gestational week (from 35 to 42 weeks) were calculated. The newborn was considered as birth weight >90 th percentile if the birthweight was greater than the 90th percentile in the study population according to gestational age. Birth trauma was defined if the newborn had nerve palsy, clavicle fracture, shoulder dystocia or subcutaneous hematoma. Among the three newborns with subcutaneous hematoma, none of them were delivered by vacuum-assisted delivery. Jaundice was defined by neonatal hyperbilirubinemia requiring phototherapy with at least one laboratory report of a bilirubin level exceeding 15 mg/dL. Neonatal hypoglycemia was diagnosed by pediatricians, which was defined as plasma glucose ≤ 45 mg/dL 12 h after birth²¹. The study was reviewed and approved by the research ethics committee of the National Taiwan University Hospital titled as 'Applied One-step Screening for Gestational Diabetes in Taiwan: Effect on Prevalence and Perinatal Outcome.' Written informed consent was obtained from each patient before enrolment.

Statistical Analysis

Data are presented as means and standard deviations for continuous variables, and as number and/or percentages for categorical variables. The Student's *t*-test, χ^2 -test and Fisher's exact test were used to identify the differences in clinical characteristics and results of GDM diagnosis and treatment between the two diagnostic methods. Multiple logistic regression analyses were carried out to estimate the odds ratios (OR) of adverse pregnancy outcomes between the two diagnostic methods, using 50-g GCT followed by 100-g OGTT as the reference

group (OR 1). Parity (not adjusted for primary cesarean section), maternal age, gestational weight gain, maternal bodyweight at delivery, gestational week, history of macrosomia (adjusted for birthweight >90th percentile) and history of PIH and pre-eclampsia (adjusted for pre-eclampsia and PIH), were regarded as potential confounders and were adjusted. A two-tailed *P*-value below 0.05 was considered significant. The statistical analyses were carried out using Stata/SE 11.0 for Windows (StataCorp, College Station, TX, USA).

RESULTS

A total of 1,840 pregnant women were included in the present study. Among them, 952 women were screened by the IADPSG criteria, and 888 women were screened by the C&C criteria. The clinical characteristics between the two groups are summarized in Table 1. There was no significant difference in age, parity, bodyweight at first visit, and maternal history of GDM, preterm delivery, PIH and pre-eclampsia. The gestational weeks were slightly shorter in the IADPSG group (38.7 weeks vs 39.0 weeks, *P* = 0.003). The frequency of maternal history of chronic hypertension was higher in the IADPSG group (1% vs 0.2%, *P* = 0.04). Women screened by the IADPSG criteria showed less bodyweight gain at delivery (9.4 kg vs 10.0 kg, *P* < 0.001), which could be due to the fact that more women were diagnosed as GDM and treated in the IADPSG group than in the C&C group (GDM 13.44% vs 2.59%). The birthweight of the newborns in the IADPSG group were lighter than that in the C&C group (3,065 g vs 3,128 g, *P* = 0.004).

In Table 2, the prevalence of GDM was significantly higher by the IADPSG criteria (13.44% vs 2.59%, *P* < 0.001). A total of 148 (16.7%) women in the C&C group had abnormal results in 50-g GCT (≥ 140 mg/dL) and received 100-g OGTT. A delay in the diagnosis of GDM was observed in the C&C group (30.5 weeks in the C&C group vs 27 weeks in the IADPSG group, *P* < 0.0001). As women in the C&C group received 50-g GCT as a screening test, fasting plasma glucose in the C&C group was higher than fasting plasma glucose in the IADPSG group (88 mg/dL vs 78 mg/dL, *P* < 0.0001). There was no difference in the treatment of GDM between the two groups.

Table 3 showed the pregnancy outcomes of the two groups. For maternal outcomes, women screened by the IADPSG criteria had a lower primary cesarean rate than women screened by the C&C criteria (21.7% vs 24.7%, adjusted OR 0.79, 95% confidence interval 0.63–0.998, *P* < 0.05). There was no significant difference in the risk of cesarean section for all reasons, PIH and pre-eclampsia. For fetal outcomes, the adjusted ORs were below 1 for birthweight >90th percentile, jaundice, admission to neonatal intensive care unit, birth trauma and neonatal hypoglycemia. However, none of them reached statistical significance when analyzed individually (all *P* > 0.05). When analyzed together, the adjusted OR for having any one of aforementioned fetal adverse outcome was 0.79 (95% confidence interval 0.64–0.98, *P* < 0.05), which means that

