

Racial Disparities on Glycemic Control and Lipid Profiles in Children with Type 1 Diabetes

Ambika Ashraf¹, Yufeng Li², Frank Franklin³, Kenneth McCormick¹ and Elaine Moreland¹

¹Department of Pediatrics/Division of Pediatric Endocrinology and Metabolism, University of Alabama at Birmingham. ²The Department of Biostatistics and bio informatics unit, Comprehensive Cancer Center, UAB. ³Department of Maternal and Child health, UAB School of Public Health, Birmingham.

Abstract

Objective: We assessed the racial (Black–White) differences in glycemic control, prevalence of abnormal lipid profiles and factors influencing temporal trends in children with type 1 diabetes (T1DM).

Methods: This retrospective study was done in children with T1DM. The outcome measure was based on glycemic control and all lipid determinations which were stratified according to the published guidelines.

Results: The study included 181 children; 76.2% Whites and 23.8% Blacks. The mean glycated hemoglobin (A1C) was higher in Blacks than in Whites ($p < 0.0001$). Blacks had elevated total cholesterol (TC) ($p = 0.0013$), lower TC/HDL ratio ($p < 0.0001$) and higher concentration of HDL (<0.0001) when compared to Whites. The longitudinal analyses over a 5 year period showed changes in A1C significantly associated with changes in the lipid profiles. The lipid profiles in Blacks were more altered by the trend in A1C with changes in the TC ($p = 0.0079$), non-HDL ($p < 0.0001$) and HDL ($p < 0.0001$).

Conclusions: Black children with T1DM have poorer glycemic control. However they retained excellent levels of HDL when compared to Whites.

Keywords: type 1 diabetes, dyslipidemia, glycemic control, racial differences

Introduction

Both diabetes and dyslipidemia are independent risk factors for cardiovascular disease. Moreover, in long standing type 1 diabetes (T1DM), there is an increased likelihood for atherosclerosis.^{1,2} Amongst the reports on prevalence of abnormal lipid profiles in children with T1DM,^{3–12} there is only few on temporal trends.¹² Limited information is available on Black–White difference on lipid abnormalities in children with T1DM.¹³ It is well known that racial differences exist in glycemic control and development of diabetic complications in adults with type 2 DM.^{14,15}

This retrospective study aimed to assess the racial differences in glycemic control and lipid profiles in children with T1DM. We also assessed the prevalence of abnormal lipid profiles in children with T1DM and characterized the factors influencing the trends in dyslipidemia in these subjects. Identification of such risk factors could lead to preventive measures and intervention strategies in this high risk population. To our knowledge this is the first study to address the temporal trends in glycemic controls and lipid profiles in children with T1DM with regard to race.

Methods

Children with T1DM, who are being followed by the department of Pediatric Endocrinology, Metabolism and Diabetes at the Children's Hospital of Birmingham, Alabama, were included in the study. Patient records over a 5 year period of time, 2001–2006 were abstracted. Patients were identified using the diagnosis code of 250.1 for T1DM. Only insulin dependent patients with positive autoimmune

Correspondence: Ambika Ashraf, M.D., Division of Pediatric Endocrinology, UAB Pediatrics, Children's Hospital, University of Alabama at Birmingham, Children's Park Place, Suite 230, 1600 Fourth Ave S., Birmingham, AL 35233. Tel: 205 939 9107; Fax: 205 939 5257; Email: aashraf@peds.uab.edu



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markers against islet cell or GAD-65 antigens and those with more than one lipid measurement were included in the study. Children with biochemical criteria for hypo or hyperthyroidism, those on thyroid medications, children who had hemoglobinopathies, celiac disease and children with type 2 diabetes were excluded. All children with T1DM received similar diabetes education according to the endocrine division policy and patients were given similar instructions to contact the pediatric endocrinologist frequently for ongoing insulin adjustments to maintain euglycemia. In addition, the insulin dose was also adjusted during the clinic visits based on the blood sugar logs. All patients were initially on multiple daily dose injection (MDI).

The information on the race was collected based on the demographic data provided by the patient. We collected longitudinal data on BMI and A1C from the charts.

