# Hemoglobin $A_{1c}$ Versus Oral Glucose Tolerance Test in Postpartum Diabetes Screening

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**OBJECTIVE**—To determine the usefulness of measuring hemoglobin $A_{1c}$ (A1C), alone or combined with the fasting glucose test, compared with the oral glucose tolerance test (OGTT) for the reassessment of the carbohydrate metabolism status in postpartum women with a history of gestational diabetes mellitus (GDM).

**RESEARCH DESIGN AND METHODS**—We evaluated the status of carbohydrate metabolism by performing the OGTT and fasting glucose and A1C tests in 231 postpartum women with prior GDM 1 year after delivery.

**RESULTS**—The prevalence of abnormal carbohydrate metabolism was 45.89% by the OGTT criterion, 19.05% by the A1C test criterion, 38.10% by the fasting glucose test criterion, and 46.75% by the A1C-fasting glucose test criteria. Using the OGTT as the gold standard, abnormal carbohydrate metabolism according to the A1C test criterion had 22.64% sensitivity and 54.55% positive predictive value; abnormal carbohydrate metabolism by the fasting glucose criterion had 83.02% sensitivity and 100% positive predictive value. The A1C-fasting glucose test criteria classified 18 women with normal carbohydrate metabolism as having abnormal carbohydrate metabolism. Abnormal carbohydrate metabolism by the A1C-fasting glucose test criteria had 83.02% sensitivity and 81.48% positive predictive value.

**CONCLUSIONS**—Our results seem to indicate that the A1C test criterion alone or in combination with fasting glucose test criterion does not provide a sensitive and specific diagnosis of abnormal carbohydrate metabolism in women who have had GDM.

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Gestational diabetes mellitus (GDM) is described as any degree of glucose intolerance with onset or first recognition during pregnancy (1). The prevalence of GDM varies worldwide and among racial and ethnic groups within a country (2,3). Variations in prevalence also depend on the method and diagnostic criteria used. According to the International Association of Diabetes and Pregnancy Study Groups diagnostic criteria, ~18% of women in the world would be diagnosed with diabetes during pregnancy (4). In Spain, the prevalence of GDM is estimated to be 8.8% according to the National Diabetes Data Group (5).

Nearly all women with GDM (~90%) are normoglycemic just after delivery but they are at high risk for abnormal carbohydrate metabolism and recurrent GDM (6). The recurrence rate of GDM in successive pregnancies is ~35%, increasing with the age and weight of the mother (7). As a prior history of GDM is predictive of an increased risk of developing type 2 diabetes and cardiovascular disease (8), it is important to reevaluate these women and detect as many cases as possible.

The American College of Obstetricians and Gynecologists (9), the American Diabetes Association (ADA) (10), and the Fifth International Workshop-Conference on Gestational Diabetes Mellitus (11) recommend long-term follow-up for women with GDM using a 2-h, 75-g oral glucose tolerance test (OGTT). This long-term follow-up is essential, and reassessment of glycemic status should be undertaken at a minimum of 3 years because a negative postpartum screening test only excludes the presence of type 1 or type 2 diabetes at the time of the test.

During the last decade, the ADA has updated its screening recommendations for abnormal carbohydrate metabolism. Previously, to identify patients at high risk for diabetes, the ADA preferred the use of the fasting blood glucose test instead of the OGTT due to its logical advantage (12). However, individuals still need to fast for at least 8 h before testing. As the hemoglobin $A_{1c}$ (A1C) test is a nonfasting test, it has significant practical advantages over the OGTT, and it is now becoming the preferred test to diagnose abnormal carbohydrate metabolism (13).

With this background, the purpose of this study was to evaluate the usefulness of A1C (alone or combined with a fasting glucose test) for the reassessment of carbohydrate metabolism status in postpartum women with a history of GDM.

