Published in final edited form as:

Pediatr Diabetes. 2021 November ; 22(7): 951–959. doi:10.1111/pedi.13253.

Glycemic Control is Associated with Dyslipidemia Over Time in Youth with Type 2 Diabetes: the SEARCH for Diabetes in Youth Study

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Author Contributions: R.P.B. interpreted data and wrote the manuscript. A.S.S. designed study, interpreted data, and edited the manuscript. E.T.J. designed study, interpreted data and edited the manuscript. J.M.S. designed study, conducted analysis and edited the manuscript. R.B.D. designed study, conducted analysis, interpreted data and edited the manuscript. L.M.D. designed study and edited the manuscript. L.K. contributed to discussion and edited the manuscript. G.I. designed study and edited the manuscript. C.B.T. contributed to discussion and edited the manuscript. A.D.L. contributed to discussion and edited the manuscript. E.M.U. designed study and edited the manuscript. J.M.L designed study, contributed to discussion and edited the manuscript. C.P designed study and edited the manuscript. S.M. researched data and edited the manuscript. D.D. designed study, interpreted data, edited the manuscript. All authors have approved the final article. R.P.B. is the guarantor of this work and, as such, had full access to the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Conflict of Interest: The authors have disclosed no conflicts of interest

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention and the National Institute of Diabetes and Digestive and Kidney Diseases.

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Abstract

Background: Dyslipidemia has been documented in youth with type 2 diabetes. There is a paucity of studies examining dyslipidemia over time in youth with type 2 diabetes and associated risk factors.

Objectives: To evaluate lipids at baseline and follow-up and associated risk factors in youth with type 2 diabetes.

Methods: We studied 212 youth with type 2 diabetes at baseline and after an average of 7 years of follow-up in the SEARCH for Diabetes in Youth Study. Abnormal lipids were defined as HDL-C <35, LDL-C >100, or triglycerides >150 (all mg/dL). We evaluated participants for progression to abnormal lipids (normal lipids at baseline, abnormal at follow-up), regression (abnormal lipids at baseline, normal at follow-up), stable normal and stable abnormal lipids over time for HDL-C, LDL-C and triglycerides. Associations between HbA1c and adiposity over time (area under the curve, AUC) with progression and stable abnormal lipids were evaluated.

Results: HDL-C progressed, regressed, was stable normal, and stable abnormal in 12.3%, 11.3%, 62.3%, and 14.2% of participants, respectively. Corresponding LDL-C percentages were 15.6%, 12.7%, 42.9% and 28.8% and triglycerides were 17.5%, 10.8%, 55.7% and 16.0%. Each 1% increase in HbA1c AUC was associated with a 13% higher risk of progression and stable abnormal triglycerides and a 20% higher risk of progression and stable abnormal LDL-C. Higher adiposity AUC was marginally (p=0.049) associated with abnormal HDL-C.

Conclusions.—Progression and stable abnormal LDL-C and triglycerides occur in youth with type 2 diabetes and are associated with higher HbA1c.

Keywords

type 2 diabetes; dyslipidemia; youth

1. INTRODUCTION

Type 2 diabetes in youth is increasing in prevalence [1] and appears to be more aggressive in youth compared to adults [2], requiring insulin therapy earlier, experiencing more diabetes associated complications and increased mortality [3–6]. Cardiovascular disease is one of the leading causes of morbidity and mortality in adults with type 2 diabetes [7], the antecedents of which are already present in youth [8], and dyslipidemia is a known modifiable cardiovascular risk factor in adults [9].

Dyslipidemia has been documented in youth with type 2 diabetes [10–13], however, there is a paucity of longitudinal studies, and published data are limited by small sample sizes, retrospective nature of studies, shorter duration of follow-up, and inclusion of individuals on lipid lowering medication [11,14–16].

The objectives of this study were to assess changes in lipid concentrations and status between baseline and follow-up in a prospective manner in adolescents and young adults with youth-onset type 2 diabetes and to assess factors that are associated with abnormal lipid levels over time. Identifying risk factors that influence progression of dyslipidemia in youth-onset type 2 diabetes may guide screening and future interventions for an important modifiable cardiovascular risk factor in this high-risk population.

