OBJECTIVE: To test the hypothesis that a hemoglobin A1C value (A1C) in early pregnancy is predictive of overt diabetes mellitus (DM) postpartum in women with gestational diabetes (GDM).

STUDY DESIGN: In this case-control analysis of women with an early pregnancy diagnosis of GDM, we estimated the association between an early pregnancy A1C and subsequent diagnosis of DM. Women with a normal postpartum diabetic screen (controls) were compared against those with confirmed postpartum DM (cases). Ability of A1C levels to predict DM was examined via logistic regression analysis and corresponding receiver operating characteristic values.

RESULTS: During the 10-year study period 166 women met the inclusion criteria: 140 (84%) had normal postpartum testing (controls), and 26 (16%) were diagnosed with DM (cases). The mean A1C value was significantly higher among cases than controls (6.7 vs. 5.6, p < 0.0001, SD 1.3–5). Cases had A1Cs ranging from 5.5–11.7%, while controls had A1Cs ranging from 4.3–7.8%. The best discriminatory cut point for postpartum DM was an A1C > 5.9% (sensitivity 81%, specificity 83%, positive predictive value 47%, negative predictive value 96%).

CONCLUSION: Our findings suggest that an elevated early pregnancy A1C may be predictive of overt DM. Larger studies are needed to further validate this association. (J Reprod Med 2014; 59:343–347)

Keywords: diabetes, early pregnancy, gestational diabetes mellitus, hemoglobin A1C, overt diabetes mellitus.

The differentiation between gestational diabetes mellitus (GDM) and overt diabetes mellitus (DM) is in a state of controversy at present. Since 2010 the International Association of Diabetes and Pregnancy Study Groups (IADPSG) has concluded that women who meet standard criteria for the diagnosis of DM at their first prenatal visit should be diagnosed as having DM, not GDM.1 A hemoglobin A1C value (A1C) of ≥ 6.5% is one of the standard diagnostic criteria for DM.1,2 The American Dia-
The American Diabetes Association (ADA) and the IADPSG also proposed use of the 2-hour, 75-g glucose tolerance test for the diagnosis of GDM.\textsuperscript{1,2} The American Congress of Obstetricians and Gynecologists (ACOG) did not support these new diagnostic criteria for GDM and has not commented directly on the ADA position statement regarding diagnosis of overt DM during pregnancy.\textsuperscript{3} ACOG currently recommends postpartum screening at 6–12 weeks for women who had GDM in order to identify women with DM.\textsuperscript{4} With postpartum screening rates as low as 20–40%,\textsuperscript{5} however, the opportunity to diagnose overt DM postpartum is often lost. Given the association between pregestational DM and higher risk for adverse perinatal outcomes,\textsuperscript{6} the ability to diagnose overt DM during pregnancy and provide these women with postpartum resources for diabetic care has the potential to improve outcomes for both the woman and for subsequent pregnancies.

In the context of the current debate on the diagnosis of gestational versus overt DM in early pregnancy, the aim of our study was three-fold: (1) to test the hypothesis that a high early pregnancy A1C is predictive of overt diabetes, (2) to find a population-specific A1C cutoff value for our patients (a largely homogeneous Hispanic/Latino population), and (3) to test the validity of the cutoff of A1C of 6.5% as suggested by the IADPSG by looking at the percentage of women with elevated A1C who were confirmed to have overt DM based on postpartum testing.

Materials and Methods

In this case-control analysis we accessed the records of all women diagnosed with GDM and DM who delivered at Ben Taub General Hospital (BTGH), an academic hospital affiliation of Baylor College of Medicine, between January 1, 2000, and June 30, 2010. Approval from our institutional review board was obtained prior to data collection.

Inclusion criteria consisted of a diagnosis of GDM in the first half of pregnancy (up to 20\% of gestation), an A1C value obtained at < 20 weeks of gestation, and an evaluation within 12 weeks postpartum for DM. All patients with a known history of type 1 or type 2 DM or a diagnosis of GDM in the first half of pregnancy but without a hemoglobin A1C and/or postpartum follow-up were excluded. The diagnosis of GDM was based on either a 50-g 1-hour Glucola result of > 200 mg/dL or 2 abnormal values on a 100-g 3-hour glucose tolerance test (GTT) using the Carpenter-Coustan diagnostic criteria. Postpartum screening for DM was accomplished by at least one of three methods, with a diagnosis of overt DM consisting of one of the following: (1) a fasting plasma glucose ≥ 126 mg/dL, (2) a random plasma glucose ≥ 200 mg/dL and symptoms of diabetes, (3) an A1C of ≥ 6.5%, or (4) a 2-hour plasma glucose ≥ 200 mg/dL in the 75-g GTT.\textsuperscript{2} Women with a normal postpartum diabetes screen were considered controls, and those with confirmed diabetes served as cases.

