

Racial and Ethnic Differences in Hemoglobin A1c among Patients with Impaired
Glucose Tolerance in the Diabetes Prevention Program

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Abstract

Objective To examine racial and ethnic differences in hemoglobin A1c (HbA1c) in people with Impaired Glucose Tolerance (IGT).

Research Design and Methods We studied 3,819 individuals ≥ 25 years of age with IGT found to be eligible to participate in the Diabetes Prevention Program. HbA1c was compared among five racial and ethnic groups before and after adjustment for factors that differed among groups or might affect glycemia including age, sex, education, marital status, blood pressure, adiposity (BMI and waist circumference), hematocrit, fasting and post glucose load glucose levels, glucose area under the curve, β -cell function, and insulin resistance.

Results Mean \pm SD HbA1c was $5.91 \pm 0.50\%$. Among Whites, HbA1c was $5.80 \pm 0.44\%$, among Hispanics $5.89 \pm 0.46\%$, among Asian American $5.96 \pm 0.45\%$, among American Indians $5.96 \pm 0.46\%$ and among African Americans $6.19 \pm 0.59\%$. Age, sex, SBP, DBP, BMI, fasting glucose, glucose area under the curve, corrected insulin response and insulin resistance were each independent predictors of HbA1c. Adjusting for these and other factors, mean HbA1c levels were 5.78% for Whites, 5.93% for Hispanics, 6.00% for Asian Americans, 6.12% for American Indians, and 6.18% for African Americans ($p < 0.001$).

Conclusions HbA1c levels are higher among U.S. racial and ethnic minority groups with IGT after adjustment for factors likely to affect glycemia. Among patients with IGT, HbA1c may not be valid for assessing and comparing glycemic control across racial and ethnic groups or as an indicator of health care disparities.

Carbohydrates are covalently attached to the N-terminal valine of the β -chain of hemoglobin by a slow non-enzymatic process. The most common modification, glucose attachment, can be measured as hemoglobin A1c (HbA1c). Since the early 1980s, HbA1c has been used as a clinical measure of average glycemia over the preceding weeks and months (1,2). With publication of the results of the Diabetes Control and Complications Trial and the United Kingdom Prospective Diabetes Study, HbA1c has also come to be used as a measure of risk for the development of diabetic complications.

In a recent systematic review, Kirk and colleagues summarized 21 studies which compared glycosylated hemoglobin levels across racial and ethnic groups (3). Seven of the 9 studies that tested differences between African Americans and non-Hispanic Whites and 4 of the 5 that tested differences between Hispanic Americans and non-Hispanic Whites demonstrated higher glycosylated hemoglobin levels among African Americans or Hispanic Americans. The authors concluded that African Americans and Hispanics with diabetes have poorer glycemic control than do non-Hispanic Whites (3). Five additional studies have compared glycosylated hemoglobin levels among racial and ethnic groups within organized systems of health care and carefully adjusted for processes of care (4-8). Although adjustment for covariates attenuated racial differences in glycosylated hemoglobin, the differences between racial groups remained statistically significant. Two

reports have also assessed the association between glycosylated hemoglobin and race and ethnicity in nondiabetic populations. Eberhardt and colleagues analyzed data from a community-based sample of 3,175 adults in the South Carolina Cardiovascular Disease Prevention Project (9). After adjusting for age and body mass index, glycosylated hemoglobin remained 0.3% and 0.4% higher in black men and women with no reported diabetes compared to white men and women with no reported diabetes ($p < 0.05$). More recently, Saaddine and colleagues described HbA1c by race for 7,968 young and apparently healthy participants in the Third National Health and Nutrition Examination Survey (10). Subjects were 5-24 years of age and had not been treated for diabetes. Mean HbA1c was $4.93\% \pm 0.04\%$ (SD) in non-Hispanic Whites, $5.05\% \pm 0.02\%$ in Mexican Americans, and $5.17\% \pm 0.02\%$ in non-Hispanic Blacks. After adjusting for age, sex, overweight, and education, HbA1c for non-Hispanic Blacks and Mexican Americans remained 0.2 and 0.1% higher than for non-Hispanic Whites.

