Racial Disparity in A1C Independent of Mean Blood Glucose in Children With Type 1 Diabetes

JODI L. KAMPS, PHD[1,2]
JAMES M. HEMPE, PHD[2,3]
STUART A. CHALEW, MD[2,3,4]

OBJECTIVE — Mean blood glucose (MBG) and MBG-independent factors both influence A1C levels. Race was related to A1C independent of MBG in adults. The goal of this study was to determine if racial disparity exists in A1C independent of MBG in children with diabetes.

RESEARCH DESIGN AND METHODS — Participants included 276 children with type 1 diabetes. A1C and MBG were obtained from multiple clinic visits, and a hemoglobin glycation index (HGI) (an assessment of A1C levels independent of MBG) was calculated. A1C and HGI were analyzed controlling for age, diabetes duration, and MBG.

RESULTS — African Americans had statistically significantly higher A1C (9.1 ± 0.1) and HGI (0.64 ± 0.11) than Caucasians (A1C 8.3 ± 0.1, HGI −0.15 ± 0.07) independent of covariates.

CONCLUSIONS — Because of racial disparity in A1C, which is independent of MBG, we recommend that A1C and MBG be used together to make therapeutic decisions for children with diabetes.

Diabetes Care 33:1025–1027, 2010

Our group previously demonstrated that A1C levels are determined by mean blood glucose (MBG) and MBG-independent factors (1–3). Identification of MBG-independent factors that influence A1C levels is important for proper interpretation of A1C results and assessment of glycemic control in patients with diabetes, particularly because patients with higher than average A1C levels independent of MBG have greater risk of microvascular complications (2). Recent data from adults (4–8) indicate that ethnicity/race is associated with differences in A1C independent of MBG. Race may also be associated with variation in A1C levels in children with or without diabetes (9,10), although these findings were not shown to be independent of MBG. The goal of the current study was to determine if racial disparity exists in A1C independent of MBG in children with type 1 diabetes.

RESEARCH DESIGN AND METHODS

— Participants included 276 children from Children's Hospital of New Orleans with type 1 diabetes who self-identified as either African American or Caucasian. Patient participation was approved by the relevant institutional review boards.

MBG and A1C were obtained from participant medical records between 2002 and 2008, and average values were calculated for each participant. MBG was calculated as the mean of self-monitored blood glucose data downloaded from strip-based patient glucose meters during periods of at least 30 days. Most A1C assays (98%) were performed at Children's Hospital by the DCA 2000+ Analyzer (78%) and later the VITROS 5,1 chemistry system. A few samples (2%) were measured at outside commercial reference laboratories. All assays reported results in National Glycohemoglobin Standardization Program (NGSP) equivalents (11). Statistical analysis indicated no differences in A1C by assay method.

Evidence for a glucose-independent effect of race on A1C was tested by using MBG as a covariate in the analysis, or in a separate statistical model using the calculated hemoglobin glycation index (HGI) described elsewhere in detail (1,2,12). HGI was calculated by subtracting the patient's predicted A1C from the observed A1C measured at each clinic visit. Predicted A1C was determined by inserting the patient's MBG into a population regression equation {A1C [%] = [MBG (mg/dl) × 0.021] + 4.3}. Patients were divided into low, moderate, and high HGI groups based on mean HGI tertile (33%) rank using predetermined delimiters (low HGI was <-0.41, high HGI was >0.26, and moderate HGI was equal to all values in between) (12).

Demographic results are presented as means (± 1 SD). Appropriate transformations were applied to variables that were not normally distributed before ANOVA, although findings using raw and transformed data were both statistically significant and results using raw data are presented.

RESULTS

— Participants included 141 females (51.1%) and 198 Caucasians (71.7%) with a mean age of 12.5 years (± 3.6) and mean diabetes duration of 4.9 years (± 3.4). The mean number of clinic visits was 7.7 (± 2.8). Mean A1C was 8.5% (± 1.3), and mean HGI was 0.08 (± 1.08).