Due to the retrospective nature of the data collection we could not reliably ascertain the family history of lipid abnormalities and, hence, this issue is not included in this study. Once the insulin therapy was initiated lipid measurements were not taken under fasting conditions and hence, we did not incorporate triglyceride and LDL levels into our analysis. Non-HDL is calculated from the difference between the levels of total and HDL cholesterol. Non-HDL is a comprehensive measure of all potential atherogenic lipoproteins (VLDL, intermediate-density lipoprotein [IDL], LDL, and lipoprotein[a]). It can be calculated in the non-fasting state or in the setting of hypertriglyceridemia. The primary advantages of calculating non-HDL is due to the fact that it requires measurement of only TC and HDL, both of which can be measured reasonably accurately in a non-fasting sample.¹⁶ Non-HDL cholesterol >160mg/dL is designated as “high” according to ATP III guidelines.¹⁷

Measurements of total cholesterol (TC) and HDL were done by standard enzymatic methods. Hypercholesterolemia was stratified according to the American Heart Association optimal lipid levels for children and adolescents¹² as: TC level <170 mg/dL acceptable, 170–199 mg/dL borderline, >200 mg/dL high. Optimal HDL level for children with diabetes was defined as >35mg/dL.¹⁸ A1C values measured by DCA2000 assay included in the analysis were those determined at the time of the lipid profile measurements.

Statistical analysis

Standard procedures in SAS® (Statistical Analysis Software) version 9.1 were used for descriptive and comparative statistical analysis. We have confirmed the normality of continuous variables. Linear correlation between A1C, BMI and lipid variables (TC, HDL) was examined using Pearson correlation coefficient. These correlations were further examined with linear regression model (ANOVA) with adjustments for age, gender and race factors. Longitudinal analysis with mixed linear model was used to evaluate the changes of A1C and lipid abnormality over time. The association between non-HDL, TC categories and race and sex were tested with Mantel-Haenszel statistics. A nominal *p* value of <0.05 was considered statistically significant. The data are expressed as mean ± S.D.

Results

After excluding those patients with the aforementioned exclusion criteria, the study included 181 children diagnosed with diabetes from age 2.6 to 16 years. Among these children, 94 (51.9%) are males and 87 (48.1%) are females. There were 76.2% Whites and 23.8% Blacks. The mean age of diagnosis of diabetes was not different between Black and White children (7.8 ± 2.9 years). The mean BMI did not differ statistically among races at the time of diagnosis and at follow up.

There were 181 patients with lipid profiles at two different time points, 115 with lipid profiles at three time points, 40 with lipid profiles at four time points, 7 children with five time points, and 3 children with 6 lipid profiles since diagnosis of diabetes. We examined all longitudinal data points for lipid values. The lipid measurements were further characterized based on the duration of diagnosis of diabetes.

Females had higher TC ($p = 0.05$), and non-HDL ($p = 0.05$) when compared to males. Based on all the observations, Black children had A1C of $10.6\% \pm 2.2\%$ and White children had $8.7\% \pm 1.6\%$ ($p < 0.0001$). In Blacks serum TC was 175.5 ± 35.0 mg/dl, whereas Whites had 164.9 ± 30.3 mg/dl ($p = 0.0013$). Similarly Black children had serum HDL of 66.6 ± 15.9 mg/dl, whereas White children had 56.3 ± 13.0 mg/dl ($p < 0.0001$).

In univariate analysis, there was a statistically significant association between A1C and TC ($p < 0.001$, Pearson correlation coefficient = 0.28). The multivariable regression analysis, after controlled

for age, sex, BMI and race still showed a strong positive association with TC ($p < 0.0001$, β coefficient = 408.89), non-HDL ($p < 0.0001$, β coefficient = 486.62) and negative association with HDL ($p = 0.02$, β coefficient = -77.74) between the lipid variables and A1C. There was also a strong negative association between BMI and HDL ($p < 0.0001$, β coefficient = -0.69) and a strong positive association between BMI and non-HDL ($p = 0.004$, β coefficient = 1.01), when adjusted for age, sex and race.