2. METHODS

2.1 Study Participants

Participants included in this study were enrolled in the SEARCH for Diabetes in Youth study, a multicenter study investigating the prevalence, incidence, and complications in youth with type 1 and type 2 diabetes. Comprehensive details pertaining to the recruitment and study components of the SEARCH study have been published [17]. Individuals included in this study had a diagnosis of type 2 diabetes based on an etiologic definition utilizing two main markers, no evidence of autoimmunity (negative diabetes autoantibodies), and insulin resistance (defined as an insulin sensitivity calculated as >8.15). This measure of insulin sensitivity is based on a validated equation developed using direct measurements of glucose disposal rate from euglycemic-hyperinsulinemic clamps in youth with type 2 diabetes and includes HbA1c, triglycerides and waist circumference; Exp [4.647252 - (0.02032*[waist, cm])– (0.09779*[A1c, %])– (0.002350*[TG, mg/dl])][18,19].

Participants with type 2 diabetes in this analysis were seen at two visits where lipids were measured. There were 409 individuals with type 2 diabetes that were recruited as incident cases in 2002–2006 and 2008 per SEARCH study design [17], participated in a baseline study visit, and were eligible for a follow-up visit. Of these, 290 individuals were seen in follow-up (n=119 not seen for follow-up). Those who participated in a follow-up visit were more likely to be female compared to those not seen (65.9% female and 49.6% female, respectively; p=0.0022), but did not differ in age at baseline visit, race-ethnicity or HbA1c. Of the 290 seen for follow-up, those excluded from this analysis (total n=78) were those that did not have a fasting lipid profile at baseline (n=14), those that did not have a fasting lipid profile at follow-up visit (n=26), or those ever on self-reported lipid lowering medication (n=38). Individuals ever on lipid-lowering medication were excluded in order to assess the change in lipids over time in patients with type 2 diabetes. Those excluded (n=78) were slightly older than those included (n=212) (age 22.9 years and 21.9 years, respectively, p=0.0276), but were not different in sex, race-ethnicity or HbA1c. Thus, this study included 212 individuals with type 2 diabetes who had a baseline and follow-up visit and who had never been on a lipid lowering medication. The study was reviewed and approved by the local institutional review boards at each of the 5 SEARCH study sites (California, Colorado, Ohio, South Carolina and Washington) and all participants and their parents/guardians provided informed assent and/or consent.

2.2 Anthropometric and Metabolic Measurements

Medical history and current medications were obtained through questionnaires completed by study participants. Sex and race/ethnicity were self-reported, and race/ethnicity was

categorized as non-Hispanic white (NHW), non-Hispanic black (NHB), Hispanic, or other. Current cigarette smoking was defined as self-reported cigarette smoking in the last 30 days. Individuals who had tried smoking but were not current smokers were considered former smokers. Individuals who had never smoked were considered nonsmokers. Physical activity was self-reported and defined as either occurring 0–2 days/week or 3–7 days/week.

Height was measured in centimeters using a stadiometer and weight in kilograms using a standardized scale. Anthropometric measurements were taken twice and averaged. Body mass index (BMI) was calculated using weight and height measurements, weight (kg)/height (m^2). The Centers for Disease Control and Prevention (CDC)-derived BMIz scores were utilized. Waist to height ratios (WHtR) were ascertained by measuring waist circumference and dividing by height in centimeters. Waist circumference was measured utilizing Natural Waist, the mid-point between the lower rib and the iliac crest, or the line at natural side bend [20]. Resting systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured 3 times using an aneroid sphygmomanometer and an appropriately sized cuff. Participants were seated for 5 minutes prior to measurements and the average of the 3 measurements was used.

A blood draw was obtained after an 8-hour overnight fast and with no reported episodes of diabetic ketoacidosis in the prior month. Biochemical measurements of HbA1c, total cholesterol, HDL-C, and triglycerides were performed as described previously [21]. LDL-C was either calculated by the Friedewald equation or if triglycerides were greater than 400 mg/dL, LDL-C was measured utilizing the beta quantification procedure.

2.3 Definitions of Abnormal Lipids

The main outcomes analyzed in this study were changes in lipid status from baseline to follow-up. Fasting lipids (total cholesterol, HDL-C, LDL-C and triglycerides) were measured at the baseline and follow-up study visit (mean interval between visits 7.0 years). At both baseline and follow-up, abnormal lipids were defined as any one of the following 1) HDL-C <35 mg/dL, 2) LDL-C >100 mg/dL, or 3) triglycerides >150 mg/dL; definitions based on guidelines for adults and children with diabetes [22,23]. Using the cut-offs above, progression to abnormal lipids was defined for each lipid (HDL-C, LDL-C and triglycerides) as normal lipid concentration at baseline and abnormal at follow-up and regression was defined as abnormal lipid concentration at baseline and normal at follow-up. Stable normal was defined as normal lipid concentration at both baseline and follow-up and stable abnormal as abnormal lipid concentration at both baseline and follow-up. Therefore, each lipid (HDL-C, LDL-C and triglycerides) was separately analyzed for progression, regression, stable normal or stable abnormal. In secondary analysis, we also examined the percent of participants with high-risk lipids at baseline and follow-up, defined as LDL-C >130 mg/dL or triglycerides >400 mg/dL, thresholds which suggest pharmacological lipid lowering therapy would be considered for LDL-C and triglycerides [22,23].