These studies raise the question whether racial or ethnic differences in hemoglobin glycation or red cell survival rather than average glycemia might account for differences in HbA1c. We assessed baseline data from the Diabetes Prevention Program to compare HbA1c levels by race/ethnicity among 3,819 participants with impaired glucose tolerance before and after adjustment for factors that differed among groups

or were likely to affect glycemia including age, sex, education, marital status, blood pressure, adiposity (BMI and waist circumference), hematocrit, fasting and post glucose load glucose levels, glucose area under the curve, β -cell function, and insulin resistance.

Methods

The Diabetes Prevention Program was a 27 center randomized controlled clinical trial designed to evaluate the safety and efficacy of interventions to delay or prevent the development of diabetes in people at increased risk for type 2 diabetes. The baseline characteristics of the cohort have been described elsewhere (11). In brief, eligibility required age ≥ 25 years, BMI ≥ 24 kg/m² (≥ 22 kg/m² for Asian Americans), and plasma glucose two hours after a 75-gm oral glucose load of 140-199 mg/dl (7.8-11.1 mmol/L) plus a fasting plasma glucose of 95-125 mg/dl (5.3-6.9 mmol/L) (or any fasting glucose ≤ 125 mg/dl (6.9 mmol/L) for American Indians).

The data reported here were obtained before randomization and are based on the 3,819 participants screened and found to be eligible to participate in the DPP. Standardized interviewer-administered questionnaires were used to obtain data on race/ethnicity, education, and marital status. Seated blood pressures were measured twice with a mercury sphygmomanometer. Standing height and weight were determined in duplicate with stadiometers and calibrated balance beam scales by certified clinic staff. Waist circumference was measured at the midpoint between the iliac crest and the costal margin in the

midaxillary line. The oral glucose tolerance test was preceded by instructions to consume a usual diet with adequate carbohydrates and was initiated between 0700 and 1100 hours after an overnight fast. Blood was sampled from a vein before (0 minutes) and after 75 g oral glucose (Trutol 75: Custom Laboratories, Baltimore, MD). Blood was drawn during the fasting state for hematocrit, plasma glucose, and insulin; at 30 minutes for plasma glucose and insulin; and at 120 minutes for plasma glucose. The area under the 120 min glucose curve (AUC in mmol/L/120 min) was computed using the trapezoidal rule. Dividing the AUC by 120 min yields the corresponding AUC mean glucose in mmol/L. β -cell function was measured as corrected insulin response (CIR) where CIR = $(100 * 30\text{-min insulin } (\mu\text{u/ml})) / (30\text{-min glucose (mg/dl)} * [30\text{-min glucose (mg/dl)} - 70 \text{ mg/dl}])$. Insulin resistance was measured as HOMA IR where HOMA-IR = $\text{fasting insulin } (\mu\text{u/ml}) * (\text{fasting glucose (mg/dl)} / 18.01) / 22.5$.

Blood samples were collected and processed following the DPP Standardized Manual of Operations. Serum and plasma samples were stored at -20°C for a few days then shipped on dry ice in batches. Whole-blood samples for HbA1c analysis were shipped by overnight express within 24 hours of sample collection. Fasting specimens for A1c were obtained in eligible participants immediately before randomization. The average time interval between OGTT specimens and HbA1c was 60 ± 20 days (mean \pm SD). The time interval ranged from 52 days for

Hispanics to 60 days for Asians and African Americans to 62 days for Caucasians and 69 days for Native Americans. Hematocrit was performed locally. All other analytical measurements were performed at the Central Biochemistry Laboratory at the University of Washington, Seattle, Washington. Plasma glucose was measured on a chemistry autoanalyzer by the glucokinase method. Insulin measurements were performed by a radioimmunoassay method using an anti-guinea pig antibody that measures total immunoreactive insulin. HbA1c was measured by a dedicated ion-exchange high-performance liquid chromatography instrument (Variant: BioRad, Hercules, California). The intra-assay coefficient of variation was 1.36% and the inter-assay CV was 1.70%.

