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The Association between Adiponectin/Leptin Ratio and Diabetes Type: The SEARCH for Diabetes in Youth Study

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Abstract

We tested the association of adiponectin/leptin ratio (ALR) with diabetes type after adjusting for multiple factors in 1,156 youth with newly diagnosed diabetes in the SEARCH study. Although ALR is associated with diabetes type in youth, it is due to differences in adiponectin, but not leptin levels.

Keywords

adiponectin; leptin; adiponectin/leptin ratio; type 1 diabetes; type 2 diabetes; pediatrics; youth

The adiponectin/leptin ratio (ALR) differ between type 1 and type 2 diabetes mellitus in youth (1) and may be a tool to distinguish between major diabetes types in youth(2). However, it is unclear whether ALR and its components are associated with diabetes type above and beyond differences in obesity. The objective of this study was to test the hypothesis that ALR is associated with diabetes type in analyses adjusted for demographic factors, A1c and obesity in a larger cohort of youth with diabetes.

Methods

A detailed description of the study methods in SEARCH has been published(3). SEARCH is a multi-center study conducting population-based ascertainment of diabetes in youth <20 years in the U.S. in racial/ethnically diverse populations. The study was approved by the local institutional review boards that had jurisdiction over the local study populations.

During the study visit, survey information was collected and blood was drawn fasting under conditions of metabolic stability for measurement of A1c and adipocytokines. Height, weight, and waist circumference were obtained(3). BMI z-score was calculated using a normalized standard deviation score(4). Diabetes type was based on health care provider's report and validated with biochemical markers, including diabetes auto-antibodies and C-peptide in a subset(5). Of the 3,484 youth registered for SEARCH, 1,156 youth with newly diagnosed diabetes in 2002–2004 aged 3–19 years at diagnosis with complete data were included in this analysis. Race/ethnicity was self-reported using the 2000 U.S. census questions format. Adiponectin and leptin levels were measured using commercially available RIA assays with sensitivities of 1 ng/ml and 85.4 pg/ml, respectively.

Descriptive statistics (means/standard deviations or counts/percents) were calculated for variables of interest. Comparisons were made by diabetes type using t-tests or chi-squared tests for continuous and categorical variables, respectively. Next, a series of general linear models were fit to estimate mean levels of adipocytokines and ALR in type 1 and type 2 diabetic youth, adjusted for demographic factors, A1c, and obesity. In these models, because leptin and ALR were highly skewed, data were log transformed to make these variables more normally distributed. Four sequential models were fit: model 1) unadjusted, model 2) adjusted for age, sex, race/ethnicity, model 3) additionally adjusted for diabetes duration and A1c, model 4) additionally adjusted for BMI-z score and waist circumference. SAS software version 9.1 was used.

Results

Our sample included 976 youth with type 1 and 180 with type 2 diabetes (Table). Compared with youth with type 2 diabetes, those with type 1 diabetes were younger (11.2 ± 3.8 vs 15.3 ± 2.6 years), had shorter diabetes duration (10.1 ± 6.8 vs 11.3 ± 7.6 months), were thinner (mean BMI z-score = -0.57 ± 0.99 vs 2.02 ± 0.82), had less abdominal fat (mean waist circumference 67.1 ± 12.1 vs 101.2 ± 22.7 cm), and were more likely to be non-Hispanic White (75.9 vs 25.0%).

Unadjusted adiponectin levels were higher in youth with type 1 than type 2 diabetes (18.22 ± 0.22 vs 9.33 ± 0.48 , $p < 0.0001$) and with sequential adjustments decreased slightly in type 1 youth and increased in type 2 (17.13 ± 0.47 vs 13.85 ± 0.65 , $p < 0.0001$) (Figure, A). Unadjusted leptin concentrations were much lower in type 1 as compared with type 2 youth (geometric mean 4.46 ± 0.22 vs 17.81 ± 1.79 , $p < 0.0001$) until adjusted for obesity (6.09 ± 0.64 vs 5.50 ± 0.99 , $p = 0.20$) (Figure, B).