## RESEARCH DESIGN AND METHODS

### Subjects

A total of 231 Spanish women with previous GDM underwent an OGTT at the Division of Endocrinology, Virgen de la Victoria Hospital, 1 year after delivery, as the cumulative incidence of abnormal carbohydrate metabolism in postpartum GDM women is increased at this time (14). The participants completed a structured interview to obtain the following data: age, personal history of GDM and macrosomia in previous pregnancies, family history of diabetes, type of delivery, the need for insulin during pregnancy, and BMI before pregnancy. The following data were also

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collected: weight, height, waist circumference, BMI, and blood pressure.

The capture rate of women with previous GDM was less than one-half (31.5%), which is similar to the rate found in the study of Russell et al. (15). No significant differences were observed in the following variables between those attending and those not attending the reassessment: age, BMI before pregnancy, gestational age at which GDM monitoring began, history of GDM in previous pregnancies, history of macrosomia, family history of diabetes, and the need for insulin treatment. Women were excluded if they extended breastfeeding more than 6 months postpartum, were diagnosed with diabetes just after delivery, or had anemia.

### Measurements

Blood pressure was measured twice, at 8:00 A.M., with the subject seated and with an interval of 5 min between measurements. The blood pressure measurements were taken on the right arm, which was relaxed and supported by a table, at an angle of 45° from the trunk (ELKA aneroid manometric sphygmomanometer; Von Schlieben Co., Manheim, Germany).

Blood samples were collected after a 12-h fast at 8:15 A.M. The women underwent a 75-g oral glucose overload with a commercial preparation. Only water was permitted during the process, and no physical exercise was undertaken. The blood samples were collected before and 2 h after a tolerance test.

Plasma biochemical parameters were measured in duplicate by standard enzymatic methods. Glucose, cholesterol, HDL cholesterol, triglycerides, and uric acid were measured using a Dimension Vista analyzer (Siemens AG). LDL cholesterol was calculated by the Friedewald formula. A1C was measured using the VARIANTTM II TURBO A1C-2.0 kit.

The patients were classified according to their fasting glucose level as normal (fasting plasma glucose [FPG] <100 mg/dL), prediabetes (FPG = 100–125 mg/dL), or diabetes (FPG ≥126 mg/dL). The OGTT results were classified by the ADA criteria. The patients were also grouped as having normal glucose tolerance (FPG <100 mg/dL and/or 2-h plasma glucose <140 mg/dL), prediabetes (impaired fasting glucose [IFG]: FPG = 100–125 mg/dL and/or impaired glucose tolerance [IGT]: 2-h plasma glucose = 140–199 mg/dL), and diabetes (2-h plasma glucose ≥200 mg/dL). The patients were also classified according to the A1C criteria as normal (A1C <5.7%), prediabetic (A1C = 5.7–6.4%), and diabetic (A1C ≥6.5%).

The study was approved by the Ethics Committee of Virgen de la Victoria Hospital, and all the participants provided signed consent after being fully informed of the goal and characteristics of the study.

### Statistical analysis

The results are given as the mean ± SD. All clinical parameters are summarized by descriptive statistics. Normal distributions of data were tested using a Kolmogorov-Smirnov test. The relationships between clinical parameters of the patients were analyzed using the Student *t* test. Differences in the frequency distribution of qualitative variables between groups were assessed by the Fisher exact test. The agreement between the diagnoses resulting from A1C, fasting glucose, or the combination of both test criteria and OGTT criteria was estimated by calculation of the Cohen κ coefficient (κ). Using the OGTT as the gold standard, the diagnostic values for the A1C, FPG, or a combination of both were assessed for sensitivity, specificity, and positive and negative predictive values. The sample size was estimated assuming that the sensitivity was ~50% (16,17), which corresponds to the worst-case scenario of maximum uncertainty. With 97 patients, the precision of the estimate of the 95% CI for this sensitivity would be 10%. Since we estimated that the prevalence of abnormal carbohydrate metabolism could be ~50% (14), and assuming a loss rate of 16%, 231 patients would be sufficient to have the power to achieve the above-mentioned precision.