A normal errors multiple linear regression model was employed to assess differences between groups and the effects of covariates on levels of HbA1c (12). Collinearity diagnostics indicated that no statistical problems existed with the use of all the covariates simultaneously in a single multiple regression model. The normal errors assumption was verified using the Shapiro-Wilks test of the residuals (13). However, White's test of homoscedasticity was significant (14). Thus models were re-fit using White's asymptotic (consistent) robust information-sandwich estimate of the covariance matrix of the estimates, and these robust estimates used to construct a robust large sample test of the significance of each effect in the models. The results were unchanged and thus the model-based tests of

significance are presented. The strength of the effect of a covariate is expressed using the semi-partial R^2 that is the proportion decrease in the total sum of squares $[(N-1)*\text{Variance}]$ when that covariate is removed from the regression model containing all other covariates. For multiple comparisons among ethnic groups versus Caucasians, the Holm step-down Bonferroni method was used to adjust p-values for multiple tests (15). All analyses were performed using the Statistical Analysis System (SAS Institute, Cary, NC).

Results

Table 1 presents the characteristics of DPP participants at randomization by self-reported race and ethnic group. Of the 3,819 participants, 55% were white, 20% were African American, 16% were Hispanic, 5% were American Indian, and 4% were Asian American. Mean age was 51 years. Two-thirds were women. Approximately two-thirds were married and one quarter had college or higher educations. Mean blood pressure was 124/78 mm/Hg. Among women, mean BMI was 35 kg/m² and mean waist circumference was 104 cm. Among men, mean BMI was 32 kg/m² and mean waist circumference was 108 cm. Mean hematocrit was 41.1%. Mean fasting glucose was 106 mg/dl (5.9 mmol/L) and fasting insulin was 184.5 pmol/L. Mean CIR was 0.6 and mean HOMA IR was 7. Mean HbA1c was 5.91%.

Compared to Whites, African Americans, Hispanics, American Indians, and Asian Americans tended to be younger. Compared to Whites, African Americans, Hispanics, and

American Indians were more likely to be women and Asian Americans were more likely to be men. Compared to Whites, Asian Americans and Hispanics were more likely to be married and Asian Americans were more likely to be college graduates. Compared to Whites, African Americans and Asian Americans had higher and American Indians had lower blood pressure levels. Compared to Whites, African Americans had slightly higher BMIs and Hispanics and American Indians had slightly lower BMIs. Asian Americans had substantially lower BMIs reflecting the fact that Asian Americans with IGT and BMIs ≥ 22 kg/m² were eligible to participate. A similar pattern was observed with respect to waist circumference with the exception that African American and American Indian women had the highest waist circumferences. Compared to Whites, African Americans had lower and Asian Americans had higher hematocrits. Fasting plasma glucose levels were quite similar across groups except for American Indians who had lower fasting glucose levels, reflecting the fact that American Indians with IGT had no lower eligibility limit for FPG to participate in the DPP, a protocol variation based on their known high rate of conversion to diabetes regardless of FPG level. Compared to Whites, Hispanics, Asian Americans, African Americans and American Indians tended to have lower 30-minute post glucose load glucose values. Because all DPP participants were required to have IGT, 2-hour plasma glucose levels did not differ among groups. Whites and Hispanics had similar glucose AUCs, African

Americans and American Indians had lower glucose AUCs, and Asian Americans had higher glucose AUC means. Whites and Asian Americans had lower corrected insulin responses and were less insulin resistant. Compared to Whites, all race and ethnic groups had significantly higher HbA1c levels.

Table 2 presents a multiple regression model of the joint association of all covariates in Table 1 with HbA1c. The racial and ethnic differences in HbA1c persisted after adjusting for variables that might be related to the differences in HbA1c. The covariate-adjusted mean HbA1c levels estimated from the model were 5.78% for Whites, 6.18% for African Americans, 5.93% for Hispanics, 6.12% for American Indians, and 6.00% for Asian Americans. The values for all race and ethnic groups were significantly higher than for whites (each $p < 0.0001$ adjusted for multiple comparisons). Nonwhite race, older age, female sex, lower SBP, higher DBP, greater BMI, higher FPG, greater glucose AUC, lower CIR and higher HOMA IR were all independently associated with higher HbA1c and together, explained 22% of the variance.

Because the DPP used race- and ethnic- group-specific cutpoints for BMI (BMI ≥ 24 kg/m² except ≥ 22 kg/m² for Asian Americans) and FPG (95-125 mg/dl except ≤ 125 mg/dl for American Indians), we reran the analyses using common criteria for all groups (i.e. BMI ≥ 25 kg/m² and FPG 95-125 mg/dl (5.3-6.9 mmol/L)). The results were not substantially changed and all differences between racial and

ethnic groups remained statistically significant ($p < 0.0001$ adjusted for multiple comparisons).