Participants were classified into HGI categories: low HGI (n = 89, 32.1%), moderate HGI (n = 94, 33.9%), and high HGI (n = 93, 33.7%). Results of χ^2 analyses indicated significant differences in HGI group by race ($P < 0.001$) but not by sex. Specifically, 25.6% of African American children were in the low HGI group, 16.7% were in the moderate HGI group, and 57.7% were in the high

From the [1]Department of Psychology, Children's Hospital, New Orleans, Louisiana; the [2]Department of Pediatrics, Louisiana State University Health Sciences Center, New Orleans, Louisiana; the [3]Children's Hospital Research Institute for Children, New Orleans, Louisiana; and the [4]Department of Endocrinology, Children's Hospital, New Orleans, Louisiana.
Corresponding author: Jodi L. Kamps, jkamps@chnola.org.
Received 3 August 2009 and accepted 8 February 2010. Published ahead of print at http://care.diabetesjournals.org on 25 February 2010. DOI: 10.2337/dc09-1440.

Table 1—*Results of ANOVA/ANCOVA (controlling for MBG, participant age, and diabetes duration) evaluating differences in A1C and HGI between African American and Caucasian participants*

	African American	Caucasian
n	78	198
Unadjusted (mean ± SD)		
A1C (%)	9.4 ± 1.5	8.2 ± 1.0*
HGI (%)	0.65 ± 1.44	−0.15 ± 0.79*
Adjusted (mean ± SEM)		
A1C (%)	9.1 ± 0.1	8.3 ± 0.1*
HGI (%)	0.64 ± 0.11	−0.15 ± 0.07*

*$P < 0.001$; values within a row are significantly different.

HGI group. For Caucasian participants, 34.8% were in the low HGI group, 40.9% were in the moderate HGI group, and 24.2% were in the high HGI group.

ANOVA was also conducted to evaluate differences between African Americans and Caucasians. The analysis yielded significantly different results for participant age and MBG, with African Americans exhibiting older age (mean 13.2 years for African Americans, 12.2 years for Caucasians, $P < 0.05$) and higher MBG (mean 206 mg/dl for African Americans, 189 mg/dl for Caucasians, $P < 0.001$) but not longer diabetes duration (mean 5.1 years for African Americans, 4.8 years for Caucasians, $P = 0.53$).

Results of ANOVA also yielded statistically higher A1C and HGI for African Americans compared with Caucasians (Table 1, unadjusted results). ANCOVA also indicated significantly higher A1C ($P < 0.001$) and HGI ($P < 0.001$) for African Americans compared with Caucasians, even when controlling for participant age, diabetes duration, and MBG (Table 1, adjusted results).

CONCLUSIONS — This study demonstrates that African American children with diabetes have higher A1C levels than Caucasians independent of MBG. This finding extends similar observations in adults (7,8) to children with diabetes and suggests that race was a factor accounting for between-individual differences in A1C previously described by our group (9). Previous analyses suggest that between-individual differences in A1C independent of MBG are not due to red blood cell turnover (1) or artifacts in the measurement of A1C or calculation of MBG (12). Biological factors that may influence intracellular A1C levels independent of MBG include those that influence nonenzymatic glycation (e.g., pH, glucose transport, and oxidative status) or enzymatic deglycation (13,14). However, further research will be necessary to clarify the mechanism of racial disparity in A1C.

These results indicate that discrepancies exist in the information provided by MBG versus A1C, particularly for children from different racial groups, and that MBG or A1C alone may not provide complete information about metabolic status. Because A1C differences independent of MBG contribute to risk for microvascular complications (2), this finding may help explain why African Americans are at increased risk of diabetes complications (4,9,15). Given that MBG-independent disparity in A1C is unlikely to be modifiable by glucose-lowering agents, simply increasing insulin doses to achieve a lowered target A1C could lead to greater risk of hypoglycemia in African American patients. Evidence of higher A1C levels in African Americans independent of MBG also has implications for diagnosis of diabetes, whether diagnosis is based on blood glucose concentration or A1C. We recommend that both A1C and MBG be evaluated when making therapeutic decisions in individuals with diabetes, especially in African Americans, who, based on current results, exhibit a tendency for higher A1C levels at any given MBG.

Acknowledgments — This research was supported by a grant from the American Diabetes Association (7-04-CR-04); by the Department of Pediatrics, Louisiana State University Health Sciences Center; and by the Children's Hospital of New Orleans.

No potential conflicts of interest relevant to this article were reported.