In all cases, the rejection level for a null hypothesis was $\alpha = 0.05$ for two tails. The statistical analysis was done with SPSS (version 15.0 for Windows; SPSS, Chicago, IL).

**RESULTS**—The age of the study subjects was 34.63 ± 4.65 years and their BMI was 27.74 ± 5.95 kg/m$^2$. The evaluation was performed at 13.2 ± 3.0 months postpartum. Table 1 shows the distribution of the clinical and medical history variables in women with normal and abnormal carbohydrate metabolism according to oral glucose tolerance, fasting glucose, and A1C test criteria. All the diagnostic tests found that the group of women with abnormal carbohydrate metabolism had a higher BMI, waist circumference, blood pressure (except A1C), glucose levels, and lipid abnormalities, all variables associated with a raised vascular risk.

Based on the OGTT results, 125 women (54.11%) had normal glucose tolerance, 92 (39.83%) had prediabetes (58 with IFG, 16 with IGT, and 18 with IFG + IGT), and 14 (6.06%) had diabetes. Based on the fasting glucose results, 143 women (61.91%) had normal glucose tolerance, 82 (35.50%) had prediabetes, and 6 (2.60%) had diabetes. In contrast, using the A1C test, 187 women (80.95%) had normal glucose metabolism, 43 (18.62%) had prediabetes, and 1 had diabetes (0.43%). With the combination of the fasting blood glucose and A1C test, 123 women (53.25%) had normal glucose metabolism, 101 (43.72%) had prediabetes, and 7 had diabetes (3.03%).

Figure 1 represents the women classified as having abnormal carbohydrate metabolism according to at least one of the diagnostic tests. The prevalence of abnormal carbohydrate metabolism by the OGTT (gold standard) was 45.89%. However, 20 women classified as having normal carbohydrate metabolism with the OGTT criteria (16% of all these women) were diagnosed as having abnormal carbohydrate metabolism according to the A1C test and fasting glucose test criteria (Table 2). In turn, 82, 18, and 18 women classified as having abnormal carbohydrate metabolism by the OGTT criteria (77.36, 16.98, and 16.98%, respectively) were diagnosed as having normal carbohydrate metabolism according to the A1C test, fasting glucose, and the combination of both criteria, respectively.

The sensitivity, specificity, and positive and negative predictive values of A1C, fasting glucose, and the combination of both diagnostic tests compared with the OGTT (gold-standard test) are shown in Table 2.

**CONCLUSIONS**—Our results seem to indicate that the A1C test criteria alone or in combination with fasting glucose test criteria, despite being easy to perform, do not reliably diagnose abnormal carbohydrate metabolism in postpartum women who have had GDM. Women who have had GDM are more likely than other women to develop type 2 diabetes later on (18), and it is therefore important to reevaluate them. One of the main problems for the postpartum reevaluation of women with a history of GDM is that many women fail to attend their postpartum visits. Thus, a balance must be found to capture a large number of women who attend a follow-up visit and to use diagnostic tests capable of detecting as many as possible that are at risk for type 2 diabetes.

After standardization, the A1C test is a very attractive test for the diagnosis of

**Table 1—*Distribution of clinical variables in women with normal or abnormal glucose tolerance according to different diagnostic tests***