Because there was a 60 day time interval between the OGTT and HbA1c, we reran the full model for the 2,022 participants who had not developed diabetes at one year of follow-up and had OGTTs and HbA1cs performed on the same day. Compared to Whites, the covariate-adjusted HbA1c values for all other race and ethnic groups remained significantly higher ($p < 0.0001$ adjusted for multiple comparisons).

Discussion

In this cohort of adults with IGT enrolled in the Diabetes Prevention Program, African Americans, Hispanic Americans, American Indians, and Asian Americans had higher HbA1c levels than whites. This effect persisted after adjusting for differences among groups in age, sex, education, marital status, blood pressure, body mass index, hematocrit, fasting and post glucose load glucose levels, glucose area under the curve, β -cell function, and insulin resistance. Taken together, these factors explained 22% of the variance in HbA1c.

Previous studies have demonstrated higher glycosylated hemoglobin levels among African Americans and Hispanic Americans but these results have been attributed to poorer glycemic control among racial and ethnic minority groups (3). However, studies that have compared glycosylated hemoglobin levels among racial and ethnic groups within organized systems of health care and have

carefully adjusted for processes of care, and studies of nondiabetic populations have still demonstrated persistent differences in mean HbA1c (4-8). Our findings that factors that differed among racial and ethnic groups or were likely to affect glycemia did not explain differences in HbA1c suggest that hemoglobin glycation or red cell survival may differ among racial and ethnic groups.

Previous studies in nondiabetic individuals have shown that HbA1c levels in the same individual change little over time but that levels vary markedly between individuals (16-18). Additional variation in HbA1c levels between individuals has been shown to be related to factors independent of glycemia such as female sex (19), sex hormones (20), differences in visceral fat (21), and biologic variation in hemoglobin glycation or red cell survival. Recent studies have suggested that inter-individual differences in intra-erythrocyte 2,3-diphosphoglycerate, which catalyzes the production of HbA1c, may in part account for the variability of glycosylated hemoglobin observed in nondiabetic subjects (22). Similarly, inter-individual variation in intra-erythrocyte fructosamine 3-kinase, which deglycosylates intracellular fructosamines, might partially explain nonglucose-mediated inter-individual variation in HbA1c (23). Evidence from diabetic twin studies have suggested that HbA1c levels are genetically determined (24,25). Inter-individual variation in HbA1c may also be explained by differences in erythrocyte survival. Studies in both type 1 (26) and type 2 diabetes (27) have, for example, demonstrated that

hyperglycemia is associated with decreased erythrocyte survival. In the DPP population, there were significant differences in hematocrit among racial and ethnic groups. Hemoglobinopathies were not systematically assessed but are generally more common in non-Whites and are associated with decreased erythrocyte survival and decreased glycohemoglobin percentages.

In conclusion, our analyses demonstrate that HbA1c levels are higher among U.S. racial and ethnic minority groups with impaired glucose tolerance after adjustment for differences among groups in age, sex, education, marital status, blood pressure, adiposity, hematocrit, fasting and post glucose load glucose levels, β -cell function, and insulin resistance. Thus the racial and ethnic differences in HbA1c are not explained by differences in these factors. We appreciate that these glucose levels may not be a robust reflection of the 24-hr glucose profile and that other unmeasured or suboptimally measured risk factors may explain some of these racial and ethnic differences in HbA1c. Clearly further studies are needed to confirm our observation. It is not known whether these racial and ethnic differences in HbA1c lead to differences in the risk of microvascular, neurologic, or macrovascular complications. Our results raise the possibility that HbA1c may not be valid for assessing and comparing glycemic control across

racial and ethnic groups or as an indicator of health care disparities. They also raise the important question whether HbA1c can be used as a diagnostic test for diabetes.

