Received: 3 March 2020 | Revised: 9 May 2020 | Accepted: 31 May 2020

DOI: 10.1111/pedi.13063

ORIGINAL ARTICLE

ISPAD International Society for Pediatric and Adolescent Diabetes WILEY

Prevalence of dyslipidemia in Indian children with poorly controlled type 1 diabetes mellitus

Nikhil Shah[1] | Anuradha Khadilkar[1,2] | Ketan Gondhalekar[1] | Vaman Khadilkar[1,2]

[1]Department of Growth and Pediatric Endocrinology, Hirabai Cowasji Jehangir Medical Research Institute, Jehangir Hospital, Pune, Maharashtra, 411001, India

[2]Interdiscplinary School of Health Sciences, Savitribai Phule University, Pune, Maharashtra, 411007, India

Correspondence
Nikhil Shah, Department of Growth and Pediatric Endocrinology, Hirabai Cowasji Jehangir Medical Research Institute, Jehangir Hospital, Pune 411 001, India.
Email: nikhilshah1507@gmail.com

Abstract

Background: Children with type 1 diabetes having dyslipidemia are at increased risk of developing premature atherosclerosis and cardiovascular disease. The present study aims to determine the prevalence of dyslipidemia and its predictors in poorly controlled Indian children with type 1 diabetes.

Methods: The cross-sectional study included 235 children and youth (3-18 years) with type 1 diabetes having disease duration of at least 1 year. Demographic data and laboratory findings were obtained from patients' records.

Results: The prevalence of dyslipidemia in our study was 47.2% with abnormal low-density lipoprotein cholesterol being the most common lipid abnormality. Poor glycemic control and higher thyroid stimulating hormone values were important predictors of likelihood of dyslipidemia and hypertriglyceridemia. Despite a low percentage of overweight and obese children in our study, body fat percentage was a significant predictor of likelihood of high total cholesterol and abnormal high-density lipoprootein. Interestingly, 28 children under the age of 10 years were found to have dyslipidemia, which constitutes 11.9% of the total study group.

Conclusions: We found a high prevalence of dyslipidemia in children with type 1 diabetes including children under age of 10 years, which emphasize the need for early screening and regular monitoring of lipid profile in these children.

KEYWORDS

children, cholesterol, dyslipidemia, glycemic controltriglyceridestype 1 diabetes mellitus

1 | INTRODUCTION

According to International Diabetes Federation report in 2019, among children and adolescents with type 1 diabetes, India has the highest prevalence (95.6 cases per 1000 children) and also the largest number of new cases (15.9 cases per 1000 children).[1] To add to this disease burden, the per annum increase in incidence of type 1 diabetes in India is reported to be around 3% to 5%.[2] With this increasing incidence, there is also an increasing risk of microvascular and macrovascular complications associated with type 1 diabetes. One of these complications includes cardiovascular disease (CVD), which is the leading cause of mortality and morbidity in patients with type 1 diabetes.[3]

The changes of atherosclerosis begin as early as childhood and these changes are often expedited in high-risk pediatric populations like children with type 1 diabetes.[4] Dyslipidemia plays an important role in the initiation and progression of this accelerated atherosclerosis which in turn is responsible for premature cardiovascular disease and early mortality in patients with type 1 diabetes.[5] Hence, guidelines were formed to screen children with type 1 diabetes for dyslipidemia which state that all these children should be screened after the age of 10 years with a fasting lipid profile and if LDL cholesterol (low-density lipoprotein cholesterol) is <100 mg/dL the lipid profile should be repeated after 3 to 5 years[6,7].

