RESEARCH PAPER

Association Between Metabolic Control and Lipid Parameters in Indian Children with Type 1 Diabetes

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Objectives: To compare lipid parameters between diabetics and controls and to study association between metabolic control and lipid profile.
Methods: Lipid profile and HbA1c were measured (*n*=80, 39 boys) in diabetic children [age 10.7(3.4) y] and 54 controls, tests repeated after 1 year (in 45 diabetics).
Results: Diabetic children had higher mean (SD) LDL-C [95.3(27.7) *vs* 84.5(26.4) mg/dL], lower HDL-C [48.2 (13.1) *vs* 53.1(11.9) mg/dl]. Moderate physical activity (*P*=0.014) protected against high LDL-C levels. HbA1c (*P*=0.00) predicted total and LDL-C levels. At 1year, 63% showed reduced LDL-C with improving HbA1c; 72% showed increased LDL-C with deteriorated HbA1c.
Conclusion: Improving metabolic control is cardinal to reduce cardiometabolic risk; physical activity is beneficial.

Keywords: *Cardiometabolic risk, Hyperlipidermic, Metabolic control, Prognosis*.

Impaired lipid metabolism resulting from uncontrolled hyperglycemia is implicated in cardiovascular complications in diabetes. Deranged lipids have been reported amongst adolescents and youth in the SEARCH for Diabetes in Youth study [1]. Although data on the influence of blood glucose control on development of atherosclerosis is conflicting, there is increasing evidence of an association between the two [2-5].

This study was conducted to *i*) compare lipid parameters between diabetic children and controls; *ii*) determine factors influencing lipid parameters in diabetic children; and *iii*) examine effect of lowering of glycosylated hemoglobin on lipids in diabetic children at one year.

METHODS

This cross-sectional study with one-year follow-up was done after institutional ethical committee clearance. Considering variability in LDL-C reported in past studies [6], a sample size of 80 diabetics and 54 controls was found to have a power of 0.8 at 5% level of significance and 3% margin of error. Families with diabetic children aged 5 to 17 years attending the diabetes clinic at our institution were approached, and a random sample of 80 (39 boys) were enrolled prospectively (May 2013 to October 2014). Age- and gender-matched healthy controls were recruited from private schools. Patients with known chronic disorders were excluded. Data on medications, age at onset and duration of diabetes and insulin regimen were collected in a standardized form and verified from hospital records.

Anthropometric data were collected using standard methods and were converted to Z scores [7]. Fasting blood sample was collected to measure HbA1c by HPLC (BIO-RAD, Germany) and lipid profile (enzymatic method). The GE-Lunar DPX Pro (GE Healthcare, Wisconsin, USA) was used to measure body composition. Dietary intakes were assessed by 24-hour recall on three random days (non-consecutive)/week, including one holiday. Nutrient intakes were calculated (CDIET, Version 2, Xenios Technologies, Pune, India). Physical activity data were collected using validated activity questionnaires [8,9] adapted for Indian children.

Statistical analyses were carried out using SPSS for Windows 12 (SPSS, Chicago, IL, USA). Anthropometry, biochemical parameters and body composition were recorded in 45 (20 girls) children who regularly attended the clinic at the end of one year.

RESULTS

***Table* I** summarizes the anthropometric, body composition and biochemical parameters. There were no significant differences between sexes for anthropometric and biochemical parameters (*P*>0.05). Hence, further analysis was performed on pooled data.

TABLE I ANTHROPOMETRY, BODY COMPOSITION AND BIOCHEMICAL PARAMETERS IN STUDY PARTICIPANTS

	Cases (n=80)	*Controls (n=54)*
Age (y)	10.7 (3.4)	11.7 (2.8)
Height (cm)	132.3 (18.1)	144.7* (15.2)
Weight (kg)	28.9 (11.8)	35.0* (11.2)
BMI (kg/m^2)	15.6 (3.1)	17.1 (5.8)
Height for Age Z Score	–0.9 (1.1)	0* (0.9)
Weight for Age Z Score	–1 (0.9)	–0.8 (3.4)
BMI for Age Z Score	–0.7 (0.8)	–1.3 (5.7)
Lean Mass%	73.9 (9.0)	70.7 (9.0)
Total Body Fat%	20.3 (9.1)	26.5* (12)
Android Fat%	21.9 (10.3)	29.1* (13.3)
Gynoid Fat%	33 (8.8)	35.8 (9.9)
Cholesterol (mg/dL)	157.7 (33.5)	153.5 (27.7)
Triglyceride (mg/dL)	71 (26.5)	71.5 (30.5)
HDL (mg/dL)	48.2 (13.1)	53.1* (11.9)
VLDL	14.3 (5.4)	14.3 (6.1)
LDL (mg/dL)	95.3 (27.7)	84.5* (26.4)
Cholesterol/HDL ratio	3.4 (0.8)	3* (0.8)
LDL/HDL ratio	2.1 (0.7)	1.7* (0.7)
HbA1c%	10 (2)	-