2.4 Statistical Analysis

Data are presented as mean (standard deviation; SD) or median (interquartile range, IQR) for continuous variables, or frequency (%) for categorical variables. To define the relative

change within each lipid category (progression/regression/stable), the median (IQR) percent change at follow-up relative to baseline was calculated. Basic demographic characteristics were compared across the four groups (stable normal, stable abnormal, progression and regression) using chi-square tests for categorical variables.

Three separate multivariable models were used to estimate adjusted relative risks for HDL-C, LDL-C, and triglycerides for progression and stable abnormal vs stable normal and regression (modeled using log link, Poisson distribution). Model covariates included a derived area under the curve (AUC) summary statistic (a continuous variable) for HbA1c and WHtR. The AUC variables of HbA1c and WHtR were calculated using all available values (for HbA1c and WHtR values available: mean 2.9, SD 1.1, maximum number was 5). Covariates were selected based on directed acyclic graph modeling which was developed a priori based on the literature. Model 1 evaluated the association of HbA1c AUC with progression and stable abnormal lipid value, Model 2 evaluated WHtR AUC in place of HbA1c, and Model 3 included both HbA1c AUC and WHtR AUC. WHtR was selected over other measures of adiposity, such as BMI z-score, because WHtR has been shown to be more strongly associated with adverse cardiovascular risk factors in children and adults [24,25]. Each model was adjusted for sex, race/ethnicity, age at diagnosis, age at visit follow-up time, and clinical site.

In secondary analyses, we examined the percent of participants in high risk categories for each of the lipid parameters at baseline and follow-up (LDL-C >130 mg/dL or triglycerides >400 mg/dL). These analyses examined the percentage of participants who were in each risk group at baseline and follow-up but did not examine the individual trajectories of a given participant.

3. RESULTS

Characteristics of n=212 SEARCH participants with type 2 diabetes who had lipids at baseline and at follow-up are shown in Table 1. At baseline study visit, participants had a mean age of 14.9 ± 2.7 years, a mean diabetes duration of 0.9 ± 0.6 years and a mean HbA1c of 7.3 ± 2.3% (57 ± 25 mmol/mol). In regard to race/ethnicity, 42.9% of participants identified as NHB, 26.4% as NHW, and 19.8% as Hispanic. Females comprised 67.9% of the cohort. Follow-up data was obtained an average of 7.0 ± 2.0 years later when the mean age of the participants was 21.9 ± 3.5 years. Mean HbA1c at follow-up was 9.1 ± 3.1% (76 ± 34 mmol/mol). Diabetes treatment, physical activity and smoking status are also shown in Table 1.

Baseline lipids [expressed as mean ± SD or median (IQR)] were as follows: total cholesterol 164 ± 36 mg/dL, HDL-C 42 ± 12 mg/dL, LDL-C 96 ± 28 mg/dL, and triglycerides 110 (76, 156) mg/dL. Follow-up lipids were as follows: total cholesterol 176 ± 45 mg/dL, HDL-C 42 ± 12 mg/dL, LDL-C 103 ± 37 mg/dL, and triglycerides 112 (77, 182) mg/dL.

3.1 Lipid Concentrations and Lipid Status Over Time

We examined the number (and percent) of participants who progressed, regressed, were stable normal and stable abnormal for each lipid category (HDL-C, LDL-C and

triglycerides) over an average of 7 years of follow-up (see x-axis of Figure 1). Additionally, the median (IQR) for HDL-C, LDL-C and triglyceride concentrations at baseline and follow-up are shown as bars in Figure 1. Finally, the median percent change of lipid concentration for HDL-C, LDL-C and triglycerides at follow-up relative to baseline is reported (above bars in Figure 1) to reflect the extent of change in lipid concentrations within each category.

