

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

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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.

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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 indepen-

dent 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 $\{A1C [\%] = [MBG (mg/dl) \times 0.021] + 4.3\}$. 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

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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
<i>n</i>	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, glu-

cose 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.

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

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