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References

1. Nathan DM, Singer DE, Hurxthal K, Goodson JD. The clinical information value of the glycosylated hemoglobin assay. *N Engl J Med* 310:341-346, 1984.
2. Goldstein DE, Little RR, Wiedmeyer H-M, England JD, McKenzie EM. Glycated hemoglobin: methodologies and clinical applications. *Clin Chem* 32B:64-70, 1986.
3. Kirk JK, Bell RA, Bertoni AG, Arcury TA, Quandt SA, Goff DC, Narayan KMV. Ethnic disparities: control of glycemia, blood pressure, and LDL cholesterol among US adults with type 2 diabetes. *Ann Pharmacother* 39:1489-1501, 2005.
4. Summerson JH, Konen JC, Dignan MB. Race-related differences in metabolic control among adults with diabetes. *Southern Medical J* 85:953-956, 1992.
5. Wisdom K, Fryzek JP, Havstad SL, Anderson RM, Dreiling MC, Tilley BC. Comparison of laboratory test frequency and test results between African-Americans and Caucasians with diabetes: opportunity for improvement. Findings from a large urban health maintenance organization. *Diabetes Care* 20:971-977, 1997.
6. Gary TL, McGuire M, McCauley J, Brancati FL. Racial comparisons of health care and glycemic control for African American and White diabetic adults in an urban managed care organization. *Dis Management* 7:25-34, 2004.
7. Brown AF, Gerzoff RB, Karter AJ, Gregg E, Safford M, Waitzfelder B, Beckles GLA, Brusuelas R, Mangione CM, for the TRIAD Study Group. Health behaviors and quality of care among Latinos with diabetes in managed care. *Am J Public Health* 93:1694-1698, 2003.
8. Brown AF, Gregg EW, Stevens MR, Karter AJ, Weinberger M, Safford MM, Gary TL, Caputo DA, Waitzfelder B, Kim C, Beckles GL. Race, ethnicity, socioeconomic position, and quality of care for adults with diabetes enrolled in managed care. The Translating Research Into Action for Diabetes (TRIAD) Study. *Diabetes Care* 28:2864-2870, 2005.
9. Eberhardt MS, Lackland DT, Wheeler FC, German RR, Teutsch SM. Is race related to glycemic control? An assessment of glycosylated hemoglobin in two S. Carolina communities. *J Clinical Epidemiol* 47:1181-1189, 1994.
10. Saaddine JB, Fagot-Campagna A, Rolka D, Narayan KMV, Geiss L, Eberhardt M, Flegal KM. Distribution of HbA1c levels for children and young adults in the U.S.: Third National Health and Nutrition Examination Survey. *Diabetes Care* 25:1326-1330, 2002.
11. The Diabetes Prevention Program Research Group. The Diabetes Prevention Program. Baseline characteristics of the randomized cohort. *Diabetes Care* 23:1619-1629, 2000.
12. Hocking, R.R. *The Analysis of Linear Models*. Belmont, CA. Brooks/Cole Publishing Co, 1985.

