HEMOGLOBIN A_{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

Purpose: Although the prevalence of diabetes among various racial/ethnic groups has been well studied, little is known about the racial/ethnic differences in Hemoglobin A_{1c} (HbA_{1c}) in diagnosed and undiagnosed diabetes. HbA_{1c} correlates with morbidity and mortality in diabetes. Knowledge of the racial/ethnic differences in HbA_{1c} would impact screening and intervention in primary care settings. This study describes racial/ethnic differences in HbA_{1c} among US Black, Hispanic, and White diagnosed and undiagnosed persons with diabetes.

Methods: This study included participants in the 1999–2000 National Health and Nutrition Examination Survey who were ≥20 years old with a HbA_{1c} measurement. The association between HbA_{1c} and race in diagnosed and undiagnosed persons with diabetes (with body mass index [BMI] and age as covariates) was determined. The distribution of HbA_{1c} and mean HbA_{1c} in diagnosed and undiagnosed diabetes and the rates of diagnosed and undiagnosed diabetes with their corresponding HbA_{1c} levels are described by race/ethnicity.

Results: Estimated diabetes prevalence in US persons ≥20 years is 8.2%, with 2.3% having undiagnosed diabetes. Whites with diabetes had lower mean HbA_{1c} levels (7.6%, standard error [SE] 0.2) than Blacks (8.1%, SE 0.3) or Hispanics (8.2%, SE .3). Whites with diagnosed diabetes were less likely to have HbA_{1c}≥11% (1.7%) than Blacks (11.1%) or Hispanics (10.4%). Hispanics with undiagnosed diabetes were more likely to have HbA_{1c}≥7% (60.5%) than Blacks (39.3%) or Whites (37.8%).

Conclusions: Significant numbers of persons with diabetes are undiagnosed. There are significant racial/ethnic differences in HbA_{1c} levels, which are significantly higher in Blacks and Hispanics. Comprehensive risk-based screening and intervention for diabetes is needed in order to address racial and ethnic disparities, especially in minorities. (*Ethn Dis.* 2005;15:562–567)

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

From the Department of Family Medicine, Mercer University School of Medicine, Macon (JB, MD); Institute of Public Health, Georgia State University, Atlanta (IO); College of Health and Human Sciences, Georgia Southern University, Statesboro (RV); Georgia.

Address correspondence and reprint requests to John M. Boltri, MD; Mercer University School of Medicine; Department of Family Medicine; 3780 Eisenhower Parkway; Macon, GA 31206; 478-633-5550; 478-784-5496 (fax); boltri.john@mccg.org

INTRODUCTION

Hemoglobin A_{1c} (HbA_{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_{1c} (HbA_{1c}) is highly correlated with long-term morbidity associated with DM, including retinopathy and nephropathy.[1–6] The 2003 American Diabetes Association (ADA) Standards of Medical Care position statement recommends maintaining a virtually normal HbA_{1c} of <7.0% for all persons with diabetes.[7]

While some studies have shown a trend of increasing prevalence of DM in Black, Hispanic, and White Americans,[8–11] little has been described with respect to racial/ethnic differences in HbA_{1c} among persons with diagnosed and undiagnosed DM. A significant gap exists in the knowledge of racial variations in HbA_{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_{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_{1c} in a probability sample of Americans age ≥20 years with diagnosed and undiagnosed diabetes. The study also sought to compare the distribution of HbA_{1c} among Blacks, Hispanics, and Whites, and to determine the association of HbA_{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.[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 ≥12 years of age by using the Boronate Affinity High Performance Liquid Chromatography system. Total GHb was then transformed to the equivalent HbA_{1c}. This system is standardized to the Diabetes Control and Complications Trial, is less sensitive to

A significant gap exists in the knowledge of racial variations in HbA_{1c} 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 HbA_{1c} 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 HbA_{1c}.