**significantly different between diabetic children and controls (P<0.05); #significantly different between HbA1c>median group and controls (P<0.05).*

35% diabetic children had high LDL-C, 18% had low HDL-C and 2% had high triglycerides [10]. HDL-C was significantly lower and LDL-C was significantly higher in diabetic children. Mean (SD) HbA1c of diabetic children was 10 (2), signifying suboptimal blood glucose control.

Using linear regression, metabolic control (HbA1c) (*P*=0.002) was identified as positive predictor and age at diagnosis (*P*=0.012) as a negative predictor of total cholesterol. For LDL-C, metabolic control (*P*=0.001) and age at diagnosis (*P*=0.027) were predictors. Total body fat % or android fat % did not affect lipid profile. When diabetic children were divided into two groups according to median HbA1c (9.7%) and then compared to controls, diabetic children with HbA1c above median had significantly higher LDL-C and lower HDL-C as compared to controls (***Fig.* 1**).

To study impact of lifestyle factors on lipid profile, linear regression models were utilized. Mean (SD) daily intake of energy was 1632 (43) Kcal, protein was 44 (12) g, fat was 45 (12) g and carbohydrate was 267 (75) g. Mean (SD) time spent in moderate activities by children was 37 (25) min/d. Moderate physical activity (*P*=0.014) was identified as protective factor against LDL-C. Dietary intakes did not affect any of the lipid profile parameters.

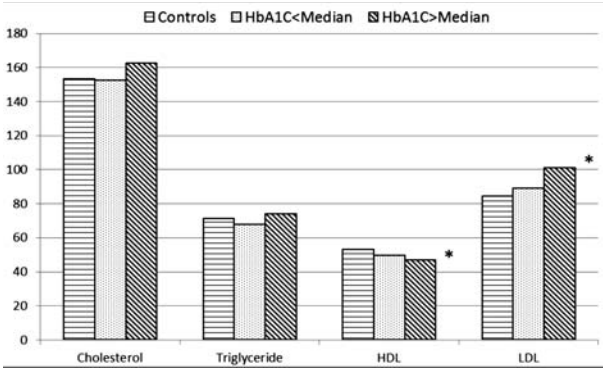

FIG. 1 *Comparison of lipid profile parameters between groups of diabetic children according to HbA1C and controls.*

Follow-up: Lipid profile parameters and HbA1c were repeated after one year in a subset of diabetic children (*n*=45) and percentage change of LDL-C and HbA1c were computed. A positive association (r^2=0.2059) between percentage change in LDL-C and HbA1c was seen (***Fig.* 2**). In the group of children whose metabolic control improved, 63% children showed a reduction in LDL-C levels. Whereas, in the group where the metabolic control deteriorated, 72% children showed increase in LDL-C.

DISCUSSION

Our cross-sectional data shows that Indian children and adolescents with type 1diabetes have deranged lipids as compared to healthy controls. Deterioration was related to poor metabolic control and age at diagnosis. Physical activity was protective against LDL-C. One year follow-up data showed deterioration in HbA1c to be associated with an increase in LDL-C and *vice versa.*

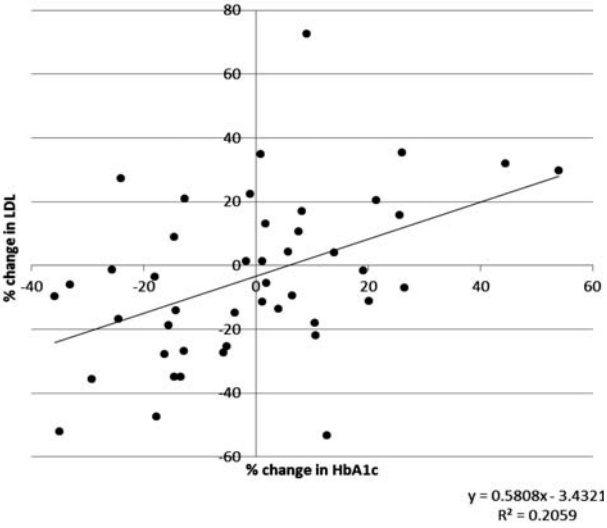

FIG. 2 *Relationship between percentage change of LDL-C and HbA1c over the one year period.*

WHAT THIS STUDY ADDS?