The prevalence of dyslipidemia reported in children and young adults with type 1 diabetes in different parts of the world widely

varies and ranges from as low as 26% to as high as 75%.[8-10] Poor glycemic control, increased duration of diabetes, and increased body mass index (BMI) are some of the important risk factors associated with the development of dyslipidemia in children with type 1 diabetes.[9,11] In addition, studies have also shown that children with unfavorable socioeconomic status are at a higher risk of having altered glycated hemoglobin values due to poor glycemic control.[12] With the knowledge that poor glycemic control is associated with increased risk of dyslipidemia in children with type 1 diabetes and underprivileged children with type 1 diabetes have poor glycemic control, their risk of developing complications like dyslipidemia and premature cardiovascular disease is greater.

With such a wide variation in the occurrence of dyslipidemia and limited data available on dyslipidemia in Indian underprivileged children with type 1 diabetes, we conducted a study to estimate prevalence and predictors of dyslipidemia in Indian children and youth with poorly controlled type 1 diabetes.

2 | METHODOLOGY

2.1 | Subjects

Underprivileged children and adolescents (3-18 years) with type 1 diabetes along with their parents who were attending the diabetes clinic at a tertiary care hospital in Pune, India were approached to take part in this cross sectional, observational study. Due to the fluctuation of weight and metabolic instability, which is usually seen at the onset and during the initial therapy for diabetes, children and young adults with diabetes duration less than 1 year were not included in the study.[13] Children with other major illnesses or comorbidities (like celiac disease, untreated hypothyroidism, eating disorders, and/or polyendocrinopathies) were excluded from the study. All 291 patients who were approached agreed to take part in the study, of these, 235 met the inclusion and exclusion criteria mentioned as above. Of the 56 children who were not included, 23 children had disease duration less than 1 year, 23 patients were above the age of 19 years, and 10 children had poorly controlled/untreated hypothyroidism. None of the 235 children included in the study were on any lipid lowering or antihypertensive medications (except for insulin and levothyroxine). Using the formula n = z*z*P*(1-P)/d*d, where (z = 1.96 for 95% confidence interval, p = prevalence based on previous studies, and d = precision), a sample size of 235 was adequate for a power of 0.8 at a significance level of 0.05.[14] The precision of the study was 0.06 with 95% confidence interval.

The study was approved by the Institutional Ethics Committee. Parents provided written informed consent and children gave assent for the study. For illiterate parents, the information was read out to them in their native language. If they agreed to take part in the study, then their signature or thumbprint was witnessed by an independent witness, usually one of the senior members unrelated to the study from the hospital. This study was conducted between October 2018 and March 2019.

2.2 | Clinical history and examination

Data on age of the subjects, age at onset of diabetes, duration of diabetes, current medications, family and personal medical history, type of insulin regimen, and total dose of insulin per day were collected using standardized questionnaires by physicians. Medical history provided by parents was verified from hospital medical records. Physical activity data using validated activity questionnaires adapted for Indian children were also collected by physicians.[15] Tanner staging for sexual maturity was performed by a pediatric endocrinologist.[16,17] After at least 5 minutes rest, blood pressure (BP) was recorded in the sitting or supine position and the cubital fossa was supported at the heart level. BP was measured using a mercury sphygmomanometer, with appropriate sized cuff. In case of a high reading, BP was measured again after 10 minutes and also confirmed by another examiner. Systolic BP (SBP) and/or diastolic BP (DBP) >90th percentile and <95th percentile was considered as prehypertension and SBP and/or DBP >95th percentile were classified as hypertensive in children less than 18 years.[18] In adults, BP readings within the reference range were defined as SBP <120 mm Hg and DBP <80 mm Hg, hypertension was defined at 140/90 mm Hg reading and higher.[19] BP percentiles were computed using the American Academy of Pediatrics (AAP, 2017) reference standards.[20]

2.3 | Anthropometry

Standing height using a portable stadiometer (Leicester Height Meter, Child Growth Foundation, UK) was measured to the nearest millimeter and weight was measured using an electronic scale to the nearest 100 g. BMI was computed by dividing weight in kilograms by height in meter square. Subsequently, the height, weight, and BMI were converted to Z scores using Indian references.[21] Using the above reference standards, BMI z-scores above 0.67 in girls and above 0.55 in boys (23 adult equivalent BMI percentile) were considered as overweight and BMI z-score above 1.64 in girls and above 1.34 in boys (27 adult equivalent BMI percentile) were considered as obese.[21]