Demographic data were abstracted from the prenatal and inpatient records. Maternal age, race/ethnicity, height, and prepregnancy weight were self-reported. Pregnancy outcomes of interest included history of spontaneous preterm birth (defined as delivery prior to 37 weeks’ gestation), gestational hypertension, and preeclampsia as identified using the National High Blood Pressure Education Program Working Group Guidelines.\textsuperscript{7}

All continuous variables were checked for normality. Women with and without overt DM were compared via $\chi^2$/Fisher’s exact test for grouped data or $t$ test for continuous variables. Wilcoxon rank test (a nonparametric method) was used for nonnormal data. A logistic regression analysis was performed for determination of receiver operating characteristic (ROC) values. $p < 0.05$ was considered statistically significant. All analysis was performed in SAS statistical software (SAS Institute Inc., Cary, North Carolina).

Sample size and power was based on the study’s primary objective of assessing ability of A1C to discriminate postpartum diabetes via estimation of ROC curve. With sample size of 26 cases and 140 controls we have 80% power to detect a ROC of at least 0.85 or better when a minimum and baseline value of ROC = 0.7 for A1C was set, and with alpha equal to 0.05 and using a two-sided test.

Results

We identified 6,439 women who delivered at BTGH during the 10-year study period with a diagnosis of GDM. Of the 6,439 women, 166 (2.6%) met all inclusion criteria. The primary basis for exclusion was lack of postpartum follow-up. Of the 166 women included for analysis, 140 (84%) had normal laboratory results in the postpartum check (controls), and 26 (16%) were diagnosed with DM in the postpartum follow-up (cases). The method of postpartum diabetes evaluation for the study subjects was primarily via fasting plasma glucose (44%, $N = 73$) or
2-hour GTT (45%, N = 76), and by the A1C criteria mentioned earlier (10%, N = 17). Both groups were similar with respect to demographic and previous pregnancy characteristics, except for higher end of pregnancy weight in women with postpartum DM (Table I).

We examined several laboratory parameters along with A1C (Table II) in an effort to determine if there was a better indicator other than A1C for the diagnosis of overt DM. Although cases had higher mean values for all parameters than did controls, the variable with the highest ability to discriminate women with and without overt DM was A1C (ROC value of 0.88, 95% CI 0.83–0.95, p < 0.0001). Although women with overt DM had a significantly higher A1C mean value than did those without (6.7% vs. 5.6%, p < 0.0001), there was a substantial overlap in these values between the two groups.

The value that provided the best discriminatory cut point in our population was an A1C > 5.9% (sensitivity 81%, specificity 83%, positive predictive value [PPV] 47%, negative predictive value [NPV] 96%). In addition, none of the cases had an A1C of < 5.4%, and none of the controls had an A1C of > 9% (Figure 1).

**Discussion**

In this study, our primary aim was to test the hypothesis that a high early-pregnancy A1C is predictive of overt diabetes mellitus. Our secondary aims were to find a population-specific A1C cutoff value for our patients as well as how this value compared to that recommended universally by the IADPSG. We did not find a discrete hemoglobin A1C value that will always predict a postpartum diagnosis of overt DM in women with a diagnosis of GDM in the first half of pregnancy. In our predominantly Hispanic/Latino population we did identify a discriminatory cut point of > 5.9%, with a sensitivity and specificity comparable to our current diagnostic criteria for GDM. This value, in fact, performs well at predicting which women will not be diag-

### Table 1  Patient Characteristics by Case-control Status

<table>
<thead>
<tr>
<th>Variable*</th>
<th>Total (N = 166)</th>
<th>Cases (N = 26)</th>
<th>Controls (N = 140)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age</td>
<td>31.9 (4.7)</td>
<td>32 (5.5)</td>
<td>31.9 (4.6)</td>
<td>0.93</td>
</tr>
<tr>
<td>Gravidity</td>
<td>3.3 (1.6)</td>
<td>3.7 (1.6)</td>
<td>3.3 (1.6)</td>
<td>0.24</td>
</tr>
<tr>
<td>Term pregnancy</td>
<td>1.8 (1.3)</td>
<td>1.8 (1.6)</td>
<td>1.8 (1.4)</td>
<td>0.91</td>
</tr>
<tr>
<td>Prepregnancy weight (kg)</td>
<td>75.3 (15)</td>
<td>78.5 (10.9)</td>
<td>75.3 (15.9)</td>
<td>0.017</td>
</tr>
<tr>
<td>End of pregnancy weight (kg)</td>
<td>80.7 (15.9)</td>
<td>85.7 (13.2)</td>
<td>79.8 (15.9)</td>
<td>0.03</td>
</tr>
<tr>
<td>GA at GDM diagnosis</td>
<td>14.9 (3.9)</td>
<td>13.7 (4.2)</td>
<td>15.2 (3.8)</td>
<td>0.07</td>
</tr>
<tr>
<td>GA at delivery</td>
<td>37.8 (2.1)</td>
<td>38.8 (1.3)</td>
<td>37.9 (2.2)</td>
<td>0.90</td>
</tr>
<tr>
<td>Infant's weight (g)</td>
<td>3,298 (662)</td>
<td>3,507 (628)</td>
<td>3,260 (664)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

*Quantities given as mean (SD).
GA = gestational age, GDM = gestational diabetes mellitus, HTN = hypertension, VBAC = vaginal birth after cesarean section.
nosed with overt DM postpartum, with a negative predictive value of 96%.