For HDL-C, 12.3% of participants progressed, 11.3% regressed, 62.3% remained stable normal, and 14.2% remained stable abnormal. For those that progressed to abnormal HDL-C the median percent change in HDL-C was −25.9%, while for those participants that regressed for HDL-C the median percent change was +24.3%. For participants who remained stable normal for HDL-C the median percent change was +2.3% and for those that remained stable abnormal for HDL-C the median percent change was +1.5%.

For LDL-C, 15.6% of participants progressed, 12.7% regressed, 42.9% remained stable normal, and 28.8% remained stable abnormal. For those that progressed to abnormal LDL-C the median percent change in LDL-C was +50.6%, while for those participants that regressed for LDL-C the median percent change was −23.1%. For participants who remained stable normal for LDL-C the median percent change was 0.0% and for those that remained stable abnormal for LDL-C the median percent change was +8.3%.

For triglycerides, 17.5% of participants progressed, 10.8% regressed, 55.7% remained stable normal, and 16.0% remained stable abnormal. For those that progressed to abnormal triglycerides the median percent change in triglycerides was +74.8%, while for those participants that regressed for triglycerides the median percent change was −43.4%. For participants who remained stable normal for triglycerides the median percent change was +1.2% and for those that remained stable abnormal for triglycerides the median percent change was +19.3%.

Differences in the frequency of progression, regression, stable normal and stable abnormal for each lipid (HDL-C, LDL-C and triglycerides) by sex and race/ethnicity (Supplementary Table S1) was also examined. While no differences across lipid categories (progression, regression, stable normal, stable abnormal) were identified by sex, differences were observed in triglycerides by race/ethnicity, with NHB found to have the highest percentage of stable normal.

3.2 Factors Associated with Abnormal Lipids at Follow-up

Next, we sought to examine the relationship between HbA1c and WHtR over time and the risk of having abnormal lipids at follow-up (combined stable abnormal and progression groups vs stable normal and regression groups, Table 2). In models that adjusted for age at diagnosis, age at visit, sex, race/ethnicity, follow-up time, and clinical site, each 1% increase in HbA1c AUC was associated with a 13% higher risk [RR (95%CI) 1.13 (1.05, 1.22)] of having triglycerides >150mg/dL at follow-up. Similarly, each 1% increase in HbA1c AUC was associated with a 20% higher risk [RR (95%CI) 1.20 (1.14, 1.27)] of having an LDL-C >100mg/dL at follow-up. HbA1c was not found to be associated with progression and stable abnormal HDL-C at follow-up. When adiposity measured by WHtR AUC was included in

the model (Model 3), the association for HDL-C, LDL-C, and triglycerides was essentially unchanged. Increase in WHtR AUC had a borderline association (p=0.049) with abnormal HDL-C. WHtR AUC was not associated with LDL-C or triglycerides.

In secondary analyses, we also assessed the percent of participants in high risk lipid categories at both baseline and follow-up (Table 3). High risk LDL-C (defined as LDL-C>130mg/dL that may require statin therapy per ADA guidelines) was present in 9.4% of participants at baseline and 20.8% at follow-up. High risk triglycerides (triglycerides>400mg/dL) were present in 2.4% at baseline and 5.7% of participants at follow-up.

4. DISCUSSION

This study describes the changes in lipid concentrations and lipid status over an average of 7 years in a large multi-ethnic cohort of adolescents and young adults with youth-onset type 2 diabetes not on lipid lowering therapy. We demonstrated that 44.4% of participants with youth-onset type 2 diabetes had progression to abnormal LDL-C or continued to have abnormal LDL-C at follow-up and 33.5% had progression to or stable abnormal triglycerides at follow-up. Additionally, after adjusting for covariates, HbA1c, a modifiable risk factor, was associated with abnormal LDL-C and abnormal triglycerides at follow-up. These results suggest that without lipid lowering therapy, adolescents and young adults with youth-onset type 2 diabetes are at risk for progression to or persistent abnormal lipids, and that glycemic control may be associated with dyslipidemia.