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 over sampling 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 HbA_{1c} and BMI and between HbA_{1c} and age, education, income and sex. The distributions of HbA_{1c} in the diagnosed and undiagnosed DM populations were evaluated using nonparametric smoothed curves, based on empiric HbA_{1c} 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 HbA_{1c}. 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 HbA_{1c} 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 HbA_{1c} 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). HbA_{1c} 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

	All Persons With Diagnosed Diabetes			
	Blacks (*n*=108)	Hispanics (*n*=164)	Whites (*n*=120)	*P* value
FBG (mmol/L)	10.1 (1.1)[a]	9.0 (0.8)[b]	8.3 (0.4)[c]	<.001
FBG (mg/dL)	182.3 (19)[a]	162.3 (14)[b]	149.9 (8)[c]	<.001
HbA_{1c}	8.2 (0.3) [a]	8.1 (0.4) [b]	7.5 (0.3) [c]	<.001
BMI (kg/m)	33.7 (1.0) [a]	31.0 (0.9) [b]	32.8 (0.9) [c]	<.001
Age (years)	59.0 (1.7) [a]	56.5 (1.6) [b]	60.2 (1.5) [c]	<.001
Education ≥HS	42.3% (6) [a]	23.7% (6) [b]	69.8% (4) [c]	<.001
Income ≥$20K	42.4% (6) [a]	43.4% (8) [a]	65% (5) [c]	<.05
Female sex	57.7% (5) [a]	55.6% (7) [b]	42.9% (5) [c]	<.001
Prevalence of DM	11.1% (0.5)	8.9% (0.7)	4.2% (0.5)	<.001
	All Persons With Undiagnosed Diabetes			
	Blacks (*n*=28)	Hispanics (*n*=38)	Whites (*n*=37)	P-value
FBG (mmol/L)	10.3 (0.6)[a]	9.3 (0.7)[b]	10.1 (0.8)[c]	<.001
FBG (mg/dL)	184.7 (11) [a]	167.2 (13) [b]	182.3 (15) [c]	<.001
HbA_{1c}	7.8 (.70) [a]	8.7 (.70) [b]	7.8 (.40) [a]	<.001
BMI (kg/m)	33.6 (.70) [a]	30.4 (.50) [b]	31.3 (1.3) [c]	<.001
Age (years)	53.8 (.40) [a]	54.1 (2.9) [b]	60.5 (2.3) [c]	<.001
Education ≥HS	29.0% (10) [a]	16.9% (9) [b]	70.5% (8) [c]	<.001
Income ≥$20K	47.9% (12) [a]	38.5% (14) [b]	60.1% (9) [c]	<.001
Female sex	71.3% (10) [a]	51.0% (15) [b]	46.7% (5) [c]	<.001
Prevalence of DM	3.0% (0.5)	2.8% (0.2)	2.4% (0.2)	<.001
	All Persons With Diabetes (Diagnosed plus Undiagnosed)			
	Blacks (*n*=136)	Hispanics (*n*=202)	Whites (*n*=157)	P-value
FBG (mmol/L)	10.1 (0.9)[a]	9.1 (0.6)[b]	8.7 (0.9)[c]	<.001
FBG (mg/dL)	182.8 (17) [a]	163.4 (11) [b]	157.4 (17) [c]	<.001
HbA_{1c}	8.1 (.30) [a]	8.2 (.30) [b]	7.6 (.20) [c]	<.001
BMI (kg/m)	33.7 (.80) [a]	30.8 (.70) [b]	32.5 (.74) [c]	<.001
Age (years)	57.6 (1.4) [a]	56.0 (2.1) [b]	60.2 (1.3) [c]	<.001
Education ≥HS	39.6%(5) [a]	22.3% (5) [b]	69.9% (4) [c]	<.001
Income ≥$20K	43.6%(5) [a]	42.7% (7) [b]	64.0% (4) [c]	<.001
Female sex	60.9%(5) [a]	54.7% (6) [b]	43.8% (4) [c]	<.001
Prevalence of DM	13.9% (0.8)	10.7% (0.9)	7.6% (0.5)	<.001

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.

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 HbA_{1c} 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 HbA_{1c} distribution curves for diagnosed and undiagnosed diabetes (all racial/ethnic groups combined). In both diagnosed and undiagnosed persons with diabetes, the distributions of HbA_{1c} 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 HbA_{1c} levels ≥7.0% was higher for the diagnosed diabetes group (61.5%) compared to undiagnosed diabetes group (48.5%, $P<.05$).