| | OGTT criteria | | A1C criteria | | Fasting glucose criteria | | A1C and fasting glucose criteria | |
|---|---|---|---|---|---|---|---|---|
| | Normal | Abnormal | Normal | Abnormal | Normal | Abnormal | Normal | Abnormal |
| *N* | 125 | 106 | 187 | 44 | 143 | 88 | 123 | 108 |
| One year after delivery | | | | | | | | |
| Age (years) | 34.34 ± 4.46 | 35.11 ± 5.11 | 34.55 ± 4.93 | 35.02 ± 3.18 | 34.31 ± 4.57 | 35.18 ± 4.77 | 34.23 ± 4.73 | 35.10 ± 4.54 |
| BMI (kg/m$^2$) | 25.72 ± 4.85 | 30.10 ± 6.27§ | 27.14 ± 5.42 | 30.38 ± 7.38† | 25.93 ± 4.96 | 30.67 ± 6.27§ | 25.77 ± 4.89 | 30.00 ± 6.26§ |
| Waist (cm) | 83.20 ± 10.95 | 93.78 ± 15.10§ | 86.17 ± 12.16 | 96.07 ± 18.20§ | 83.51 ± 11.22 | 95.44 ± 15.01§ | 83.00 ± 10.86 | 93.81 ± 15.01§ |
| SBP (mmHg) | 109.20 ± 12.66 | 115.92 ± 18.17† | 111.93 ± 16.40 | 113.79 ± 12.73 | 109.28 ± 13.43 | 117.21 ± 17.98§ | 109.39 ± 14.00 | 115.65 ± 17.03† |
| DBP (mmHg) | 72.33 ± 10.29 | 76.64 ± 13.48† | 74.06 ± 12.26 | 75.35 ± 11.04 | 72.31 ± 10.43 | 77.57 ± 13.71† | 72.33 ± 10.83 | 76.60 ± 12.97† |
| Fasting glucose (mg/dL) | 91.57 ± 4.92 | 105.26 ± 9.84§ | 96.83 ± 9.46 | 102.18 ± 12.08† | 91.57 ± 5.12 | 108.07 ± 7.87§ | 91.52 ± 5.21 | 105.06 ± 9.70§ |
| 120-min glucose (mg/dL) | 100.14 ± 20.51 | 138.29 ± 41.64§ | 114.74 ± 33.93 | 129.98 ± 47.08* | 108.64 ± 30.30 | 132.27 ± 42.48§ | 109.35 ± 31.62 | 127.09 ± 40.74§ |
| A1C (%) | 5.36 ± 0.32 | 5.48 ± 0.35† | 5.30 ± 0.24 | 5.90 ± 0.22§ | 5.35 ± 0.30 | 5.52 ± 0.36§ | 5.17 ± 0.25 | 5.57 ± 0.35§ |
| Cholesterol (mg/dL) | 192.70 ± 34.45 | 188.30 ± 36.53 | 192.48 ± 35.83 | 183.05 ± 32.82 | 190.50 ± 34.05 | 190.98 ± 37.71 | 191.98 ± 34.82 | 189.20 ± 36.17 |
| HDL-C (mg/dL) | 56.16 ± 12.28 | 50.59 ± 12.29§ | 54.55 ± 12.72 | 49.59 ± 11.16* | 56.13 ± 12.16 | 49.50 ± 12.19§ | 56.21 ± 12.32 | 50.64 ± 12.24§ |
| LDL-C (mg/dL) | 113.44 ± 27.57 | 112.24 ± 29.24 | 113.52 ± 29.12 | 110.20 ± 25.83 | 111.47 ± 27.01 | 115.18 ± 30.78 | 112.64 ± 27.95 | 113.16 ± 29.24 |
| Triglycerides (mg/dL) | 95.25 ± 76.15 | 117.10 ± 63.65* | 102.42 ± 71.47 | 117.41 ± 70.53 | 96.73 ± 74.56 | 119.17 ± 63.87† | 96.77 ± 77.43 | 114.96 ± 62.76* |
| Prepregnancy | | | | | | | | |
| PH of GDM (%) | 25.42 | 37.74 | 33.33 | 24.00 | 26.47 | 38.64 | 29.09 | 33.33 |
| PH of macrosomia (%) | 17.24 | 18.86 | 16.28 | 24.00 | 16.41 | 20.45 | 14.81 | 21.05 |
| FH of diabetes (%) | 65.60 | 64.15 | 65.24 | 63.63 | 63.64 | 67.05 | 64.23 | 65.74 |
| BMI bp (kg/m$^2$) | 25.21 ± 4.34 | 28.71 ± 6.15§ | 26.29 ± 4.96 | 29.07 ± 5.42* | 25.37 ± 4.50 | 29.08 ± 6.19§ | 25.18 ± 4.45 | 28.67 ± 6.01§ |
| Pregnancy | | | | | | | | |
| Insulin treatment (%) | 27.20 | 38.68* | 32.24 | 39.02 | 27.86 | 42.86* | 26.45 | 41.74* |
| Macrosomia (%) | 7.20 | 6.60 | 5.35 | 13.64* | 6.29 | 7.95 | 5.69 | 8.33 |
| Cesarean section (%) | 29.66 | 31.31 | 29.61 | 34.21 | 30.15 | 30.86 | 20.69 | 13.86 |
| Instrumental birth (%) | 19.49 | 15.15 | 18.99 | 10.53 | 19.12 | 14.81 | 19.51 | 12.96 |