Little is known about dyslipidemia in young adults with youth-onset type 2 diabetes, with the majority of studies being retrospective [12,14–16] or cross-sectional [10] in nature with limited prospective analysis [11,13]. Retrospective work by Barr et al. [16] analyzed lipids and glycemic control in youth with type 2 diabetes at 1 and 3-year follow-up time periods. They reported higher LDL-C (observed at 1-year follow-up) and non-HDL (observed at 1 and 3-year follow-up) associated with higher HbA1c. Pelham et al. [15] found that out of 93 youths with type 2 diabetes 18% had elevated LDL-C>130 mg/dL and 26% had non-HDL-C>145 mg/dL. Finally, Sellers, et al. [12] and Fortmeier-Saucier, et al. [14] analyzed Canadian First Nation heritage and Mexican-American youth, respectively. Sellers, et al. found that all components of the lipid profile were worse in youth with type 2 diabetes compared to a population of Canadian First Nation youth without diabetes [12], while Fortmeier-Saucier et al. found 75% of Mexican-American youth with type 2 diabetes in their study had two or more abnormal lipid values [14]. Cross sectional work in SEARCH assessed the prevalence of serum lipid abnormalities in US youth with both type 1 and type 2 diabetes [10]. In youth with type 2 diabetes, LDL-C >100 mg/dL was present in 57%, triglycerides >150 mg/dL in 39%, and HDL-C <40 mg/dL in 44%.

Prospective studies on dyslipidemia in youth-onset type 2 diabetes have largely been limited to the TODAY study, a randomized control trial of youth with new onset type 2 diabetes that included individuals on lipid-lowering therapy [11,13]. The TODAY study reported that over an average follow-up of 3.9 years, LDL-C, non-HDL, apoB levels, and triglycerides all rose over time despite diabetes treatment interventions [11]. Thus, studies to date have not

evaluated lipids at baseline and follow-up over this amount of time in a multi-ethnic cohort of youth with type 2 diabetes.

In this study we report prospective data on lipids in youth with type 2 diabetes, who were not on lipid-lowering medications, at baseline and over a mean follow-up time of 7 years. We demonstrated that 44.4% of the cohort had progression to or stable abnormal LDL-C at follow-up. In comparison, the TODAY study [11] showed 34.7% of individuals had LDL-C >100 mg/dL at the last follow-up (36 months), compared to 28.1% at baseline. The difference between the degree of findings in the TODAY study and our findings could be accounted for by the additional 4 years of follow-up in our cohort, or the fact that we excluded those on lipid lowering medication. Barr, et al also demonstrated worsening LDL-C with a mean LDL-C of 107 mg/dL at diagnosis and mean of 114.9 mg/dL at 3-year follow-up [16].

Progression to or stable abnormal triglycerides occurred in 33.5% of the cohort. The TODAY study [11] similarly demonstrated a worsening of triglycerides over time, albeit with a lower percentage of individuals (23%) with triglycerides >150 mg/dL at follow-up.

In regard to HDL-C, we demonstrated that 62.3% and 11.3% of individuals had stable normal and regression at follow-up, respectively, in comparison to 26.5% of the cohort which had progression to or stable abnormal HDL-C. The TODAY study [11] and Barr, et al. [16] also demonstrated improvement in HDL-C over time in their respective studies. These improvements in HDL-C over time in individuals with youth-onset type 2 diabetes are incompletely understood, as lower levels of HDL-C are typically associated with worsening insulin resistance [6,26]. However, it is postulated that HDL becomes dysfunctional in the setting of type 2 diabetes, and this may not be reflected in the HDL-C concentration [27]. Additionally, metformin is known to improve HDL-C concentrations[28].

The categories of progression/regression/stable were based on clinical cut-points[22,23]. However, we recognize that by using cut-points a small change such as an individual changing from 99 to 101 mg/dL for LDL-C would be considered progression. As a result, we report on the median percent change of lipids at follow-up relative to baseline for each category to show that in fact most individuals in the progression category had a larger change beyond simply crossing the cut-point. For example, for LDL-C progression the median percent change in LDL-C was +50.6% relative to baseline (see Figure 1). Thus, not only did all participants LDL-C progress from an LDL-C <100 mg/dL to above the ADA target of 100 mg/dL[22,23], but the majority (median) increased by 50.6%. In contrast, for participants in the stable normal category for LDL-C, the median percent change was 0.0% relative to baseline, indicating that not only did those individuals remain <100mg/dL at follow-up, but the majority (median) in this category did not have a change from baseline to follow-up. Similar findings were present for HDL-C and triglycerides.

We examined the four progression/regression/stable categories for each lipid measurement by sex and race/ethnicity and found no statistical difference except with triglycerides by race/ethnicity. In regard to triglycerides, NHB individuals were found to have the highest percentage of stable normal, the lowest percentage of stable abnormal and a lower

percentage of progression than NHWs and Hispanics. Prior studies have demonstrated lower triglyceride levels in NHBs than NHWs[29], including in youth with type 2 diabetes [11,16], potentially due to defective hepatic synthesis of very low-density lipoprotein [30], although this remains an active area of investigation[31].