Associations between HbA_{1c} and other characteristics by race are depicted in Table 2. Body mass index and age were positively correlated with HbA_{1c} in all races ($P<.001$). High school education or higher was associated with lower HbA_{1c} in all three groups. Higher income was associated with slightly higher HbA_{1c} in Blacks only. White women were slightly more likely to have lower HbA_{1c} levels.

An excessive number of persons with diabetes have HbA_{1c} ≥7% (Table 3). Of the diagnosed persons with diabetes, 245 (62.5%) had HbA_{1c}≥7%. Of the undiagnosed persons with diabetes, 48 (46.6%) have HbA_{1c}≥7%. Statistically significant racial/ethnic differences were seen in the HbA_{1c} of diagnosed and undiagnosed subjects. Blacks and Hispanics with diagnosed diabetes were more likely to have HbA_{1c}≥11%. The percentage of diagnosed persons with diabetes with HbA_{1c} 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 HbA_{1c}≥7%. The percentage of undiagnosed persons with diabetes with HbA_{1c}≥7% for Blacks, Hispanics, and Whites was 39.3%, 60.5%, and 37.8% respectively.

DISCUSSION

Hemoglobin A_{1c} (HbA_{1c}) is a marker of how well an individual's diabetes has been controlled during the previous 3–4 months. Elevated HbA_{1c} 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 HbA_{1c} than Blacks or Hispanics, whereas among undiagnosed persons with diabetes Hispanics have a significantly higher mean HbA_{1c} than Blacks and Whites. The prevalence of both diagnosed and un-

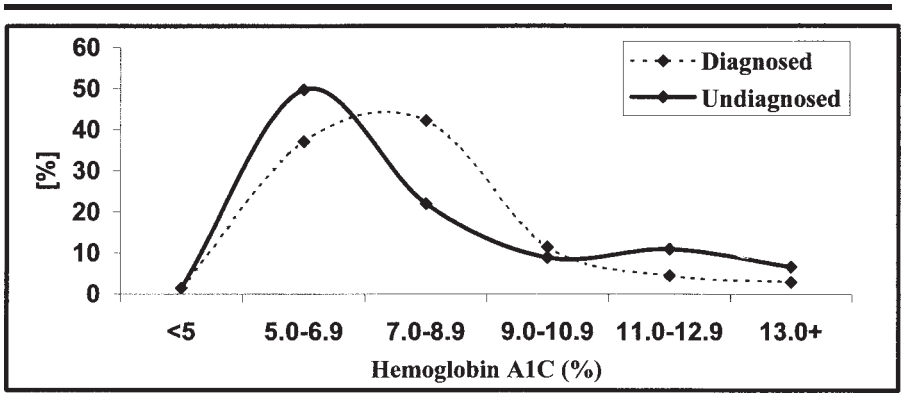

Fig 1. Distribution of HbA_{1c} in diagnosed (n=392) and undiagnosed (n=103) diabetes, in all race/ethnic groups combined

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 HbA_{1c} above the recommended 7% threshold for more intensive treatment.[7] These rates of control are lower than rates of control in patients with known hypertension,[14] 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 HbA_{1c} levels, placing them at risk for serious diabetes-related complications; however, important ethnic disparities exist. The lower mean HbA_{1c} 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 HbA_{1c} 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 $HbA_{1c} \geq 7\%$. Physicians should identify patients with elevated HbA_{1c} 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.[15] This study determined that 39% of African Americans and 61% of Hispanics with undiagnosed diabetes have $HbA_{1c} \geq 7\%$. 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.[16] The American College of Endocrinology (ACE) recommends targeted screening of high-risk persons age ≥30 years.[15] 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 HbA_{1c} and BMI consistent with previous studies.[17–20] We also found a positive correlation between HbA_{1c} and age. Previous studies have yielded conflicting results regarding such correlations, with three studies yielding a positive correlation[21–23] and two studies yielding a negative correlation.[24,25] As expected,