13. Shapiro, S.S. and Wilk, M.B. "An Analysis of Variance Test for Normality (complete samples)". *Biometrika* 52:591-611, 1965.
14. White, H. A Heteroskedasticity-Consistent Covariance Matrix Estimator and a Direct Test for Heteroskedasticity. *Econometrics* 48:817 -838, 1980.
15. Holm, S. A Simple Sequentially Rejective Bonferroni Test Procedure. *Scandinavian Journal of Statistics* 6:65 -70, 1979.
16. The DCCT Research Group. Diabetes Control and Complications Trial (DCCT): Results of Feasibility Study. *Diabetes Care* 10:1-19, 1987.
17. Yudkin JS, Forrest RD, Jackson CA, et al. Unexplained variability of glycated hemoglobin in non-diabetic subjects not related to glycaemia. *Diabetologia* 33:208-215, 1990.
18. Meigs JB, Nathan DM, Cupples LA, et al. Tracking of glycated hemoglobin in the original cohort of the Framingham-Heart Study. *J Clin Epidemiol* 49:411-417, 1996.
19. Strickland MH, Paton RC, Wales JK. Hemoglobin A1c concentrations in men and women with diabetes. *Br Med J* 289:733, 1984.
20. Kalish GM, Barrett-Connor E, Laughlin GA, Gulanski BI. Postmenopausal Estrogen/Progestin Intervention Trial. Association of endogenous sex hormones and insulin resistance among postmenopausal women: results from the Postmenopausal Estrogen/Progestin Intervention Trial. *J Clin Endocrinol Metab* 88:1646-1652, 2003.
21. Araneta MR, Barret-Connor E. Ethnic differences in visceral adipose tissue and type 2 diabetes: Filipino, African-American, and White women. *Obesity Research* 13:1458-1465, 2005.
22. Gould BJ, Davie SJ, Yudkin JS. Investigation of the mechanism underlying the variability of glycated haemoglobin in non-diabetic subjects not related to glycaemia. *Clinica Chimica Acta* 260: 49-64, 1997.
23. Delpierre G, Collard F, Fortpied J, Van Schaftingen E. Fructosamine 3-kinase is involved in an intracellular deglycation pathway in human erythrocytes. *Biochem J* 365: 801-808, 2002.
24. Snieder H, Sawtell PA, Ross L, Walker J, Spector TD, Leslie RD. HbA1c levels are genetically determined even in type 1 diabetes: evidence from healthy and diabetic twins. *Diabetes* 50:2858-2863, 2001.
25. Cohen RM, Snieder H, Lindsell CJ, Beyan H, Hawa MI, Blinko S, Edwards R, Spector TD, Leslie RDG. Evidence for independent heritability of the glycation gap (glycosylation gap) fraction of HbA1c in nondiabetic twins. *Diabetes Care* 29:1739-1743, 2006.
26. Peterson CM, Jones RL, Koenig RJ, Melvin ET, Lehrman ML. Reversible hematologic sequelae of diabetes mellitus. *Ann Intern Med* 86:425-429, 1977.
27. Virtue MA, Furne JK, Nuttall FQ, Levitt MD. Relationship between GHb concentration and erythrocyte survival determined from breath carbon monoxide concentration. *Diabetes Care* 27:931-935, 2004.