We demonstrate that HbA1c over time was independently associated with progression to and stable abnormal LDL-C and triglycerides. While regression was not looked at directly, based on these multivariable models for progression and stable abnormal lipids, it can be inferred that a lower HbA1c is associated with regression and normal lipid status over time in regard to LDL-C and triglycerides. Prior studies in adults [32] and youth [15,16,33] with type 2 diabetes have demonstrated an association between higher HbA1c values and dyslipidemia, although these were biochemical measurements at a single time point. Longitudinal studies assessing HbA1c over time in relation to dyslipidemia in youth with type 2 diabetes have been sparse, but have also demonstrated trends of higher LDL-C and triglycerides with higher HbA1c [11,34]. The pathophysiology of dyslipidemia in diabetes has been well studied, classically attributed to increased free fatty acid flux secondary to insulin resistance, but other factors such as inflammation likely play a role [35,36]. Our study demonstrates the association of higher HbA1c with abnormal and worsening LDL-C and triglycerides in youth with type 2 diabetes at 7-years follow-up. Given HbA1c is a potentially modifiable risk factor, additional studies are needed to determine whether lowering of HbA1c improves lipids over time.

Obesity over time as measured by WHtR, was not significantly associated with relative risk of abnormal lipids at follow-up, although was borderline for HDL-C. This observation could be explained by the fact that our study cohort did not experience significant change in BMI or WHtR over the course of the study as prior work has demonstrated greater weight loss resulting in greater improvement in lipids [37]. Additionally, bariatric weight loss surgery is associated with remission of dyslipidemia [38,39]. Substantial changes in weight may be needed before changes in lipid profiles are apparent.

We also sought to determine the percent of individuals in clinically high-risk categories at baseline and follow-up as this stratification signifies the need for lifestyle intervention and potentially lipid-lowering medication if no improvement [40]. The percent of individuals with high risk LDL-C and triglycerides doubled at follow-up (9.4% to 20.8% and 2.4% to 5.7%, respectively). These are participants who likely need but are not receiving lipid lowering pharmacologic therapy. Potential barriers to care of youth and young adults with type 2 diabetes could include lack of insurance, lack of consistent medical care, transition of medical care, or lack of experience of pediatric providers with issues associated with type 2 diabetes [41,42], such as utilization of lipid-lowering therapy.

Strengths of this study include a large cohort of youth with type 2 diabetes, inclusion of a diverse race/ethnic cohort, the ability to monitor the change in lipids over time in the course of type 2 diabetes, standardized lipid measurements, follow-up data over a 7-year time period, and the ability to assess associations between burden of risk factors and lipid measurements over time. By excluding participants on lipid-lowering medications, we likely under-represent the percentage of progression and stable abnormal categories. Additional limitations include lack of frequent lipid measurements over the 7-year time course, some

attrition from baseline visit, no direct multivariable modeling assessing regression and absence of variables including thyroid function testing, pubertal status, diet, alcohol use and family history of dyslipidemia that are known to affect lipid levels. Specific type 2 diabetes therapies were not ascertained in the initial study design and therefore would only be reported as “other” diabetes medication. Finally, we lacked a control group and race/ethnicity and sex were not evenly distributed in our study population, but are representative of racial/ethnic and sex make-up of the type 2 diabetes in youth population in the US [41].

In conclusion, we demonstrate that a substantial proportion of youth with type 2 diabetes had progression to or stable abnormal LDL-C and triglycerides over time. Additionally, glycemic control may be associated with progression to and stable abnormal LDL-C and triglycerides over time. The results of this study stress the importance of lipid screening in adolescents and young adults with youth-onset type 2 diabetes and the potential impact of glycemic control to improve long-term cardiovascular health to lessen long-term disease burden.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGEMENTS

The SEARCH for Diabetes in Youth Study is indebted to the many youth and their families, and their health care providers, whose participation made this study possible.

SEARCH 3/4: The authors wish to acknowledge the involvement of the Kaiser Permanente Southern California’s Clinical Research Center (funded by Kaiser Foundation Health Plan and supported in part by the Southern California Permanente Medical Group); the South Carolina Clinical & Translational Research Institute, at the Medical University of South Carolina, NIH/National Center for Advancing Translational Sciences (NCATS) grant number UL1 TR000062, UL1 Tr001450; Seattle Children’s Hospital and the University of Washington, NIH/NCATS grant number UL1 TR00423; University of Colorado Pediatric Clinical and Translational Research Center, NIH/NCATS grant Number UL1 TR000154; the Barbara Davis Center at the University of Colorado at Denver (DERC NIH grant number P30 DK57516); the University of Cincinnati, NIH/NCATS grant number UL1 TR000077, UL1 TR001425; and the Children with Medical Handicaps program managed by the Ohio Department of Health. This study includes data provided by the Ohio Department of Health, which should not be considered an endorsement of this study or its conclusions.

