Hemoglobin A\textsubscript{1c} Levels in Diagnosed and Undiagnosed Black, Hispanic, and White Persons with Diabetes: Results from NHANES 1999–2000

John M. Boltri, MD; Ike S. Okosun, PhD; Monique Davis-Smith, MD; Robert L. Vogel, PhD

INTRODUCTION

Hemoglobin A\textsubscript{1c} (HbA\textsubscript{1c}) is an important tool for evaluating the management of diabetes mellitus (DM) because it reflects the mean blood glucose concentrations over the previous few months. Hemoglobin A\textsubscript{1c} (HbA\textsubscript{1c}) is highly correlated with long-term morbidity associated with DM, including retinopathy and nephropathy.\textsuperscript{1–6} The 2003 American Diabetes Association (ADA) Standards of Medical Care position statement recommends maintaining a virtually normal HbA\textsubscript{1c} of $<$7.0% for all persons with diabetes.\textsuperscript{7}

While some studies have shown a trend of increasing prevalence of DM in Black, Hispanic, and White Americans,\textsuperscript{8–11} little has been described with respect to racial/ethnic differences in HbA\textsubscript{1c} among persons with diagnosed and undiagnosed DM. A significant gap exists in the knowledge of racial variations in HbA\textsubscript{1c} levels among diagnosed and undiagnosed Americans with diabetes. Because of racial differences in diabetes, epidemiologic understanding of the factors that are associated with racial differences in elevated HbA\textsubscript{1c} is critical for crafting diabetes management programs across at-risk population groups.

The purpose of this study is to describe the distribution of HbA\textsubscript{1c} in a probability sample of Americans age $\geq$20 years with diagnosed and undiagnosed diabetes. The study also sought to compare the distribution of HbA\textsubscript{1c} among Blacks, Hispanics, and Whites, and to determine the association of HbA\textsubscript{1c} with body mass index (BMI), age, educational level, income, and sex.

METHODS

Data from the 1999–2000 National Health and Nutrition Examination Survey (NHANES) collected by the National Center for Health Statistics of the Center for Disease Control and Prevention (CDC) was used for this analysis.\textsuperscript{12} The measurement and sampling procedures have been previously described. Briefly, the NHANES 1999–2000 is a national, cross-sectional, multistage probability sample of the US civilian, non-institutionalized population, selected using a complex, stratified, multistage probability cluster sampling design. Consent was obtained from all subjects for the interview (which included collection of demographic data) and for the physical examination and laboratory testing. Height and weight were measured and laboratory samples were obtained in the mobile examination center. All techniques and equipment were standardized. Total glycosylated hemoglobin (GHb) measurements were performed on subjects $\geq$12 years of age by using the Boronate Affinity High Performance Liquid Chromatography system. Total GHb was then transformed to the equivalent HbA\textsubscript{1c}. This system is standardized to the Diabetes Control and Complications Trial, is less sensitive to

Key Words: Diabetes Mellitus, Epidemiologic Factors, Ethnic Groups, Glycosylated, Hemoglobin A, Population Groups

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A significant gap exists in the knowledge of racial variations in HbA1c levels among diagnosed and undiagnosed Americans with diabetes.

Hemoglobin degradation, and is not affected by hemoglobin variants S, C, D, and elevated hemoglobin F. [12]

Inclusion/Exclusion Criteria
All African Americans, Hispanics, and Whites who were >20 years old with a reported HbA1c level were included in this study. All other subjects were excluded. This study was approved by the Mercer University Institutional Review Board.

Definition of Terms
In NHANES 1999–2000, subjects were asked the following questions: 1) “Other than during pregnancy, have you ever been told by a doctor or health professional that you have diabetes or sugar diabetes?” 2) “Are you now taking insulin?” and 3) “Are you now taking diabetic pills to lower your blood sugar?” Subjects were included in the diagnosed diabetes group if they answered “yes” to any of these three questions. If they did not answer “yes” but their fasting blood glucose (FBG) met the American Diabetes Association (ADA) cutoff for DM (FBG ≥ 126 mg/dL), they were included in the undiagnosed diabetes group. In NHANES 1999–2000, annual income was reported as <$20,000 or ≥$20,000 and education was reported as less than high school, high school, or more than high school. We combined “high school” with “more than high school” to assess the association between education and HbA1c.