Table 1 classifies the lipid variables in terms of duration of diabetes. Figures 1 and 2 depict the mean changes in A1C, TC and HDL by race and duration. Mixed-model longitudinal data analysis, using A1C as the independent variable showed that the changes in A1C from baseline are strongly associated with the changes of TC ($p < 0.0001$, $\beta = 0.000195$), non-HDL ($p < 0.0001$, $\beta = 0.000283$), TC/HDL ($p < 0.0001$, $\beta = 0.004065$) and with moderate association with the changes HDL

($p < 0.07$, $\beta = -0.00027$) when controlled for age, sex and race, time and baseline. These changes were significantly different between races. Blacks were more affected by the changes in the A1C over time with changes in the TC (blacks vs. whites $\beta = 0.007358$, $p = 0.04$), TC/HDL ratio (blacks vs. whites $\beta = 0.00856$, $p = 0.01$), non-HDL (blacks vs. whites $\beta = 0.00755$, $p = 0.027$) and HDL (blacks vs. whites $\beta = 0.00820$, $p = 0.03$). Elevations in TC and HDL persisted in Blacks even when controlled for A1C. Longitudinal analysis using mixed model, the changes of TC, HDL, and Non-HDL with time are strongly correlated with the changes of A1C (all $p < 0.0001$), when controlled for age, sex and race.

Discussion

In agreement with other researchers^{3,12,19} our data clearly indicate that TC, non-HDL and HDL are significantly affected by chronic glycemic control,

Table 1. Descriptive statistics of lipid variables and A1C with duration of diabetes.

	Black		White		P value
Duration of diagnosis	N		N		
Total cholesterol					
At diagnosis	10	160.9 (36.16)	42	170.4 (27.9)	0.34
1–2 years	27	183.4 (42.2)	101	160.4 (30.3)	0.01
3–4 years	42	179.6 (41.2)	110	162.7 (27.8)	0.02
5–6 years	38	169.9 (25.5)	97	167.5 (30.0)	0.66
Non-HDL					
At diagnosis	10	99.7 (20.8)	42	115.8 (27.2)	0.09
1–2 years	27	116.85 (36)	101	103.4 (28.3)	0.04
3–4 years	42	109.0 (30.2)	110	104.9 (27.3)	0.42
5–6 years	38	105.4 (23.4)	97	111 (30.3)	0.31
HDL					
At diagnosis	10	61.2 (21.5)	42	54.5 (13.8)	0.23
1-2 years	27	66.6 (17.7)	101	57.0 (14.6)	0.005
3-4 years	42	70.6 (18.4)	110	57.8 (12.9)	<0.0001
5-6 years	38	64.6 (10.5)	97	56.5 (10.6)	<0.0001
HbA1C					
At diagnosis	10	9.0 (2.5)	42	9.3 (2.0)	0.38
1–2 years	27	10.9 (2.5)	101	8.4 (1.7)	<0.0001
3–4 years	42	10.8 (2.2)	110	8.5 (1.5)	<0.0001
5–6 years	38	10.3 (1.9)	97	8.8 (1.3)	<0.0001

Values are expressed as mean ($\pm$ SD).

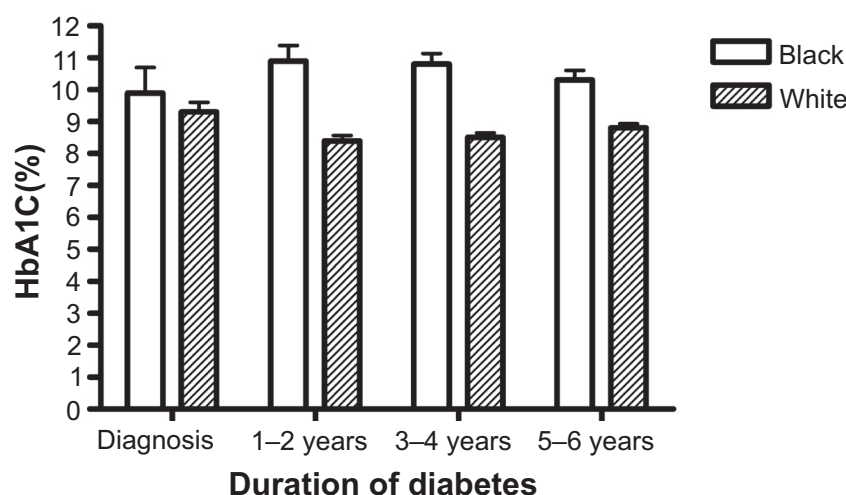


Figure 1. Mean A1C by race and duration of diabetes. Even though there was no significant difference in A1C at diagnosis between black and white children, over time Black children had higher A1C.