Table 2. Associations between HbA_{1c} and other characteristics

	Pearson's Correlation Coefficient (*P* value)		
	Blacks	**Hispanics**	**Whites**
BMI (kg/m^2)	.182 (<.001)	.172 (<.001)	.245 (<.001)
Age (years)	.297 (<.001)	.329 (<.001)	.325 (<.001)
	Beta from linear regression model (*P* value)		
	Blacks	**Hispanics**	**Whites**
Education ≥HS	−.126 (<.0001)	−.276 (<.001)	−.275 (<.001)
Income ≥$20,000	.090 (<.0001)	.021 (.443)	.081 (.603)
Female sex	−.020 (.960)	−.040 (.970)	−.101 (<.0001)

Values in parentheses are *P* values.

Table 3. Number of subjects (percent) by race across various HbA_{1c} cutpoints

	Persons with Diagnosed Diabetes						
	Blacks *n*=108	Hispanics *n*=164	Whites *n*=120	*P*	Total *n*=392	Mean FBG mmol/L	mg/dL
HbA_{1c} <7%	34 (31.3%)	63 (38.4%)	50 (41.7%)	.270	147 (37.5%)	6.1	110
HbA_{1c} 7% to <9%	46 (42.6%)	61 (37.2%)	53 (44.2%)	.452	160 (40.8%)	8.6	155
HbA_{1c} 9% to <1%	16 (14.8%)	23 (14.0%)	15 (12.5%)	.873	54 (13.8%)	11.9	215
HbA_{1c} ≥11%	12 (11.1%)	17 (10.4%)	2 (1.7%)	.010	31 (7.9%)	19.0	343
HbA_{1c} ≥7%	74 (68.5%)	101 (61.6%)	70 (58.3%)	.270	245 (62.5%)	8.9	160
	Persons With Undiagnosed Diabetes						
	Blacks *n*=28	Hispanics *n*=38	Whites *n*=37	*P*	Total *n*=103	Mean FBG mmol/L	mg/dL
HbA_{1c} <7%	17 (60.7%)	15 (39.5%)	23 (62.2%)	.095	55 (53.4%)	7.8	141
HbA_{1c} 7% to <9%	6 (21.4%)	12 (31.6%)	7 (18.9%)	.406	25 (24.3%)	9.1	164
HbA_{1c} 9% to <11%	3 (10.9%)	5 (13.2%)	1 (2.7%)	.252	9 (8.7%)	11.2	201
HbA_{1c} ≥11%	2 (7.1%)	6 (15.8%)	6 (16.2%)	.805	14 (13.6%)	16.9	305
HbA_{1c} ≥7%	11 (39.3%)	23 (60.5%)	14 (37.8%)	<.001	48 (46.6%)	9.7	174

an inverse relationship exists between HbA_{1c} and education, indicating that better education is associated with lower HbA_{1c} levels. Although income <$20,000 was not significantly associated with HbA_{1c} in Hispanics or Whites, it was associated with a very small increase in HbA_{1c} in Blacks. Finally, female sex among White subjects was associated with lower HbA_{1c} levels, whereas there was no association between HbA_{1c} 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 make 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 HbA_{1c} 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 A_{1c} (HbA_{1c}) 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 HbA_{1c} than Whites. Obesity was found to be correlated with high HbA_{1c} 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.

This study demonstrates that White persons with diabetes have lower HbA_{1c} than Blacks or Hispanics, a result not explained by differences in BMI, age, or sex.

ACKNOWLEDGMENTS

This project was supported in part by HRSA grant #5D16HP00136-02.