Since women with GDM are at increased risk of developing type 2 DM later in life, ACOG recommends screening all women with GDM at 6–12 weeks postpartum for overt DM.\(^4\) Diabetes will be diagnosed in some women soon after pregnancy, suggesting that they had preexisting DM that was not diagnosed prior to pregnancy.\(^5\) Populations with a high prevalence of type 2 DM who do not have access to screening when not pregnant are at particularly high risk for this phenomenon.\(^5\) Since many women do not follow up for their postpartum visit or screening is not performed at that time, the opportunity to diagnose overt DM and improve periconceptional glycemic control in subsequent pregnancies may be lost. In addition, poorly controlled pregestational DM leads to serious end-organ damage that may eventually become life threatening,\(^6\) which can result from undiagnosed, and therefore untreated, DM.

The new guidelines for diagnosis of GDM and DM as proposed by the ADA and IADPSG recommend that women at high risk and who are found to have DM at their initial prenatal visit, using standard criteria, receive a diagnosis of overt DM and not GDM.\(^1\)^\(^2\) The standard criteria refer to the same diagnostic criteria we used in our study for postpartum overt DM, including an A1C of ≥ 6.5%. The performance of the commonly used IADPSG cutoff of ≥ 6.5% in our population gave us 46% sensitivity, 96% specificity, 67% PPV and 91% NPV. Therefore, with further analysis we were able to identify a population-specific cutoff of 5.9% of our predominantly Hispanic/Latino women. This underscores the need for larger-scale studies in pregnant women to validate the IADPSG cutoff value and also to find population-specific cutoffs in high-diabetic-volume centers.

Our study does have limitations. The retrospective nature of our study and the lack of adequate postpartum follow-up led to a small sample size. In addition, our patients are predominantly Hispanic/Latino, which may impair the ability to generalize these results to pregnant women of different ethnicities. The Hispanic population, however, is a high-risk group for GDM and pregestational DM as compared to other ethnicities, and therefore it is important to study this group specifically.\(^5\) The inability to find a discriminatory value that reliably predicts postpartum overt DM in our study is likely due to the fact that there is substantial overlap in the A1C values of the cases and controls. Although no controls were identified with an A1C > 9%, there were not enough cases with an A1C value this high to assign any statistical significance to this finding. Despite these limitations, our findings suggest that an elevated early pregnancy hemoglobin A1C may be predictive of overt DM and that this value may differ from that which is recommended by the ADA.

### Table II  Means and ROC Values for Various Laboratory Parameters by Case-control Status

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases Mean (SD)</th>
<th>Controls Mean (SD)</th>
<th>ROC</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c</td>
<td>6.7 (1.3)</td>
<td>5.6 (5)</td>
<td>0.88</td>
<td>0.83–0.95</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Glucola</td>
<td>213.9 (50.7)</td>
<td>187.9 (33.4)</td>
<td>0.71</td>
<td>0.58–0.84</td>
<td>0.001</td>
</tr>
<tr>
<td>GTT (fasting)</td>
<td>122.9 (22.6)</td>
<td>100.5 (26.5)</td>
<td>0.83</td>
<td>0.69–0.96</td>
<td>0.0006</td>
</tr>
<tr>
<td>1 hr</td>
<td>277.4 (31.3)</td>
<td>198.8 (23.2)</td>
<td>0.81</td>
<td>0.69–0.92</td>
<td>0.004</td>
</tr>
<tr>
<td>2 hr</td>
<td>206.9 (33.4)</td>
<td>170.4 (27.3)</td>
<td>0.82</td>
<td>0.70–0.95</td>
<td>0.003</td>
</tr>
<tr>
<td>3 hr</td>
<td>155.0 (45)</td>
<td>128.9 (36.2)</td>
<td>0.66</td>
<td>0.44–0.89</td>
<td>0.12</td>
</tr>
</tbody>
</table>

**Cases:** women with a diagnosis of postpartum diabetes. **Controls:** women without postpartum diabetes. **ROC** = receiver operating characteristic, **CI** = confidence interval, **GTT** = Glucola tolerance test.

### Figure 1  Hemoglobin A1C values in cases and controls.
and IADPSG. Since the diagnosis of overt DM may have significant long-term health care implications, we should proceed with caution before adopting universal A1C criteria for the diagnosis of overt DM in pregnancy until more rigorous evaluation of these criteria in pregnant women with follow-up testing is performed.

References