Values are presented as means ± SD unless otherwise indicated. bp, before pregnancy; DBP, diastolic blood pressure; FH, family history; HDL-C, HDL cholesterol; LDL-C, LDL cholesterol; PH, personal history; SBP, systolic blood pressure. Relationships of quantitative variables between women with normal and abnormal glucose tolerance were analyzed using the Student *t* test for independent samples. Relationships of qualitative variables between women with normal and abnormal glucose tolerance were analyzed using the Fisher exact test. *$P < 0.05$. †$P < 0.01$. §$P < 0.001$.

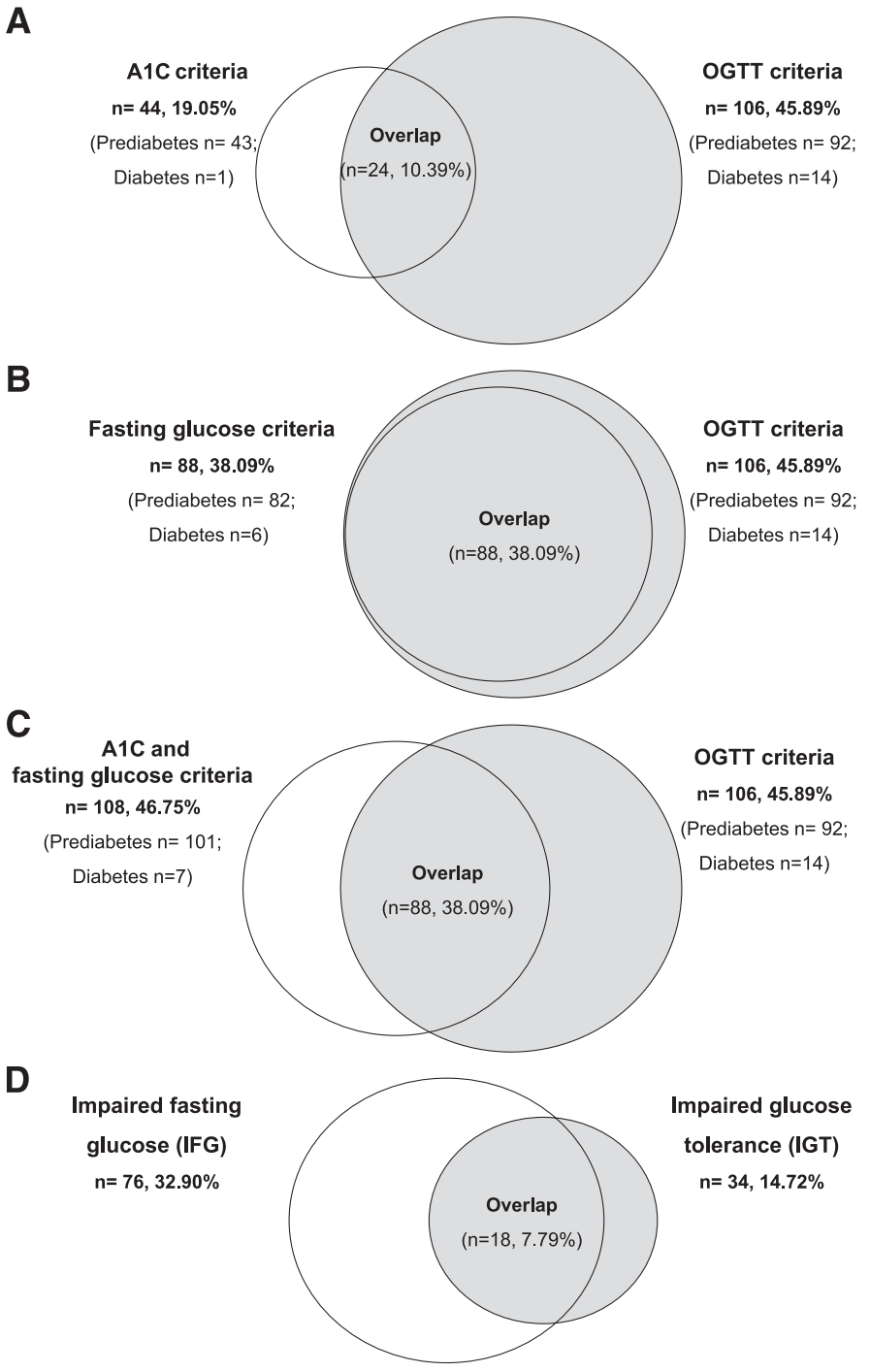


**Figure 1**—*Overlap of abnormal carbohydrate metabolism by OGTT criteria and A1C test criteria alone or in combination with fasting glucose criteria.* A*: OGTT criteria and A1C test criteria (the* κ *coefficient was 0.070,* P = *0.200).* B*: OGTT and fasting glucose criteria (the* κ *coefficient was 0.841,* P = *0.000).* C*: OGTT and the combination of A1C test and fasting glucose criteria (the* κ *coefficient was 0.669,* P = *0.000).* D*: Women classified as having IFG vs. women classified as having IGT (the* κ *coefficient was 0.141,* P = *0.017).*

diabetes and prediabetes because it is easy to perform; it requires no prior fasting or glucose overload. Moreover, unlike glucose, A1C remains relatively stable after collection and has less intraindividual variation compared with FPG (19). The A1C test result reflects longer-term blood glucose levels and it is less affected by recent physical/emotional stress than the OGTT. The A1C test could be a solution to the problem of the lack of monitoring experienced by GDM women after delivery. However, the diagnostic test used should be able to detect carbohydrate metabolism disorders at early stages.