REFERENCES

1. Standards of medical care for patients with diabetes mellitus. *Diabetes Care.* 2002; 25(suppl 1):S33–S49.
2. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes

mellitus. The Diabetes Control and Complications Trial Research Group. *N Engl J Med*. 1993;329(14):977–986.
3. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. *Lancet*. 1998;352(9131):837–853.
4. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). UK Prospective Diabetes Study (UKPDS) Group. *Lancet*. 1998;352(9131):854–865.
5. Lawson ML, Gerstein HC, Tsui E, Zinman B. Effect of intensive therapy on early macrovascular disease in young individuals with type 1 diabetes. A systematic review and meta-analysis. *Diabetes Care*. 1999;22(suppl 2):B35–B39.
6. Stratton IM, Adler AI, Neil HA, et al. Association of glycemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ*. 2000;321(7258):405–412.
7. Standards of medical care for patients with diabetes mellitus. *Diabetes Care*. 2003; 26(suppl 1):S33–S50.
8. Prevalence of diabetes and impaired fasting glucose in adults – United States, 1999–2000. *Morb Mortal Wkly Rep*. 2003;52(35):833–837.
9. Dunstan DW, Zimmet PZ, Welborn TA, et al. The rising prevalence of diabetes and impaired glucose tolerance: the Australian Diabetes, Obesity and Lifestyle Study. *Diabetes Care*. 2002;25(5):829–834.
10. Harris MI, Flegal KM, Cowie CC, et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in US adults. The Third National Health and Nutrition Examination Survey, 1988–1994. *Diabetes Care*. 1998;21(4):518–524.
11. Hotu S, Carter B, Watson P, Cutfield W, Cundy T. Increasing prevalence of type 2 diabetes in adolescents. *J Pediatr Child Health*. 2004;40(4):201–204.
12. National health and nutrition examination survey. Center for Disease Control. Available at: www.cdc.gov.
13. Shah BV, Barnwell BG, Bieler GS. *SUDAAN User's Manual*. Release 7.5 ed. Research Triangle Park, NC: Research Triangle Institute; 1997.
14. Chobanian AV, Bakris GL, Black HR, Cushman WC. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA*. 2003;289(19):2560–2572.
15. American College of Endocrinology. Consensus statement on guidelines for glycemic control. *Endocr Pract*. 2002;8(suppl 1):5–11.
16. Dallo FJ, Weller SC. Effectiveness of diabetes mellitus screening recommendations. *Proc Natl Acad Sci U S A*. 2003;100(18):10574–10579.
17. Hogel J, Grabert M, Sorgo W, Wudy S, Gaus W, Heinze E. Hemoglobin A_{1c} and body mass index in children and adolescents with IDDM. An observational study from 1976–1995. *Exp Clin Endocrinol Diabetes*. 2000;108(2):76–80.
18. Domargard A, Sarnblad S, Kroon M, Karlsson I, Skeppner G, Aman J. Increased prevalence of overweight in adolescent girls with type 1 diabetes mellitus. *Acta Pediatr*. 1999;88(11): 1223–1228.
19. Pena-Valdovinos A, Jimenez-Cruz A, Leyva-Pacheco R, Bacardi-Gascon M. Metabolic control in diabetic patients at the primary care level in Mexico. *Diabetes Res Clin Pract*. 1997;37(3):179–184.
20. Jacobs ML, Elte JW, van Ouwerkerk BM, et al. Effect of BMI, insulin dose, and number of injections on glycemic control in insulin-using diabetic patients. *Neth J Med*. 1997; 50(4):153–159.
21. Yang Y, Lu F, Wu J, Chang C. Age and sex effects on HbA_{1c}: a study in a healthy Chinese population. *Diabetes Care*. 1997;20(6):988–991.
22. Arnetz BB, Kallner A, Theorell T. The influence of aging on hemoglobin A_{1c}(HbA_{1c}). *J Gerontol*. 1982;37(6):648–650.
23. Hashimoto Y, Futamura A, Ikushima M. Effect of aging on HbA_{1c} in a working male Japanese population. *Diabetes Care*. 1995; 18(10):1337–1340.
24. El-Keebi IM, Cook CB, Ziemer DC, Miller CD, Gallina DL, Phillips LS. Association of younger age with poor glycemic control and obesity in urban African Americans with type 2 diabetes. *Arch Intern Med*. 2003;163:69–75.
25. Gilliland SS, Carter JS, Skipper B, Acton KJ. HbA_{1c} levels among American Indian/Alaska native adults. *Diabetes Care*. 2002;25(12): 2178–2183.

AUTHOR CONTRIBUTIONS

Design and concept of study: Boltri, Okosun, Vogel
Acquisition of data: Boltri
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