In the NHANES 1999–2000 survey subjects were asked to identify their race/ethnicity as Mexican-American, other Hispanic, Black (non-Hispanic Black), White (non-Hispanic White), or other (including multiracial). For the analysis presented in this paper we combined Hispanics plus Mexican Americans into a single group: Hispanics. We compared Hispanics with Blacks and Whites.

Statistical Analysis
Statistical analyses were carried out using SUDAAN version 7.5. [13] NHANES 1999–2000 used a complex cluster sampling design with intentional oversampling of sub-groups. In order to account for the unequal sub-group sample size and non-responses, sample weights for each subject, also provided by NHANES 1999–2000 were applied to the data. This sampling technique renders the data representative of the total national (civilian non-institutionalized) population of the United States. Ethnic differences for continuous and categorical variables were assessed with one-way analysis of variance (ANOVA) and chi-square statistics, respectively. Prevalence estimates were weighted to account for cluster design and to represent the total civilian non-institutionalized population of the US. Prevalences of diagnosed and undiagnosed diabetes were age-adjusted by direct methods using the 2000 US population census data. Multiple linear regression models were used to determine the relationship between elevated HbA1c and BMI and between HbA1c and age, education, income and sex. The distributions of HbA1c in the diagnosed and undiagnosed DM populations were evaluated using nonparametric smoothed curves, based on empiric HbA1c cut-points. The customary P value of <.05 was used to indicate statistical significance.

RESULTS
Of the 4880 subjects >20 years old in NHANES 1999–2000, 4076 met eligibility for this study; 776 were African-American, 1419 were Hispanic, and 1881 were Caucasian. Of the excluded subjects, 641 did not have a recorded HbA1c. The remaining 163 were listed in the “other” category for race. Four hundred ninety-five subjects were identified as having diabetes by either self-report or glucose level. The estimated age-adjusted population prevalence and SE (standard error) of diabetes was 8.2% (0.5) with the prevalence (SE) of diagnosed and undiagnosed diabetes being 6% (0.4) and 2.3% (0.4), respectively. Of the 495 persons with diabetes in the sample, 392 (79.2%) were diagnosed and 103 (20.8%) were undiagnosed.

The sample mean HbA1c for all 495 persons with diabetes was 7.8%, SE 0.1. Subject characteristics for the diagnosed (392), undiagnosed (103), and all persons with diabetes (495) are summarized in Table 1. Several statistically significant differences were seen among the variables studied between the three racial/ethnic groups. Overall, Whites were older and had higher education and higher income. More Blacks were female and had higher BMI. More Hispanics had lower education and income and lower mean BMI. Fasting blood glucose was lowest in Whites (157 mg/dL, SE .17) and highest in Blacks (182 mg/dL, SE .17), whereas HbA1c was lowest in Whites (7.6%, SE .2) and highest in Hispanics (8.2%, SE .3). The mean BMI for all subjects in all groups was in the obesity range (BMI ≥ 30). The prevalences of diabetes were higher in diagnosed and undiagnosed Blacks compared with their White and Hispanic counterparts (P<.001).