Table 1. Participant Characteristics by Racial and Ethnic Group

Clinical Characteristic	All	White	African American	Hispanic	American Indian	Asian American	P
N	3819	2117	752	609	174	167	
Age, y	50.7 ± 10.6	51.9 ± 10.6	50.5 ± 10.1*	48.4 ± 10.1 ⁺⁺	44.5 ± 9.8 ⁺⁺	49.8 ± 10.1*	<0.001
Sex, women	2576 (67.5%)	1387 (65.5%)	559 (74.3%) ⁺⁺	408 (67.0%)	153 (87.9%) ⁺⁺	69 (41.3%) ⁺⁺	<0.001
Marital status (married/living together)	2493(65.3%)	1471(69.5%)	353(46.9%) ⁺⁺	421(69.1%)	113(64.9%)	135(80.8%) ⁺	<0.001
Education 13-16 years	1821(47.7%)	1048(49.5%)	335(44.6%) ⁺⁺	260(42.7%) ⁺⁺	92(52.9%) ⁺	86(51.5%)	<0.001
≥ 17 years	1018(26.7%)	667(31.5%)	204(27.1%) ⁺⁺	71(11.7%) ⁺⁺	18(10.3%) ⁺⁺	58(34.7%)	<0.001
Blood Pressure							
Systolic, mmHg	123.9 ± 14.6	123.8 ± 14.1	127.0 ± 15.3 ⁺⁺	122.2 ± 14.3*	116.0 ± 12.4 ⁺⁺	124.8 ± 16.3	<0.001
Diastolic mmHg	78.4 ± 9.3	78.0 ± 9.1	79.8 ± 10.0 ⁺⁺	77.9 ± 8.7	75.3 ± 8.6 ⁺⁺	82.2 ± 9.7 ⁺⁺	<0.001
BMI, kg/m ²	33.9 ± 6.7	34.1 ± 6.8	35.2 ± 7.0 ⁺⁺	33.1 ± 5.7 ⁺	33.6 ± 6.1	29.5 ± 5.3 ⁺⁺	<0.001
Men	32.0 ± 5.6	32.4 ± 5.9	32.6 ± 5.8	31.4 ± 4.8	31.2 ± 4.0	28.5 ± 3.8 ⁺⁺	<0.001
Women	34.9 ± 6.9	34.9 ± 7.1	36.2 ± 7.1 ⁺⁺	33.9 ± 5.9*	33.9 ± 6.3	30.9 ± 6.5 ⁺⁺	<0.001
Waist circumference, cm							
Men	107.7 ± 13.5	110.2 ± 13.4	106.9 ± 13.9 ⁺⁺	104.5 ± 12.3 ⁺	107.0 ± 11.0	97.1 ± 9.6 ⁺⁺	<0.001
Women	103.6 ± 14.9	104.1 ± 14.8	106.1 ± 16.3*	99.6 ± 12.6 ⁺⁺	105.2 ± 13.2	93.5 ± 14.0 ⁺⁺	<0.001
Hematocrit (%)	41.1 ± 3.5	41.4 ± 3.3	39.6 ± 3.4 ⁺⁺	41.2 ± 3.7	41.5 ± 3.5	42.9 ± 3.7 ⁺⁺	<0.001
Plasma glucose, mmol/L							
Fasting	5.9 ± 0.5	5.9 ± 0.5	6.0 ± 0.5	5.9 ± 0.5	5.6 ± 0.5	6.0 ± 0.4	<0.001
30 minute	9.4 ± 1.4	9.5 ± 1.4	9.0 ± 1.2	9.6 ± 1.4	9.3 ± 1.3	9.8 ± 1.5	<0.001
120 minute	9.1 ± 1.0	9.2 ± 0.9	9.1 ± 1.0	9.1 ± 1.0	9.1 ± 1.0	9.3 ± 0.9	0.211
Glucose AUC	8.9 ± 0.8	8.9 ± 0.8	8.7 ± 0.8	9.0 ± 0.9	8.8 ± 0.8	9.1 ± 0.9	<0.001
Fasting insulin, pmol/L	184.5 ± 104.1	177.8 ± 100.4	189.7 ± 98.1	198.0 ± 113.9	207.2 ± 125.0	173.4 ± 107.8	<0.001
Corrected insulin response (CIR)	0.6 ± 0.4	0.6 ± 0.4	0.7 ± 0.5 ⁺⁺	0.7 ± 0.5 ⁺⁺	0.9 ± 0.5 ⁺⁺	0.6 ± 0.4	<0.001
Insulin resistance (HOMA IR)	7.0 ± 4.2	6.8 ± 4.0	7.3 ± 3.9*	7.5 ± 4.6 ⁺⁺	7.4 ± 4.7	6.7 ± 4.3	<0.001
HbA1c (%)	5.91 ± 0.50	5.80 ± 0.44	6.19 ± 0.59 ⁺⁺	5.89 ± 0.46 ⁺⁺	5.96 ± 0.46 ⁺⁺	5.96 ± 0.45 ⁺⁺	<0.001

Data are mean ± SD or n (%). P for test of difference in means or percentages among the ethnic groups.

Glucose AUC was calculated using the trapezoidal rule from the 2 h OGTT values.

We compared the White versus other race groups (Significant p-values are shown as * <0.05, + <0.01, ++ <0.001). Step-down Bonferroni method (Holm, 1979) was used to adjust for multiple comparisons.

Table 2. Racial and Ethnic Differences in HbA1c in a Multiple Regression Model Adjusting for the Effects of Other Covariates on HbA1c

Parameter	Estimate	SE	P-value	Type II semi-partial R²
Race (vs. Caucasian)				
African American	0.404	0.0205	<.0001	0.0811
Hispanic	0.149	0.0220	<.0001	0.00959
American Indian	0.206	0.0374	<.0001	0.00630
Asian	0.343	0.0376	<.0001	0.0173
Age at Randomization	0.0105	0.000833	<.0001	0.0328
Sex (Female vs. Male)	0.0786	0.0224	0.0005	0.00256
Systolic Blood Pressure	-0.00146	0.000700	0.0371	0.00091
Diastolic Blood Pressure	0.00357	0.00105	0.0007	0.00239
BMI	0.00527	0.00234	0.0240	0.00106
Fasting Glucose	0.259	0.0205	<.0001	0.0335
Glucose AUC	0.0245	0.0112	0.0286	0.00010
Corrected Insulin Response (CIR)	-0.0641	0.0231	0.0055	0.00160
Insulin Resistance (HOMA IR)	0.00543	0.00242	0.0251	0.00104

Also adjusted for education, marital status, waist circumference and hematocrit; all not significant at 0.05 level.