2.4 | Biochemical measurements

Glycemic control was evaluated by measuring glycosylated hemoglobin (HbA1C). A fasting blood sample (5 mL) was collected between 7:00 and 9:00 AM by a pediatric phlebotomist. HbA1C was measured by high-performance liquid chromatography (HPLC, BIO-RAD, Germany). Thyroid stimulating hormone concentrations (TSH) were measured by chemiluminescent microparticle immuno assay. The fasting blood samples were then assessed for lipid profile (total cholesterol, triglycerides [TG], and high-density lipoprotein-cholesterol [HDL-C]) using the enzymatic method and LDL-C concentrations were calculated by the Friedewald formula.[22] Dyslipidemia was defined if one or more of the following lipid parameters were abnormal; LDL-C >100 mg/dL (>2.6 mmol/L), HDL-C <40 mg/dL (<1.1 mmol/L), total cholesterol (TC) >200 mg/dL (>5.2 mmol/L), and TG >130 mg/dL

(>1.5 mmol/L) in children aged >10 years and 100 to 130 mg/dL (1.1-1.5 mmol/L) in children <10 years.[6,7,23]

2.5 | Body composition

Body composition was assessed using Bioelectrical Impedance Analyzer (BIA), (Tanita Model BC-420MA) after a minimum of 3 hours of fasting and voiding before measurements.[24] BIA measures body composition as fat percentage, fat mass, fat free mass, total body water, and bone mineral amount included in the entire bone (bone mass) by measuring bioelectrical impedance in the standing position.

2.6 | Statistical analysis

All statistical analyses were carried out using the SPSS for Windows software program, version 26 (SPSS, Chicago, IL). All outcome variables were tested for normality before performing statistical analyses. Differences in means were tested using Student *t* test for parametric data, Mann-Whitney *U* test for non-parametric data, and chi-square test for categorical variables. For testing relationships between dichotomous-dependent variables and continuous predictors, binary logistic regression analysis was carried out. The dependent variables in the models were dyslipidemia, abnormal TC, TG, LDL or HDL cholesterol, whereas the independent variables were gender, disease duration, duration of physical activity, blood pressure, pubertal status using Tanner's staging, BMI z-scores, HbA1C, TSH concentrations, fat, and fat free mass percentage assessed using BIA. *P* values < .05 were considered as statistically significant.

3 | RESULTS

Of the 235 children studied, 114 (48.5%) were boys and 121 (51.5%) were girls. The mean age of the children in the study group was 12.5 ± 3.9 years and the average duration of diabetes was 5.2 ± 3.3 years. The minimum and maximum age of the participants involved in the study was 3 years and 18.9 years, respectively. The age wise distribution of children was as follows: 63 (26.8%) children were under the age of 10 years and 172 (73.2%) children were above 10 years. Of the 235 children, 123 (52.4%) children had disease duration of less than 5 years and the remaining 112 (47.6%) children had disease duration greater than 5 years. The childrens' mean HbA1C was 10.7 ± 1.9% (93 ± 21 mmol/mol). Of the 235 children, 170 (72%) children were on basal bolus regimen and remaining 65 (28%) children were on split mix or modified split mix regimen (split mix regimen plus one short acting insulin at lunch). The mean total insulin requirement in our cohort was 1.1 ± 0.3 units/kg/day. Seventy two (30.6%) children were prepubertal and the remaining 163 (69.4%) were in puberty or had completed their puberty; 78 (33.2%) children were in puberty, and 85 (36.2%) children were postpubertal. The number of obese and overweight children in our study was 7 (3%) and 27 (11.5%), respectively. The mean TSH of the study group was 1.46 ± 1.48 μIU/mL, with 229 children having TSH below 5 μIU/mL and 6 children having TSH between 5 and 10 μIU/mL. Patients' demographics and laboratory findings have been illustrated in Table 1.