Parts of this study were presented in poster format at the 69th Scientific Sessions of the American Diabetes Association, New Orleans, Louisiana, 5–9 June 2009.

We would like to express our appreciation to the patients who volunteered for this study and the staff of Children's Hospital laboratory and our diabetes nurses for their assistance with data collection.

References

1. Hempe JM, Gomez R, McCarter RJ Jr, Chalew SA. High and low hemoglobin glycation phenotypes in type 1 diabetes: a challenge for interpretation of glycemic control. J Diabetes Complications 2002; 16:313–320
2. McCarter RJ, Hempe JM, Gomez R, Chalew SA. Biological variation in HbA1c predicts risk of retinopathy and nephropathy in type 1 diabetes. Diabetes Care 2004;27:1259–1264
3. McCarter RJ, Hempe JM, Chalew SA. Mean blood glucose and biological variation have greater influence on HbA1c levels than glucose instability: an analysis of data from the Diabetes Control and Complications Trial. Diabetes Care 2006;29:352–355
4. Kirk JK, D'Agostino RB Jr, Bell RA, Passmore LV, Bonds DE, Karter AJ, Narayan KM. Disparities in HbA1c levels between African-American and non-Hispanic white adults with diabetes: a meta-analysis. Diabetes Care 2006;29:2130–2136
5. Kirk JK, Passmore LV, Bell RA, Narayan KM, D'Agostino RB Jr, Arcury TA, Quandt SA. Disparities in HbA1c levels between Hispanic and non-Hispanic white adults with diabetes: a meta-analysis. Diabetes Care 2008;31:240–246
6. Herman WH, Dungan KM, Wolffenbuttel BHR, Buse JB, Fahrbach JL, Jiang H, Martin S. Racial and ethnic differences in mean plasma glucose, hemoglobin A1c, and 1,5-anhydroglucitol in over 2000 patients with type 2 diabetes. J Clin Endorinol Metab 2009;94:1689–1694
7. Herman WH, Ma Y, Uwaifo G, Haffner S, Kahn SE, Horton ES, Lachin JM, Montez MG, Brenneman T, Barrett-Connor E, the Diabetes Prevention Program Research Group. Differences in A1C by race and ethnicity among patients with impaired glucose tolerance in the Diabetes Prevention Program. Diabetes Care 2007;30:2453–2457
8. Selvin E, Zhu H, Brancati FL. Elevated A1C in adults without a history of diabetes in the U.S. Diabetes Care 2009; 32:828–833
9. Chalew SA, Gomez R, Butler A, Hempe J, Compton T, Mercante D, Rao J, Vargas A. Predictors of glycemic control in children with type 1 diabetes: the importance of race. J Diabetes Complications 2000;14: 71–77
10. Saaddine JB, Fagot-Campagna A, Rolka D, Narayan KM, Geiss L, Eberhardt M, Flegal KM. Distribution of HbA1c levels for children and young adults in the U.S.: Third National Health and Nutrition Ex-

amination Survey. Diabetes Care 2002; 25:1326–1330
11. Little RR, Rohlfing CL, Wiedmeyer HM, Myers GL, Sacks DB, Goldstein DE, the NGSP Steering Committee. The National Glycohemoglobin Standardization Program: a five-year progress report. Clin Chem 2001;47:1985–1992
12. Soros AA, Chalew SA, McCarter RJ, Shepard R, Hempe JM. Hemoglobin glycation index: a robust measure of hemoglobin A1c bias in pediatric type 1 diabetes patients. Pediatr Diabetes. 18 January 2010 [Epub ahead of print]
13. Gould BJ, Davie SJ, Yudkin JS. Investigation of the mechanism underlying the variability of glycated haemoglobin in non-diabetic subjects not related to glycaemia. Clin Chim Acta 1997;260:49–64
14. Delpierre G, Collard F, Fortpied J, Van Schaftingen E. Fructosamine 3-kinase is involved in intracellular deglycation pathway in human erythrocytes. Biochem J 2002;365:801–808
15. Arfken CL, Reno PL, Santiago JV, Klein R. Development of proliferative diabetic retinopathy in African-Americans and whites with type 1 diabetes. Diabetes Care 1998; 21:792–795