- Children diagnosed at younger years are at higher risk of deranged lipid parameters.
- Physical activity is a protective factor against desanyed lipid profile.

One of the important factors contributing to variations in lipid profile amongst children could be family history of the child. We did not have information regarding the parent's lipid profile parameters or their risk for CVD. Hence, we could not adjust for this during analysis. Although our data support the relationship between poor metabolic control and increase in LDL-C, our sample size for the follow-up study is small, and studies with larger sample size are required to confirm our findings.

Interference in normal physiology of low-density lipoprotein (LDL) particle has been reported by studies in the past which suggest that in patients with type 1 diabetes, LDLs are often enriched in triglycerides and increased number of small dense LDL particles are observed. Our data are in keeping with findings of Guy, *et al*. [2] and Petitti, *et al*. [5] who have also reported high LDL-C among children with Type 1 diabetes.

Advantages of physical activity in diabetes management have been previously reported [11-13]. In our study as well, children who engaged in moderate physical activity for more than half an hour each day had lower LDL-C. Hence, encouraging children to participate in various forms of physical activity may be beneficial in reducing the risk of CVD in future.

In conclusion **e**ncouraging a healthy lifestyle with adequate physical activity and improving metabolic control is recommended for reducing dyslipidemia in children with diabetes. Children diagnosed younger are more likely to have deranged lipids and thus are at increased cardiometabolic risk.

Contributors: LP, AK, VK: conceptualized the study, and analyzed data; SC: performed statistical analyses. All authors contributed to the manuscript and approved its contents.

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Competing interests: None stated.

REFERENCES

1. Kershnar AK, Daniels SR, Imperatore G, Palla SL, Petitti 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;149:314-9.
2. Guy J, Ogden L, Wadwa RP, Hamman RF, Mayer-Davis EJ, Liese AD, *et al*. Lipid and lipoprotein profiles in youth with and without type 1 diabetes: the SEARCH for Diabetes in Youth case-control study. Diabetes Care. 2009;32:416-20.
3. Ladeia AM, Adan L, Couto-Silva AC, Hiltner A, Guimarães AC. Lipid profile correlates with glycemic control in young patients with type 1 diabetes mellitus.Prev Cardiol. 2006;9:82-8.
4. Petitti DB, Imperatore G, Palla SL, Daniels SR, Dolan LM, Kershnar AK, *et al*. SEARCH for Diabetes in Youth Study Group. Serum lipids and glucose control: the SEARCH for Diabetes in Youth study. Arch Pediatr Adolesc Med. 2007;161:159-65.
5. Schwab KO, Doerfer J, Naeke A, Rohrer T, Wiemann D, Marg W, *et al.* ; German/Austrian Pediatric DPV Initiative. Influence of food intake, age, gender, HbA1c, and BMI levels on plasma cholesterol in 29,979 children and adolescents with type 1 diabetes—reference data from the German diabetes documentation and quality management system (DPV). Pediatr Diabetes. 2009;10:184-92.
6. Babar GS, Zidan H, Widlansky ME, Das E, Hoffmann RG, Daoud M, *et al*. Impaired endothelial function in preadolescent children with type 1 diabetes. Diabetes Care. 2011;34:681-5.
7. Khadilkar VV, Khadilkar AV, Cole TJ, Sayyad MG. Cross-sectional growth curves for height, weight and body mass index for affluent Indian children, 2007. Indian Pediatr. 2009;46:477-89.
8. Barbosa N, Sanchez CE, Vera JA, Perez W, Thalabard JC, Rieu M. A physical activity questionnaire: Reproducibility and validity. J Sports Sci Med. 2007;6:505-18.
9. CDC, 1999. Available from: *www.cdc.gov/nccdphp/dnpa/ physical/pdf/PA_Intensity_table_2_1.pdf*. Accessed December 22, 2013.
10. American Diabetes Association. Management of dyslipidemia in children and adolescents with diabetes. Diabetes Care. 2003;26:2194-7.
11. Beraki A, Magnuson A, Särnblad S, Åman J, Samuelsson U. Increase in physical activity is associated with lower HbA1c levels in children and adolescents with type 1 diabetes: results from a cross-sectional study based on the Swedish Pediatric Diabetes Quality Registry (SWEDIABKIDS). Diabetes Res Clin Pract. 2014;105:119-25.
12. Quirk H, Blake H, Tennyson R, Randell TL, Glazebrook C. Physical activity interventions in children and young people with Type 1 diabetes mellitus: a systematic review with meta-analysis. Diabet Med. 2014;31:1163-73.
13. Leclair E, de Kerdanet M, Riddell M, Heyman E. Type 1 diabetes and physical activity in children and adolescents. J Diabetes Metab. 2013;S10:004.