The prevalence of dyslipidemia in our cohort of children with type 1 diabetes was 47.2%. The most frequent lipid abnormality was high LDL (>2.6 mmol/L) seen in 82 children (34.9%) followed by hypercholesterolemia (>5.2 mmol/L) which was seen in 29 children (12.3%). Abnormal HDL (<1.1 mmol/L) and hypertriglyceridemia (>1.5 mmol/L in children >10 years and 1.1-1.5 mmol/L in children <10 years) were seen in 29 children (12.3%) and 25 (10.6%) children, respectively. Out of the 111 children having dyslipidemia, 68 (28.9%) children had only one lipid abnormality, 33 (14%) children had two abnormal lipid parameters, and 10 (4.2%) children had three or more lipid abnormalities. In addition, if abnormal LDL cutoff was considered as >130 mg/dL (> 3.4 mmol/L), then the number of children having abnormal LDL was 24 (10.2%) and the number of children having dyslipidemia dropped to 73 (31.1%).[25] Nine children had LDL >160 mg/dL (>4.1 mmol/L) in our study group. The relationship between dyslipidemia and clinical/laboratory findings has been listed in Table 2. Children having dyslipidemia were shorter, had higher systolic BP, higher TSH, and poor glycemic control as compared to children not having dyslipidemia (*P* < .05). No significant differences either due to gender or puberty were seen among the two groups.

All children were assessed for dyslipidemia. As per the current screening guidelines, children older than 10 years need to be screened for dyslipidemia.[6,7] Of the study group, 172 children were over 10 years of age, of which 83 (48.3%) children had dyslipidemia. Sixty three children were less than 10 years old, of these, 28 (44.4%) had dyslipidemia, which constitutes 11.9% of the total study group.

Binary logistic regression model indicated that TSH concentration was a significant predictor of likelihood of dyslipidemia, abnormal LDL profile, hypercholesterolemia, and hypertriglyceridemia (*P* < .05) (Table 3). When the six children having TSH between 5 and 10 μIU/mL were excluded from the analysis, except for high TC prediction, similar results were obtained in terms of prediction of dyslipidemia, abnormal LDL profile, and hypertriglyceridemia as above (*P* < .05). HbA1C was an important predictor of hypertriglyceridemia (*P* < .05). In addition, HbA1C was also a predictor of dyslipidemia but did not reach statistical significance. Conversely, body fat percentage was a significant predictor of likelihood of high total cholesterol and abnormal HDL (*P* < .05). Overall, the percentage of correct prediction by the models as to whether the children in the study were having or not having a lipid abnormality (dyslipidemia, abnormal LDL, abnormal TC, abnormal TG, or abnormal HDL) was high. The correct prediction of children having dyslipidemia or not and similarly for LDL, TC, TG, and HDL was 68.1%, 68.1%, 89.7%, 89.2%, and 86.9%, respectively.

4 | DISCUSSION

Our cross-sectional study in underprivileged Indian children and youth with poorly controlled type 1 diabetes showed the prevalence of