The unadjusted ALR was much higher in type 1 than in type 2 youth (geometric mean 3.79 ± 0.23 vs 0.46 ± 0.07 , $p < 0.0001$), and remained significantly higher after adjustment for demographics, duration of diabetes, A1c and then BMI-z and waist circumference (obesity markers), although the difference was substantially reduced (Figure, C; geometric mean 2.51 ± 0.35 vs 1.97 ± 0.56 , $p = 0.0066$).

Discussion

ALR is significantly associated with diabetes type in youth after adjusting for multiple factors, including obesity. However, this difference is entirely driven by adiponectin levels, which

remain significantly lower in youth with type 2 vs type 1 diabetes after multiple adjustment, whereas leptin concentrations were not different after adjustment for obesity.

Low adiponectin levels were shown to be associated with insulin resistance(6) and to predict cardiovascular disease in adults(7). Although adiponectin levels were shown to be lower in adults with type 2 diabetes compared with non-diabetic controls(6,8), they were, paradoxically, higher in adults(9) and youth with type 1 diabetes(10). Adiponectin levels in youth with type 1 have been reported to be similar to controls at diagnosis, but increased at one month after diagnosis(11). In contrast, leptin was decreased at diagnosis and similar to control subjects one month after diagnosis(11). Another study has reported that leptin is higher in pubertal type 1 youth compared with controls(12). Little data exist on adipocytokines in youth with type 2 diabetes, but adiponectin seems to be lower(13) and leptin higher(14) in obese v non-obese youth.

In conclusion, our data suggest that ALR is associated with diabetes type above and beyond obesity. However this association is entirely due to differences in adiponectin, but not leptin levels. Adiponectin may be a useful measure of insulin resistance and help to better distinguish type 1 from type 2 diabetes in youth.

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Figure 1. 1A, Adiponectin Level by Type of Diabetes; 1B, Leptin Level by Type of Diabetes; 1C, Adiponectin to Leptin Ratio (ALR) by Type of Diabetes

In each Figure the following relationships are displayed: Model 1) unadjusted, 2) adjusted for age, sex, race/ethnicity, 3) additionally adjusted for diabetes duration and A1c, 4) additionally adjusted for BMI-z score and waist circumference.

Table 1

Characteristics of 1,156 Youth Recently Diagnosed with Type 1 or Type 2 Diabetes

Variable	Type 1, n=976	Type 2, n=180	p-value
Female, n, (%)	479, (49%)	112, (62%)	0.0012
Male, n, (%)	497, (51%)	68, (38%)	
Asian-Pacific Islander, n, (%)	32, (3.3%)	22, (12.2%)	<0.0001
African American, n, (%)	85, (8.7%)	51, (28.3%)	
Hispanic, n, (%)	107, (11.0%)	42, (23.3%)	
Native American, n, (%)	5, (0.5%)	17, (9.4%)	
Non-Hispanic White, n, (%)	741, (75.9%)	45, (25.0%)	
Other, n, (%)	6, (0.6%)	3, (1.7%)	
Age at visit, years	11.2±0.12	15.3±0.19	<0.0001
Diabetes duration, months	10.1±0.22	11.3±0.56	0.04
A1c, (%)	7.74±0.05	7.25±0.16	0.0038
BMI z-score	0.57±0.03	2.02±0.06	<0.0001
Waist circumference, cm	67.1±0.39	101.2±1.69	<0.0001
Adiponectin, µg/ml	18.22±0.22	9.33±0.48	<0.0001
Leptin, ng/dl	4.46±0.22	17.81±1.79	<0.0001
ALR	3.79 ±0.23	0.46 ± 0.07	<0.0001

ALR and Leptin reported as geometric means

Mean ± Standard Error