Table 1 | Clinical characteristics in women screened with the 75-g oral glucose tolerance test (by International Association of the Diabetes and Pregnancy Study Group criteria) or 50-g glucose challenge test followed by the 100-g oral glucose tolerance test (by Carpenter and Coustan criteria) for gestational diabetes

	75-g OGTT	50-g GCT + 100 g OGTT	<i>P</i>
<i>n</i>	952	888	
Age (years)	33.6 (4)	33.7 (4.2)	0.8
Gestational week (weeks)	38.7 (1.8)	39.0 (1.6)	0.003
Gestational parity, 1/2/more (%)	56.1/36.6/7.4	56.5/37.7/5.7	0.4
Bodyweight			
At first visit (kg)	57.8 (8.4)	58.3 (8.3)	0.2
At delivery (kg)	67.2 (8.3)	68.3 (8.5)	0.005
Weight gain (kg)	9.4 (4.0)	10.0 (4.0)	0.002
Smoking, <i>n</i> (%)	2 (0.2)	4 (0.4)	0.4
Alcohol consumption, <i>n</i> (%)	2 (0.2)	2 (0.2)	1.0
History of gestational diabetes, <i>n</i> (%)	4 (0.4)	2 (0.2)	0.7
History of macrosomia, <i>n</i> (%)	6 (0.6)	8 (1)	0.6
History of PCOS, <i>n</i> (%)	3 (0.3)	6 (0.6)	0.3
Chronic HTN, <i>n</i> (%)	10 (1)	2 (0.2)	0.04
History of PIH, <i>n</i> (%)	3 (0.3)	1 (0.1)	0.6
History of pre-eclampsia, <i>n</i> (%)	7 (0.7)	3 (0.3)	0.3
History of preterm delivery, <i>n</i> (%)	7 (0.7)	5 (0.5)	0.8
Delivery mode, NVD/CS/vacuum delivery/VBAC (%)	55.8/36.1/7.8/0.3	56.0/37.3/6.6/0.1	0.6
Birthweight (g)	3,065 (477)	3,128 (443)	0.004

Mean (standard deviation) were shown. CS, cesarean section; GCT, glucose challenge test; HTN, hypertension; OGTT, oral glucose tolerance test; NVD, normal vaginal delivery; PCOS, polycystic ovarian syndrome; PIH, pregnancy induced hypertension; VBAC, vaginal birth after cesarean section.

newborns born to women screened with the IADPSG criteria had a lower risk of having any one of the adverse fetal outcomes.

DISCUSSION

To the best of our knowledge, this is the first study to compare pregnancy outcomes by using the IADPSG criteria and the C&C criteria in Asian women. We found that using GDM by the IADPSG criteria is associated with a lower primary cesarean rate and less neonatal morbidity. By contrast, the prevalence of GDM by the IADPSG criteria is markedly higher than the prevalence of GDM by the C&C criteria.

In the present study, we also found that using the IADPSG criteria showed better pregnancy outcomes than using the C&C criteria. GDM was diagnosed earlier by the IADPSG criteria,

Table 2 | Results of screening and treatment of gestational diabetes in women diagnosed by 75-g oral glucose tolerance test (by International Association of the Diabetes and Pregnancy Study Group criteria) or 50-g glucose challenge test followed by 100-g oral glucose tolerance test (by Carpenter and Coustan criteria)

	75-g OGTT	50-g GCT + 100 g OGTT	P
<i>n</i>	952	888	
GDM, <i>n</i> (%)	128 (13.44%)	23 (2.59%)	<0.001
1-h plasma glucose after 50-g OGTT (mg/dL)	NA	120 (28)	
Women with 1-h plasma glucose after 50-g OGTT \geq 140 mg/dL, <i>n</i> (%)	NA	148 (16.7%)	–
Gestational week when 50-g GCT was performed	NA	26.5 (2)	–
Gestational week when OGTT was performed	27.0 (2.0)	30.5 (2.0)	<0.0001
Fasting plasma glucose (mg/dL)	78 (7)	88 (27)	<0.0001
1-h plasma glucose (mg/dL)	134 (29)	153 (38)	–
2-h plasma glucose (mg/dL)	117 (25)	133 (43)	–
3-h plasma glucose (mg/dL)	NA	115 (41)	–
Treatment of GDM			
Lifestyle modification, <i>n</i> (%)	122 (95.3%)	21 (91.3%)	0.3
Insulin or oral hypoglycemia agents, <i>n</i> (%)	6 (4.7%)	2 (8.7%)	0.44