TABLE 1 Demographic data of the children with type 1 diabetes

	Total	Boys (n = 114)	Girls (n = 121)	*P* value
Age (y)	12.5 ± 3.9	12.7 ± 3.8	12.4 ± 4.1	NS
Disease duration (y)	5.2 ± 3.3	5.5 ± 3.6	4.9 ± 3.1	NS
Height Z scores	−0.7 ± 1.1	−0.7 ± 1.1	−0.7 ± 1.1	NS
Weight Z scores	−0.6 ± 1.0	−0.7 ± 0.9	−0.5 ± 1.1	NS
BMI Z scores*	−0.4 ± 0.9	−0.5 ± 0.9	−0.2 ± 1.0	.022
Systolic BP percentile	61.4 ± 26.9	61.1 ± 27.8	61.7 ± 26.0	NS
Diastolic BP percentile	75.4 ± 19.4	76.1 ± 18.9	74.8 ± 20.0	NS
HbA1C (%) or (mmol/mol)	10.7 ± 1.9 (93 ± 21)	10.7 ± 1.9 (93.8 ± 20.5)	10.7 ± 2.0 (93.1 ± 21.9)	NS
TSH (mIU/L)	1.46 ± 1.48	1.49 ± 1.50	1.43 ± 1.47	NS
Total cholesterol (mmol/L)	4.1 ± 1.0	4.0 ± 1.0	4.1 ± 0.9	NS
Triglycerides (mmol/L)	0.8 ± 0.4	0.8 ± 0.5	0.8 ± 0.4	NS
LDL cholesterol (mmol/L)	2.3 ± 0.9	2.2 ± 0.9	2.4 ± 0.9	NS
HDL cholesterol (mmol/L)	1.3 ± 0.2	1.3 ± 0.2	1.3 ± 0.2	NS
Insulin (units/kg/day)	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3	NS
Physical activity (min)	64.8 ± 45.6	63.6 ± 42.6	66.0 ± 48.4	NS
Fat (%)*	18.1 ± 9.8	13.0 ± 7.6	23.0 ± 9.2	.000
Fat free mass (%)*	81.9 ± 9.8	87.0 ± 7.6	77 ± 9.2	.000

Note: All normal variables are mentioned as mean ± SD, all non-normal variables are expressed as medians ± inter-quartile range.
Abbreviations: BMI, body mass index; BP, blood pressure; HbA1C, glycated haemoglobin; HDL, high-density cholesterol; LDL, low-density cholesterol; NS, not significant; TSH, thyroid stimulating hormone.
*$P < .05$.

TABLE 2 Association between dyslipidemia and clinical/laboratory findings

	Dyslipidemia (n = 111)	No dyslipidemia (n = 124)	*P* value
Age (y)	12.9 ± 3.9	12.2 ± 3.9	NS
Disease duration (y)	5.2 ± 3.5	5.2 ± 3.3	NS
Height Z score*	−0.9 ± 1.1	−0.6 ± 1.1	.019
Weight Z score	−0.7 ± 1.0	−0.6 ± 1.0	NS
BMI Z score	−0.3 ± 0.9	−0.5 ± 0.9	NS
Systolic BP percentile*	65.3 ± 26.4	57.9 ± 26.9	.039
Diastolic BP percentile	77.5 ± 18.9	73.5 ± 19.8	NS
HbA1C (%)* or(mmol/mol)	11.0 ± 2.1 (97.0 ± 23.0)	10.4 ± 1.7 (90.2 ± 19.0)	.015
TSH (mIU/L)	1.66 ± 1.68	1.28 ± 1.25	.049
Total cholesterol (mmol/L)*	4.6 ± 1.0	3.6 ± 0.6	.000
Triglycerides (mmol/L)*	0.9 ± 0.6	0.8 ± 0.4	.000
LDL cholesterol (mmol/L)*	2.8 ± 0.9	1.8 ± 0.6	.000
HDL cholesterol (mmol/L)*	1.2 ± 0.3	1.3 ± 0.2	.012
Insulin (units/kg/day)	1.1 ± 0.3	1.1 ± 0.3	NS
Physical activity (min)	62.9 ± 41.1	66.6 ± 49.4	NS
Fat (%)	19.3 ± 10.2	17.1 ± 9.4	NS
Fat free mass (%)	80.7 ± 10.2	82.9 ± 9.4	NS

Note: All normal variables are mentioned as mean ± SD, all non-normal variables are expressed as median ± inter-quartile range.
Abbreviations: BMI, body mass index; BP, blood pressure; HbA1C, glycated haemoglobin; HDL, high-density cholesterol; LDL, low-density cholesterol; NS, not significant; TSH, thyroid stimulating hormone.
*$P < .05$.