In persons with diagnosed diabetes, fasting blood glucose was lowest in Whites (149.9 mg/dL, SE .8), and highest in African Americans (182.3 mg/dL, SE .19). HbA1c was also lowest in Whites (7.5%, SE .3) and highest in Blacks (8.2%, SE .3). Whites were more likely to be older, male,
Table 1. Descriptive characteristics: population means and standard errors by race and group

<table>
<thead>
<tr>
<th></th>
<th>All Persons With Diagnosed Diabetes</th>
<th>P value</th>
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<tbody>
<tr>
<td></td>
<td>Blacks (n = 108)</td>
<td>Hispanics (n = 164)</td>
</tr>
<tr>
<td>FBG (mmol/L)</td>
<td>10.1 (1.1)</td>
<td>9.0 (0.8)</td>
</tr>
<tr>
<td>FBG (mg/dL)</td>
<td>182.3 (19)</td>
<td>162.3 (14)</td>
</tr>
<tr>
<td>HbA1c (mmol/L)</td>
<td>8.2 (3.0)</td>
<td>8.1 (0.4)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>33.7 (1.0)</td>
<td>31.0 (0.9)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>59.0 (1.7)</td>
<td>56.5 (1.6)</td>
</tr>
<tr>
<td>Education ≥HS</td>
<td>42.3% (6)</td>
<td>23.7% (6)</td>
</tr>
<tr>
<td>Income ≥$20K</td>
<td>42.4% (6)</td>
<td>43.4% (8)</td>
</tr>
<tr>
<td>Female sex</td>
<td>57.7% (5)</td>
<td>55.6% (7)</td>
</tr>
<tr>
<td>Prevalence of DM</td>
<td>11.1% (0.5)</td>
<td>8.9% (0.7)</td>
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<thead>
<tr>
<th></th>
<th>All Persons With Undiagnosed Diabetes</th>
<th>P-value</th>
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<tbody>
<tr>
<td></td>
<td>Blacks (n = 28)</td>
<td>Hispanics (n = 38)</td>
</tr>
<tr>
<td>FBG (mmol/L)</td>
<td>10.3 (0.6)</td>
<td>9.3 (0.7)</td>
</tr>
<tr>
<td>FBG (mg/dL)</td>
<td>184.7 (11)</td>
<td>167.2 (13)</td>
</tr>
<tr>
<td>HbA1c (mmol/L)</td>
<td>7.8 (7.0)</td>
<td>8.7 (7.0)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>33.6 (7.0)</td>
<td>30.4 (5.0)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>53.8 (10.0)</td>
<td>51.0 (15.0)</td>
</tr>
<tr>
<td>Education ≥HS</td>
<td>47.9% (12)</td>
<td>38.5% (14)</td>
</tr>
<tr>
<td>Income ≥$20K</td>
<td>71.3% (10)</td>
<td>51.0% (15)</td>
</tr>
<tr>
<td>Female sex</td>
<td>3.0% (0.5)</td>
<td>2.8% (0.2)</td>
</tr>
</tbody>
</table>

FBG=fasting blood glucose; BMI=body mass index; HS=high school; DM=diabetes mellitus.
P values compare variable differences across ethnic groups and were assessed by one-way analysis of variance (ANOVA) for continuous variables and chi-square statistics for categorical variables.

Values with different superscripts differ significantly (P<.05) in pairwise comparisons.

DISCUSSION

Hemoglobin A₁c (HbA₁c) is a marker of how well an individual’s diabetes has been controlled during the previous 3–4 months. Elevated HbA₁c levels signify a greater risk for complications of diabetes. The results reported here indicate that among diagnosed persons with diabetes, Whites as a group have a significantly lower mean HbA₁c than Blacks or Hispanics, whereas among undiagnosed persons with diabetes Hispanics have a significantly higher mean HbA₁c than Blacks and Whites. The prevalence of both diagnosed and un-

better educated, and have a higher income. Hispanics were the youngest and were less well educated than the other groups. In persons with undiagnosed diabetes, FBG was lowest in Hispanics (167.2 mg/dL, SE .13) and highest in African Americans (184.7 mg/dL, SE .11), whereas HbA₁c was highest in Hispanics (8.7%, SE .7). Again, Whites with undiagnosed diabetes were more likely to be older, male, better educated, and have higher income. Fewer than 17% of Hispanics and 29% of African-American persons with undiagnosed diabetes had a high school education.