GCT, glucose challenge test; GDM, gestational diabetes mellitus; NA, not available; OGTT, oral glucose tolerance test.

which could lead to earlier therapeutic interventions including nutritional counseling, glucose monitoring and/or medications. Indeed, gain of maternal bodyweight and neonatal birthweight were both lower by using the IADPSG criteria, which might explain the reduced rate of primary cesarean section in the present study. A previous study showed that 20% of fetuses already had signs of macrosomia at the time when the women were referred for GDM treatment²². Besides, Landon *et al.* reported that treatment of mild gestational diabetes could reduce the risks of fetal overgrowth and cesarean delivery²³. Indeed, the present study showed that earlier interventions were associated with reduced neonatal morbidity including birthweight >90th percentile, neonatal jaundice, birth trauma, neonatal hypoglycemia and neonatal intensive care unit admission. Consistent with our findings, a report from the St. Carlos Gestational Diabetes Study has shown that shifting from the C&C criteria to the IADPSG criteria resulted in reduced risk of gestational hypertension, prematurity, cesarean section, small/large for gestational age, low Apgar 1-min score and neonatal intensive care unit admission in the Western population¹⁵. Furthermore, Sevket *et al.*²⁴ showed that the women who were defined as normal by the IADPSG criteria had a lower risk of polyhydramnios and pre-eclampsia than those by the C&C criteria²⁴.

In contrast, the IADPSG criterion is associated with increased prevalence of GDM, which might result in increased burden to healthcare systems. In the St. Carlos Gestational Diabetes Study, application of the new IADPSG criteria resulted in a huge increase in prevalence (from 10.6% to 35.5%)¹⁵. This raises a concern of there being enough healthcare professionals to take care of these women with GDM. It could be a major reason why Spain ultimately rejected the use of IADPSG criteria to diagnose GDM²⁵. In the present study, we have also shown that adopting the IADPSG criteria resulted in increased prevalence of GDM, from 2.59% to 13.44%. In Taiwan, the

birth rate is very low (8.530/1000 in 2011²⁶). Besides, for women without GDM, there are six clinical visits covered by the National Health Insurance after 28 weeks of gestation; whereas for women with GDM, an additional clinic visit is required. Therefore, the manpower of healthcare professionals is sufficient to take care of women with GDM by the IADPSG criteria. As shown in the St. Carlos Gestational Diabetes Study, adopting the IADPSG criteria from the C&C criteria is cost-saving in Spain (€143.58 saved per woman)¹⁵. In the present study, adopting the IADPSG criteria in Taiwan increased the cost by US\$186 per woman than the C&C criteria, which included the cost differences for the diagnosis and treatment of GDM, and for the medical care for the neonates. Adopting the IADPSG criteria is cost-effective in Taiwan, as US\$186 is equal to 4.06 times the daily wage. It is worth noting that the payment for cesarean section and normal vaginal delivery is the same in Taiwan, in order to encourage normal vaginal delivery by policy. Therefore, adopting the IADPSG criteria might be cost-saving if cost reduction in the reduced rate of primary cesarean section is considered. Furthermore, as the payment for medical services in Taiwan is very low, of cost difference is likely to be underestimated. Therefore, the Diabetes Association in Taiwan suggested the IADPSG criteria as an option to diagnose GDM in addition to the C&C criteria. Taken together, as there are differences in healthcare systems and the impact on the prevalence of GDM, each country should evaluate if the IADPSG criteria should be accepted based on their own considerations.

Another disadvantage of adopting the IADPSG criteria is that more pregnant women might be anxious once they were diagnosed as GDM. Indeed, women with GDM were more anxious than women without GDM, as shown by a report by Daniells *et al.*²⁷ However, the anxiety did not sustain if interventions were given²⁷. In another report, Crowther *et al.*⁴ also revealed a

Table 3 | Outcomes comparing the two diagnostic methods by multiple logistic regression analyses, using 50-g glucose challenge test followed by 100-g oral glucose tolerance test as the reference group (75-g oral glucose tolerance test by IADPSG criteria vs 50-g glucose challenge test followed by 100-g oral glucose tolerance test by Carpenter and Coustan criteria)