Using A1C alone, we found that 16% of women classified as having normal carbohydrate metabolism by OGTT were diagnosed as having abnormal carbohydrate metabolism, and that 74.47% of women classified as having abnormal carbohydrate metabolism by OGTT were diagnosed as having normal carbohydrate metabolism. The A1C test had low sensitivity and modest positive and negative predictive values, although it had a high specificity. The A1C test does not therefore seem to be a good test for abnormal carbohydrate metabolism screening in postpartum women with previous GDM. The suggested cut point of A1C had a low sensitivity for an abnormal carbohydrate metabolism status in our study participants. However, this test was able to detect higher values of variables associated with a raised vascular risk, such as BMI, glucose levels, and lipid abnormalities, in the women with abnormal carbohydrate metabolism.

In our study, we found that using fasting glucose test criteria, 16% of the women classified as having normal carbohydrate metabolism by the OGTT were diagnosed as having abnormal carbohydrate metabolism, whereas 38.3% of the women classified as having abnormal carbohydrate metabolism by OGTT were diagnosed as having normal carbohydrate metabolism. Fasting glucose test criteria had quite a high sensitivity and a very high specificity, as well as very good positive and negative predictive values. The U.K.'s National Institute for Health and Clinical Excellence recommends screening with a fasting glucose test at the 6-week postpartum visit (20). However, McClean et al. (21) concluded that a postpartum FPG measurement alone is not sensitive enough in this population to classify glucose tolerance status accurately and that an OGTT is needed to facilitate early detection and treatment.