as shown by the strong statistical correlation with A1C. In accordance with previous literature,^{9,12,20} we found that A1C also has a significant negative correlation with HDL. Other factors affecting the lipid profile in children with T1DM in our study were sex, duration of diabetes, BMI, and race. The effect of BMI on non-HDL and HDL has been previously reported.^{3,12,21}

Even though the A1C is negatively correlated with HDL levels, the Black children had higher concentration of HDL at baseline and at the end of the study period. Historically Black children are known to have higher HDL.²²⁻²⁴ Insulin therapy is reported to increase antiatherogenic particles.²⁵ It is a very important observation that in spite of the poor glycemic control, there were enhanced levels of HDL concentrations in Black children.

Further studies are required to identify the cause for these racial disparities in glycemic control outcome. Delamater et al. has previously reported that A1C was higher in black than white children after statistically adjusting for the effects of insulin dose, diabetes duration, and socioeconomic status.²⁶ Hanson et al. has previously reported poor glycemic control in Black females with T1DM. They reported that the poor glycemic control was not associated with a deficiency in the girls' knowledge about diabetes, adherence to treatment, self-concept, coping patterns, family functioning, stress, social support, or involvement in the health-care system.²⁷ Libman et al. has reported that Black children and adolescents, with type 1 diabetes frequently have features associated with insulin

resistance and type 2 diabetes and suggest a role for heterogeneous pathogenesis in Black and White children with diabetes.²⁸ All the children in the present study received the standard diabetic education provided by the Division of Pediatric Endocrinology. After the initial insulin treatment all families were instructed to contact the endocrinology department to report their blood sugars and their insulin dosages were adjusted according to blood sugars. It is also important to note that there was no BMI difference between Black and White children with type 1 diabetes in our population. Hence, one will have to attribute the reasons for disparities in the outcome to greater burden of disease among minorities or differences in access or utilization of diabetes care, socioeconomic status, and genetic predisposition to insulin resistance^{18,28} or other factors.

Limitations of the study: Familial factors are important determinants of lipid levels.²⁹ Hence lack of reliable family history to exclude an underlying genetic cause of hyperlipidemia. As there is significant fall off in the numbers of patients reported having lipid measurements by the fourth time point, potential bias in the longitudinal data is possible.

Conclusions

The results of this study illustrate that Black children with type 1 diabetes have a higher degree of chronic hyperglycemia as determined by the surrogate A1C. The main factors determining the lipid profile in children with T1DM are age, glycemic control, BMI, duration of diabetes, sex and race.