	75-g OGTT (n) (%)	50-g GCT + 100 g OGTT (n) (%)	Adjusted ORs (95% CI)
<i>n</i>	952	888	
Maternal outcome			
Primary CS	207 (21.7)	219 (24.7)	0.79 (0.63–0.998)*
CS	346 (36.3)	329 (37.1)	0.88 (0.72–1.08)
PIH	15 (1.6)	19 (2.1)	0.59 (0.26–1.32)
Pre-eclampsia	13 (1.4)	10 (1.1)	0.92 (0.39–2.18)
Fetal outcome			
BW >90th percentile	88 (9.2)	93 (10.5)	0.87 (0.62–1.21)
Jaundice	216 (22.7)	209 (23.5)	0.86 (0.68–1.09)
Admission to NICU	3 (0.3)	5 (0.6)	0.26 (0.51–1.35)
Birth trauma	7 (0.7)	7 (0.8)	0.79 (0.27–2.27)
Neonatal hypoglycemia	5 (0.5)	4 (0.5)	0.97 (0.21–4.41)
Fetal death	1 (0.1)	0 (0)	NA
Any one of above fetal adverse outcome	281 (29.5)	289 (32.6)	0.79 (0.64–0.98)*

* $P < 0.05$. Adjusted model: adjusted for parity (not adjusted for primary cesarean section [CS]), maternal age, gestational weight gain, maternal weight at delivery, gestational week, history of macrosomia (adjusted for birthweight [BW] >90th percentile), history of pregnancy-induced hypertension (PIH), pre-eclampsia (adjusted for preeclampsia and PIH) and chronic hypertension. GCT, gestational challenge test; NICU, neonatal intensive care unit; OGTT, oral glucose tolerance test; ORs, odds ratios.

lower frequency of depression among women receiving interventions for GDM. In contrast, some women with abnormal results by 50-g GCT and normal results by 100-g OGTT might not understand the test results correctly, which could also result in anxiety. Taken together, although adopting the IADPSG criteria might increase anxiety at the time of diagnosis, the anxiety is relieved after interventions are given.

According to the IADPSG criteria, three blood tests are required, compared with five blood tests by the C&C criteria (1 for 50-g GCT and 4 for 100-g OGTT). The IADPSG criteria use a similar procedure; that is, 75-g OGTT, to diagnose GM+DM as in non-pregnant adults to diagnose diabetes. Therefore, it is easier to follow the glycemic status of these women and compare the results after delivery. For the laboratory, the same procedure can simplify laboratory works and reduce the inventory of glucose to be prepared; that is, only packs of 75-g glucose are required. For healthcare providers, it is simpler to memorize the criteria. However, the disadvantage of the IADPSG criteria is that all pregnant women are advised

to receive OGTT. By contrast, just 16.7% women underwent OGTT using the C&C criteria in the present study. In other words, the number of blood sampling and screening by 50-g GCT or not are practical factors to be considered in different healthcare systems.

In 2011, the ADA suggested the use of 75-g OGTT and the IADPSG criteria for the diagnosis of GDM²⁸. In 2013, the National Institutes of Health consensus development conference recommended the use of 50-g GCT followed by 100-g OGTT to diagnose GDM, as there were a lack of clinical trial interventions showing the benefits of the IADPSG criteria and the potential negative consequences to identify a large new group of women with GDM¹. In the same time, the American College of Obstetrics and Gynecology also supported the C&C criteria in its guidelines in 2013²⁹. Therefore, the ADA suggested that either 75-g OGTT or 50-g GCT followed by a 100-g OGTT can be used to diagnose GDM in 2014 and 2015^{30,31}. In Taiwan, based on the findings from the current study, the guidelines by the diabetes association in Taiwan have added the 75-g OGTT as an option to diagnose GDM, in addition to 50-g GCT followed by 100-g OGTT³².

The strength of the present study was its comprehensiveness. We compared the prevalence of GDM, maternal adverse outcomes and fetal adverse outcomes. The present study has a larger sample size than previous reports investigating the performance of diagnostic criteria for GDM. However, this study was limited by its retrospective design. Therefore, data on the ponderal index of the newborn and neonatal C-peptide levels were not available. The populations in the present study were mainly ethnic Chinese. Studies on other ethnic groups are required.

In conclusion, we found that adopting the IADPSG criteria is associated with a reduction in the primary cesarean section rate and a decrease in neonatal adverse outcomes than adopting the C&C criteria, at the expense of increased prevalence of GDM.

DISCLOSURE

The authors declare no conflict of interest.

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