The combination of A1C with fasting glucose criteria classified 38.30% of the women as having normal carbohydrate metabolism who were classified as having abnormal carbohydrate metabolism by the OGTT criteria. The sensitivity and specificity were high, as were the positive and negative predictive values, although this combination did not improve the sensitivity and specificity obtained with fasting glucose test criteria alone. The κ coefficients indicated that the agreement between OGTT and A1C was very low, although

**Table 2—*Sensitivity, specificity, and positive and negative predictive values of the diagnostic tests (A1C, fasting glucose, and the combination of A1C and fasting glucose) in the study group (OGTT was considered the gold standard)***

| | Test characteristics (%) | | | |
|---|---|---|---|---|
| Diagnostic test | Sensitivity | Specificity | Positive predictive value | Negative predictive value |
| A1C | 22.64 | 84.00 | 54.55 | 56.15 |
| Fasting glucose | 83.02 | 100.00 | 100.00 | 87.41 |
| A1C and fasting glucose | 83.02 | 84.00 | 81.48 | 85.37 |

the combination of A1C and FPG increased the agreement with OGTT to moderate levels. However, all the diagnostic tests found high values for variables associated with a raised vascular risk in the women with abnormal carbohydrate metabolism, such as BMI, blood pressure (except A1C), glucose levels, and lipid abnormalities. These results reflect the discordance that exists between the various diagnostic tests. Mann et al. (22) showed that, if used alone, the A1C test would inappropriately diagnose many patients with prediabetes (classified by fasting glucose test) as not having prediabetes. As the cardiovascular risk is associated with abnormal carbohydrate metabolism (23), it is not permissible to diagnose prediabetes patients as having normal carbohydrate metabolism because it is very important to detect early states predisposing to diabetes. Nonetheless, a recent study (24) found that the agreement of OGTT and A1C is fair for the detection of abnormal glucose tolerance among women with a history of GDM, although further studies were recommended in order to determine the optimal test. Katon et al. (19) stated that it is important to consider the context and timing of the A1C measurement when interpreting these conflicting findings. After analyzing several studies, they suggested that a more restrictive criterion for the diagnosis of GDM could lead to a better association between A1C and postpartum abnormal glucose.

The current study needs to be interpreted in the context of certain potential limitations. Most notably, each test was only performed once; repeated tests could reinforce the results or provide more confidence. In addition, earlier identification of carbohydrate metabolism disorders might also lead to earlier prevention efforts. However, we evaluated these women 1 year after delivery because the risk of developing type 2 diabetes has a cumulative incidence that increases in the first year (25). The A1C might be affected by hemolytic anemias, although this concern is minimal considering the relative rarity of these conditions compared with prediabetes or diabetes.

The respective contribution of preprandial and postprandial glucose excursions to the A1C levels is controversial. Some authors have suggested that at A1C levels <7.3%, postprandial glucose contributes ~70% to elevated A1C levels (26,27). A possible explanation for the discrepancy in our results could be that the higher glucose levels in our study population were found in the preprandial state, and larger postprandial glucose excursions are necessary in order to be reflected as higher levels of A1C.

The strength of the current study is that it includes a relatively large number of postpartum women with a history of GDM, a heretofore unexamined group, with the performance of different diagnostic tests and completion of postpartum data.

In summary, the A1C test significantly underdiagnosed carbohydrate metabolism disorders in women who had had GDM. A large percentage of the postpartum women with a history of GDM who would have been labeled as having abnormal carbohydrate metabolism by the OGTT would in fact be diagnosed as having a normal metabolic status. Data from our study seem to indicate that the A1C test criteria, either alone or in combination with fasting glucose test criteria, does not provide a sufficiently sensitive and specific diagnosis of abnormal carbohydrate metabolism in women who have had GDM.

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M.J.P. and M.M. wrote the manuscript, researched data, contributed to discussion, and reviewed and edited the manuscript. A.M. and J.C.F.-G. researched data and contributed to discussion. R.G.-H. reviewed the manuscript. F.J.T. designed the study, contributed to discussion, and reviewed and edited the manuscript. M.M. and M.J.P. are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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