Figure 1 shows the HbA₁c distribution curves for diagnosed and undiagnosed diabetes (all racial/ethnic groups combined). In both diagnosed and undiagnosed persons with diabetes, the distributions of HbA₁c were skewed to the right (higher values). The degree of skewness was greater in diagnosed than undiagnosed diabetes (P<.05). Also, the proportion of subjects with HbA₁c levels ≥7.0% was higher for the diagnosed diabetes group (61.5%) compared to undiagnosed diabetes group (48.5%, P<.05).

Associations between HbA₁c and other characteristics by race are depicted in Table 2. Body mass index and age were positively correlated with HbA₁c in all races (P<.001). High school education or higher was associated with lower HbA₁c in all three groups. Higher income was associated with slightly higher HbA₁c in Blacks only. White women were slightly more likely to have lower HbA₁c levels.

An excessive number of persons with diabetes have HbA₁c ≥7% (Table 3). Of the diagnosed persons with diabetes, 245 (62.5%) had HbA₁c ≥7%. Of the undiagnosed persons with diabetes, 48 (46.6%) have HbA₁c ≥7%. Statistically significant racial/ethnic differences were seen in the HbA₁c of diagnosed and undiagnosed subjects. Blacks and Hispanics with diagnosed diabetes were more likely to have HbA₁c ≥11%. The percentage of diagnosed persons with diabetes with HbA₁c levels ≥11% for Blacks, Hispanics, and Whites was 11.1%, 10.4%, and 1.7% respectively. Hispanics with undiagnosed diabetes were more likely to have HbA₁c ≥7%. The percentage of undiagnosed persons with diabetes with HbA₁c ≥7% for Blacks, Hispanics, and Whites was 39.3%, 60.5%, and 37.8% respectively.

DISCUSSION

Hemoglobin A₁c (HbA₁c) is a marker of how well an individual’s diabetes has been controlled during the previous 3–4 months. Elevated HbA₁c levels signify a greater risk for complications of diabetes. The results reported here indicate that among diagnosed persons with diabetes, Whites as a group have a significantly lower mean HbA₁c than Blacks or Hispanics, whereas among undiagnosed persons with diabetes Hispanics have a significantly higher mean HbA₁c than Blacks and Whites. The prevalence of both diagnosed and un-
diagnosed diabetes is highest in Blacks and lowest in Whites. More than one in five persons with diabetes are undiagnosed. The mean BMI is in the obesity range for both diagnosed and undiagnosed persons with diabetes of all races. Nearly two thirds of diagnosed persons with diabetes and nearly half of undiagnosed persons with diabetes have HbA1c above the recommended 7% threshold for more intensive treatment. These rates of control are lower than rates of control in patients with known hypertension, reinforcing the need for increased efforts to achieve adequate control once diabetes has been diagnosed.

Our study confirms previous findings that many persons with diagnosed diabetes have very elevated HbA1c levels, placing them at risk for serious diabetes-related complications; however, important ethnic disparities exist. The lower mean HbA1c in White persons with diabetes may indicate better treatment, better access to care, and/or better compliance with recommendations than in the other groups. African Americans and Hispanics may have other confounding factors that contribute to increased prevalence of diabetes and higher HbA1c levels. These factors may include poor access to high-quality care, less health insurance, later diagnosis of diabetes, higher prevalence of obesity, and lower educational and economic status. Improving glycemic control and increasing detection rates for diabetes are critical issues for Blacks, who have the highest prevalence of both undiagnosed and diagnosed diabetes, and for Hispanics, who have the highest rate of undiagnosed diabetes with HbA1c ≥ 7%. Physicians should identify patients with elevated HbA1c levels and aggressively seek to improve control of diabetes and cardiovascular risk factors.