Funding:

Grant Support (SEARCH 1, 2, 3):

SEARCH for Diabetes in Youth is funded by the Centers for Disease Control and Prevention (PA numbers 00097, DP-05-069, and DP-10-001) and supported by the National Institute of Diabetes and Digestive and Kidney Diseases.

Sites (SEARCH 1 through 4):

Kaiser Permanente Southern California (U18DP006133, U48/CCU919219, U01 DP000246, and U18DP002714), University of Colorado Denver (U18DP006139, U48/CCU819241-3, U01 DP000247, and U18DP000247-06A1), Cincinnati’s Children’s Hospital Medical Center (U18DP006134, U48/CCU519239, U01 DP000248, and 1U18DP002709), University of North Carolina at Chapel Hill (U18DP006138, U48/CCU419249, U01 DP000254, and U18DP002708), Seattle Children’s Hospital (U18DP006136, U58/CCU019235-4, U01 DP000244, and U18DP002710-01), Wake Forest University School of Medicine (U18DP006131, U48/CCU919219, U01 DP000250, and 200-2010-35171)

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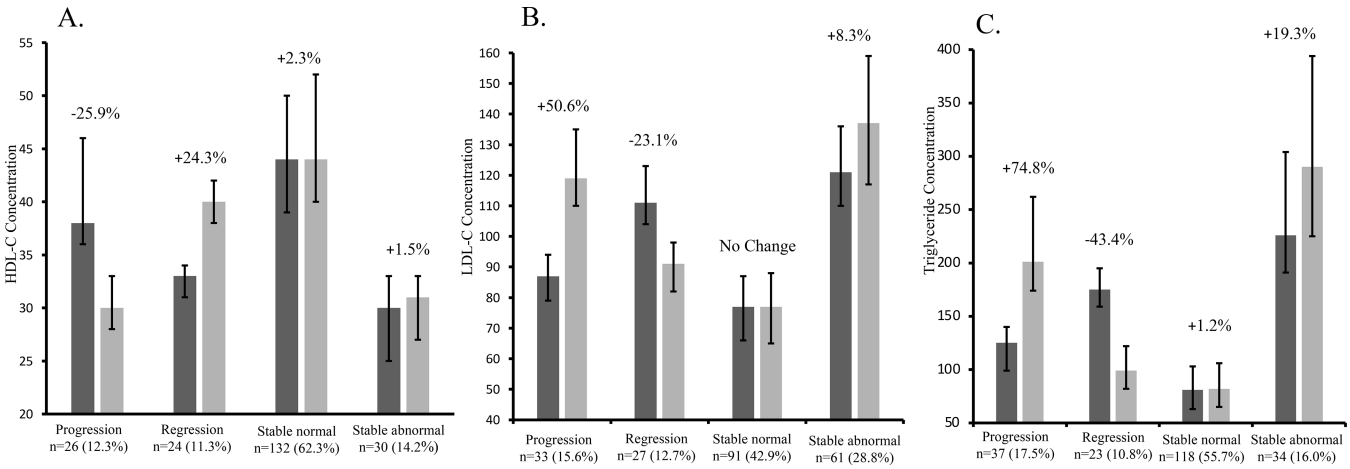

Figure 1. Change in Lipids from Baseline to Follow-up.

Data shown are the median (IQR) concentrations of A) HDL-C, B) LDL-C and C) triglycerides at baseline (dark grey bars) and follow-up (light grey bars) in each category. Categories included: Progression = normal lipid concentration at baseline, abnormal at follow-up. Regression= abnormal lipid concentration at baseline, normal at follow-up. Stable normal= normal lipid concentration at baseline and follow-up. Stable abnormal= abnormal lipid concentration at baseline and follow-up. On the x-axis are the n (%) of individuals in each category. Shown above each set of bars is the median percent (%) change of lipids relative to baseline.

Table 1.