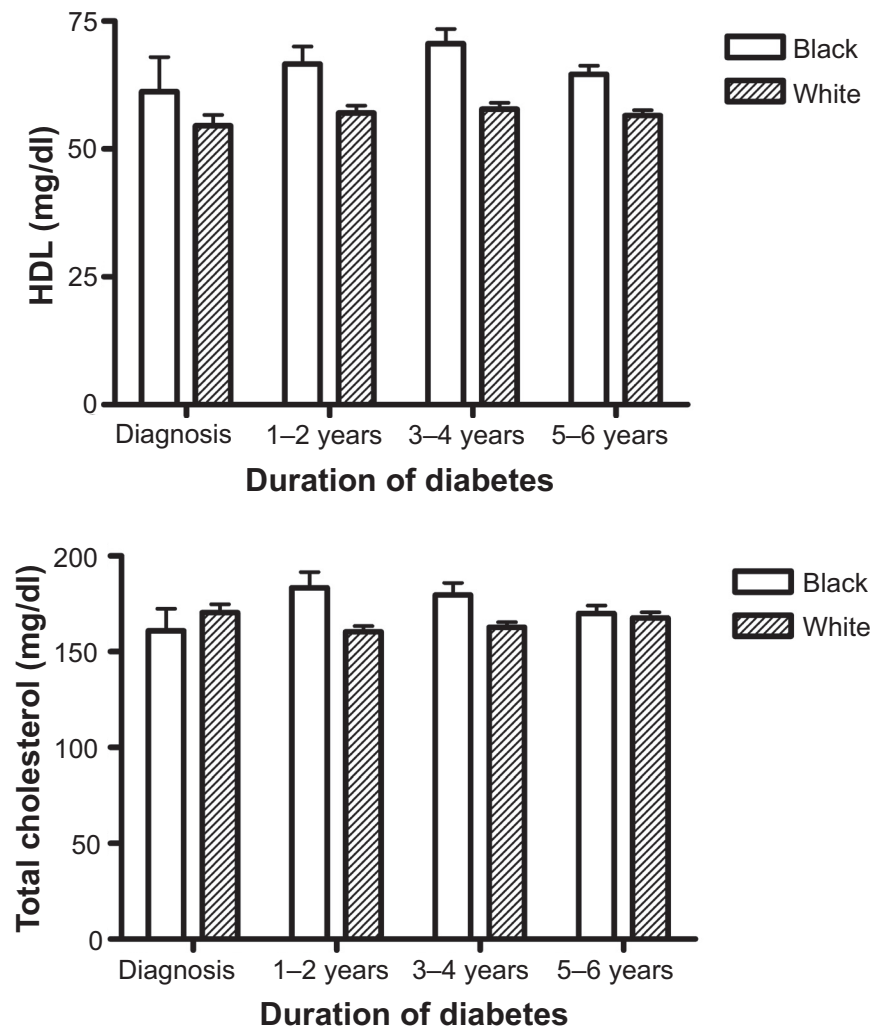


Figure 2. Mean changes in TC and HDL by race and duration of diagnosis of diabetes. Black children had higher HDL and total cholesterol with time.

Disclosure

The authors report no conflicts of interest.

References

- Krantz JS, Mack WJ, Hodis HN, Liu CR, Liu CH, Kaufman FR. Early onset of subclinical atherosclerosis in young persons with type 1 diabetes. *J Pediatr*. 2004;145:452–457.
- Krolewski AS, Kosinski EJ, Warram JH, Leland OS, Busick EJ, Asmal AC et al. Magnitude and determinants of coronary artery disease in juvenile-onset, insulin-dependent diabetes mellitus. *Am J Cardiol*. 1987;59:750–755.
- Maahs DM, Maniatis AK, Nadeau K, Wadwa RP, McFann K, Klingensmith GJ. Total cholesterol and high-density lipoprotein levels in pediatric subjects with type 1 diabetes mellitus. *J Pediatr*. 2005;147:544–546.
- Kershner AK, Daniels SR, Imperatore G, Palla SL, Pettitt DB, Pettitt DJ, et al. Lipid abnormalities are prevalent in youth with type 1 and type 2 diabetes: the SEARCH for Diabetes in Youth Study. *J Pediatr*. 2006;149:314–319.
- Chase HP, Glasgow AM. Juvenile diabetes mellitus and serum lipids and lipoprotein levels. *Am J Dis Child*. 1976;130:1113–1117.
- Parikh A, Sochett EB, McCrindle BW, Dipchand A, Daneman A, Daneman D. Carotid artery distensibility and cardiac function in adolescents with type 1 diabetes. *J Pediatr*. 2000;137:465–469.
- Traisman HS, Newcomb AL, Sever JL, Hammes R. Blood lipid and protein levels in juvenile diabetes mellitus. *Diabetes*. 1960;9:481–484.
- New MI, Roberts TN, Bierman EL, Reader GG. The significance of blood lipid alterations in diabetes mellitus. *Diabetes*. 1963;12:208–212.
- Lopes-Virella MF, Wohltmann HJ, Loadholt CB, Buse MG. Plasma lipids and lipoproteins in young insulin-dependent diabetic patients: relationship with control. *Diabetologia*. 1981;21:216–223.
- Tamborlane WV, Sherwin RS, Genel M, Felig P. Restoration of normal lipid and aminoacid metabolism in diabetic patients treated with a portable insulin-infusion pump. *Lancet*. 1979;1:1258–1261.
- Jarvisalo M, Raitakari O, Gylling H, Miettinen TA. Cholesterol absorption and synthesis in children with type 1 diabetes. *Diabetes Care*. 2006;29:2300–2304.
- Maahs DM, Wadwa RP, McFann K, Nadeau K, Williams MR, Eckel RH, et al. Longitudinal lipid screening and use of lipid-lowering medications in pediatric type 1 diabetes. *J Pediatr*. 2007;150:146–150, 150 e141–e142.
- Levitsky LL, Scanu AM, Gould SH. Lipoprotein(a) levels in black and white children and adolescents with IDDM. *Diabetes Care*. 1991;14:283–287.