In spite of the current ADA guidelines for diabetes screening, most persons with diabetes have complications at the time of diagnosis. This study determined that 39% of African Americans and 61% of Hispanics with undiagnosed diabetes have HbA1c ≥ 7%. Therefore, African Americans and Hispanics may indeed benefit from earlier screening than that currently recommended by the ADA. In an analysis by Dallo and Weller, the sensitivity for detecting diabetes increased to >95% by screening Whites ≥ 40 years old and non-Whites ≥ 30 years old. The American College of Endocrinology (ACE) recommends targeted screening of high-risk persons age ≥ 30 years. If universally applied, the ACE recommendations would significantly decrease the number of persons with undiagnosed diabetes, especially among African Americans and Hispanics. Several important barriers need to be addressed, however, in order to achieve higher screening rates. Many at-risk individuals lack knowledge about the severity of disease or benefits of treatment; few clinicians routinely screen for diabetes, even when risk factors are present; many third-party coverage payers do not pay for routine screening; and among insured patients, increasing insurance deductibles lead some individuals to delay routine screening. Education of patients and clinicians and dialogue with third-party payers may be necessary to address these barriers.

Our results also suggest that a positive correlation exists between HbA1c and BMI consistent with previous studies. We also found a positive correlation between HbA1c and age. Previous studies have yielded conflicting results regarding such correlations, with three studies yielding a positive correlation and two studies yielding a negative correlation. As expected,
an inverse relationship exists between HbA1c and education, indicating that better education is associated with lower HbA1c levels. Although income < $20,000 was not significantly associated with HbA1c in Hispanics or Whites, it was associated with a very small increase in HbA1c in Blacks. Finally, female sex among White subjects was associated with lower HbA1c levels, whereas there was no association between HbA1c and sex among Blacks or Hispanics. These results indicate that clinicians should have a lower threshold for diabetes screening in patients who are obese, older, and those of a lower income.

Limitations of the Study

This study has several limitations. First, although this sample is representative of the true sample of diagnosed and undiagnosed persons with diabetes in the United States it may be argued that the sample size is small. Second, because an oral glucose tolerance test was not performed, our results may have underestimated the true prevalence of diabetes, making it difficult to compare these results with the results from NHANES III. Third, including Mexican Americans with the other Hispanics makes this group more heterogeneous, resulting in less generalizable conclusions. Fourth, the lack of continuous data for income and education prevented an analysis of the linear relationship between these variables. Finally, because only one fasting blood sugar measure was used to include subjects or exclude them from the diabetes group rather than the recommended two measures, there may have been subjects included in the diabetes group who may not have diabetes, and vice-versa.

CONCLUSION

This study demonstrates that White persons with diabetes have lower HbA1c than Blacks or Hispanics, a result not explained by differences in BMI, age, or sex. More than 20% of persons with diabetes remain undiagnosed in the United States, with the prevalence of diagnosed and undiagnosed diabetes being highest in Blacks. Hemoglobin A1c (HbA1c) levels are ≈7% in nearly two thirds of diagnosed persons with diabetes and nearly half of undiagnosed persons with diabetes. Blacks and Hispanics have higher HbA1c than Whites. Obesity was found to be correlated with high HbA1c in both diagnosed and undiagnosed diabetes. Clinicians should screen African Americans and Hispanics who are at highest risk for diabetes including those with low income, low education, obesity and elderly, earlier and more frequently, and more aggressive treatment of DM is needed in these groups. Strategies should be developed to further study and address the disparities in the diagnosis and treatment of diabetes mellitus among different racial/ethnic groups.

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REFERENCES

Hemoglobin A1c Levels and Diabetes - Boltri et al


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Design and concept of study: Boltri, Okosun, Vogel

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Data analysis and interpretation: Boltri, Okosun, Davis-Smith, Vogel

Manuscript draft: Boltri, Okosun, Davis-Smith

Statistical expertise: Okosun, Vogel

Acquisition of funding: Davis-Smith

Administrative, technical, or material assistance: Boltri, Okosun, Davis-Smith

Supervision: Boltri, Okosun