Characteristics of participants with type 2 diabetes at baseline and follow-up

	Baseline		Follow-up	
	N	**Mean (SD) or n (%)**	**N**	**Mean (SD) or n (%)**
Age (years)	212	14.9 (2.7)	212	21.9 (3.5)
Race/ethnicity, n (%)	212			
Non-Hispanic white		56 (26.4)		-
Non-Hispanic black		91 (42.9)		-
Hispanic		42 (19.8)		-
Other		23 (10.8)		-
Female sex, n (%)	212	144 (67.9)		-
Age at DM diagnosis, (years)	212	14.0 (2.6)		-
Diabetes duration (years)	212	0.9 (0.6)	212	7.9 (2.0)
Waist to Height Ratio	211	0.61 (0.10)	212	0.63 (0.12)
Body Mass Index kg/m^2	211	34.4 (8.3)	212	35.7 (9.2)
BMI z-score	211	2.1 (0.7)	212	1.8 (0.8)
HbA1c (%)	212	7.3 (2.3)	212	9.1 (3.1)
HbA1c (mmol/mol)	212	56.7 (24.8)	212	75.5 (33.6)
Systolic blood pressure (mmHg)	211	115 (12)	212	117 (12)
Diastolic blood pressure (mmHg)	210	71 (9)	212	75 (10)
Diabetes medication categories, n (%)	212		211	
Metformin only		85 (40.1)		40 (19.0)
Insulin only		47 (22.2)		54 (25.6)
Insulin + Anything else		49 (23.1)		45 (21.3)
Other		10 (4.7)		21 (10.0)
None		21 (9.9)		51 (24.2)
Physical activity[†], n (%)			211	
0–2 days/week				134 (63.5)
3–7 days/week				77 (36.5)
Smoking Status[†], n (%)			205	
Current				69 (33.7)
Former				59 (28.8)
Never				77 (37.6)
Total cholesterol (mg/dL)	212	163.6 (35.6)	212	175.9 (44.7)
LDL-C (mg/dL)	212	96.4 (28.0)	212	103.3 (37.0)
HDL-C (mg/dL)	212	41.5 (11.9)	212	42.2 (12.3)
Triglycerides (mg/dL), median (Q1, Q3)	212	110 (76, 156)	212	112 (77, 182)

Mean interval between visits 7.0 (2.0) years. Q, quartile.

† Certain items, including smoking status and physical activity were discontinued at the baseline visit for later study participants, and are therefore only described using follow-up visit values.

Table 2:

Associations between HbA1c and WHtR with progression and stable abnormal lipids at follow-up

			Model 1† HbA1c AUC ONLY		Model 2† WHtR AUC ONLY		Model 3† HbA1c and WHtR together	
Lipid Outcome	**Total N**	**N (Progression + Stable Abnormal)**	**RR (95% CI)**	**p-value**	**RR (95% CI)**	**p-value**	**RR (95% CI)**	**p-value**
HDL-C <35 mg/dL	212	56						
HbA1c AUC (1 unit increase)			0.99 (0.91, 1.08)	0.8292	---	---	1.01 (0.92, 1.10)	0.8648
WHtR AUC (0.1 unit increase)			---	---	1.22 (1.00, 1.49)	0.0486	1.22 (1.00, 1.50)	0.0485
TG >150 mg/dL	212	71						
HbA1c AUC (1 unit increase)			1.13 (1.05, 1.22)	0.0017	---	---	1.13 (1.04, 1.22)	0.0023
WHtR AUC (0.1 unit increase)			---	---	0.94 (0.79, 1.12)	0.4997	1.00 (0.83, 1.19)	0.9606
LDL-C >100 mg/dL	212	94						
HbA1c AUC (1 unit increase)			1.20 (1.14, 1.27)	<.0001	---	---	1.21 (1.14, 1.29)	<.0001
WHtR AUC (0.1 unit increase)			---	---	0.97 (0.83, 1.12)	0.6646	1.07 (0.92, 1.25)	0.3541

†Multivariable models comparing progression and stable abnormal to regression and stable normal. Each model represents the relative risk and is adjusted for sex, race/ethnicity, age at diagnosis, age at visit follow-up time, and clinical site.

Table 3.

High-risk lipid stratification at baseline and follow-up

	Baseline, n (%)	Follow-up, n (%)
LDL-C		
≤100 mg/dL (Normal)	124 (58.5)	118 (55.7)
>100 to ≤130 mg/dL (Elevated)	68 (32.1)	50 (23.6)
>130 mg/dL (High-Risk)	20 (9.4)	44 (20.8)
Triglycerides		
≤150 mg/dL (Normal)	155 (73.1)	141 (66.5)
>150 to ≤400 mg/dL (Elevated)	52 (24.5)	59 (27.8)
>400 mg/dL (High-Risk)	5 (2.4)	12 (5.7)

Data are n and (%)