14. Harris MI, Eastman RC, Cowie CC, Flegal KM, Eberhardt MS. Racial and ethnic differences in glycemic control of adults with type 2 diabetes. *Diabetes Care*. 1999;22:403–408.
15. Young BA, Maynard C, Boyko EJ. Racial differences in diabetic nephropathy, cardiovascular disease, and mortality in a national population of veterans. *Diabetes Care*. 2003;26:2392–2399.
16. Liu J, Sempos C, Donahue RP, Dorn J, Trevisan M, Grundy SM. Joint distribution of non-HDL and LDL cholesterol and coronary heart disease risk prediction among individuals with and without diabetes. *Diabetes Care*. 2005;28:1916–1921.
17. Hirsch GA, Vaid N, Blumenthal RS. Perspectives: The significance of measuring non-HDL-cholesterol. *Prev Cardiol*. 2002;5: 156–159.
18. Gower BA, Fernandez JR, Beasley TM, Shriver MD, Goran MI. Using genetic admixture to explain racial differences in insulin-related phenotypes. *Diabetes*. 2003;52:1047–1051.
19. Petitti DB, Imperatore G, Palla SL, Daniels SR, Dolan LM, Kershner AK et al. Serum Lipids and Glucose Control: The SEARCH for Diabetes in Youth Study. *Arch Pediatr Adolesc Med*. 2007; 161:159–165.
20. Perez A, Wagner AM, Carreras G, Gimenez G, Sanchez-Quesada JL, Rigla M et al. Prevalence and phenotypic distribution of dyslipidemia in type 1 diabetes mellitus: effect of glycemic control. *Arch Intern Med*. 2000;160:2756–2762.
21. Idzior-Walus B, Mattock MB, Solnica B, Stevens L, Fuller JH. Factors associated with plasma lipids and lipoproteins in type 1 diabetes mellitus: the EURODIAB IDDM Complications Study. *Diabet Med*. 2001;18:786–796.
22. Hickman TB, Briefel RR, Carroll MD, Rifkind BM, Cleeman JI, Maurer KR et al. Distributions and trends of serum lipid levels among United States children and adolescents ages 4–19 years: data from the Third National Health and Nutrition Examination Survey. *Prev Med*. 1998;27:879–890.
23. Freedman DS, Newman WP, 3rd, Tracy RE, Voors AE, Srinivasan SR, Webber LS et al. Black-white differences in aortic fatty streaks in adolescence and early adulthood: the Bogalusa Heart Study. *Circulation*. 1988;77:856–864.
24. Li S, Chen W, Srinivasan SR, Tang R, Bond MG, Berenson GS. Race (black–white) and gender divergences in the relationship of childhood cardiovascular risk factors to carotid artery intima-media thickness in adulthood: the Bogalusa Heart Study. *Atherosclerosis*. 2007; 194:421–425.
25. Taskinen MR, Kuusi T, Helve E, Nikkila EA, Yki-Jarvinen H. Insulin therapy induces antiatherogenic changes of serum lipoproteins in noninsulin-dependent diabetes. *Arteriosclerosis*. 1988;8:168–177.
26. Delamater AM, Albrecht DR, Postellon DC, Gutai JP. Racial differences in metabolic control of children and adolescents with type I diabetes mellitus. *Diabetes Care*. 1991;14:20–25.
27. Hanson CL, Henggeler SW, Burghen GA. Race and sex differences in metabolic control of adolescents with IDDM: a function of psychosocial variables? *Diabetes Care*. 1987;10:313–318.
28. Libman IM, Pietropaolo M, Arslanian SA, LaPorte RE, Becker DJ. Evidence for heterogeneous pathogenesis of insulin-treated diabetes in black and white children. *Diabetes Care*. 2003;26:2876–2882.
29. Abroha A, Schultz C, Konopelska-Bahu T, James T, Watts A, Stratton IM et al. Glycaemic control and familial factors determine hyperlipidaemia in early childhood diabetes. Oxford Regional Prospective Study of Childhood Diabetes. *Diabet Med*. 1999;16:598–604.