TABLE 3 Binary logistic regression to determine the predictors of dyslipidemia, abnormal LDL, hypercholestrolemia, hypertriglyceridemia, and abnormal HDL

					95% CI for Exp (B)	
		OR	Wald	Sig	Lower	Upper
Model 1 dyslipidemia (Nagelkerke 0.140)	HbA1C	1.149	3.137	0.077	0.985	1.339
	TSH*	1.289	5.099	0.024	1.034	1.606
	constant	0.006	8.970	0.003		
Model 2 abnormal LDL (Nagelkerke 0.163)	HbA1C	1.065	0.597	0.440	0.908	1.248
	TSH*	1.264	4.885	0.027	1.027	1.557
	constant	0.006	8.119	0.004		
Model 3 abnormal total cholesterol (Nagelkerke 0.228)	TSH*	1.299	4.403	0.036	1.017	1.658
	Fat %*	1.056	4.355	0.037	1.003	1.112
	constant	0.003	4.096	0.043		
Model 4 abnormal triglycerides (Nagelkerke 0.236)	HbA1C*	1.564	13.104	0.000	1.228	1.993
	TSH*	1.332	4.834	0.028	1.032	1.719
	constant	0.000	6.925	0.009		
Model 5 abnormal HDL (Nagelkerke 0.204)	Gender*	0.220	7.564	0.006	0.075	0.647
	Fat %*	0.933	5.253	0.022	0.879	0.990
	constant	0.003	4.883	0.027		

Abbreviations: HbA1C, glycated haemoglobin; HDL, high-density cholesterol; LDL, low-density cholesterol; OR, odds ratio; TSH, thyroid stimulating hormone.
*$P < .05$.

dyslipidemia was around 47.2%; 11.9% children under 10 years had an abnormal lipid profile. We also recognized certain modifiable factors, such as HbA1C, TSH concentrations, and body fat percentage, as independent predictors of derangements in lipid profile in our study population.

The prevalence of dyslipidemia in children with type 1 diabetes has been documented in few large and several small cross-sectional studies and a wide variation has been noted among the different study populations.[8,11,26-28] Such a wide variation could be attributed to various factors, including differences in guidelines or reference ranges used to define dyslipidemia. In a study conducted in Brazil, dyslipidemia was defined as per the recommendations laid down by the Brazilian Society of Diabetes and the prevalence was around 72.5%.[11] The reference ranges used in the above study had lower cutoffs for the various lipid parameters and hence could be the reason for the high percentage of dyslipidemia. On the other hand, the prevalence of dyslipidemia in studies conducted in Turkey and Germany was found to be around 26.2% and 28.6%, respectively.[8,26] The above studies used higher reference ranges for defining dyslipidemia and this could be one of the reasons for the low prevalence in these studies. Other important factors for such a wide variation in the prevalence of dyslipidemia could be due to age of participants in the study, sedentary lifestyles of the participants, prevalence of obesity in the study group, local dietary habits,[11] associated risk factors like the prevalence of smoking,[8] and a degree of insulin resistance[29] in the participant group. No pediatric or adult studies, to the best of our knowledge, from India have been conducted to determine the prevalence of dyslipidemia in patients with type 1 diabetes. The only pediatric study that we found from South Asia was conducted in Bangladesh and showed a prevalence of 65% which is very high as compared to the prevalence of 47.2% in our study.[27] This could be the due to the different reference ranges used to define dyslipidemia as well as the older age group of participants in the Bangladeshi study. Similarly, a study in Lithuania reports a prevalence of 62.6%.[28] Despite using similar cutoffs to define dyslipidemia, our prevalence was lower as compared to the Lithuanian study possibly because of the lower percentage of participants greater than 18 years (6% as compared to 33.2%) and lower percentage of obese and overweight subjects (14.5% as compared to 23%).

There are only a handful of Indian pediatric studies on the prevalence of dyslipidemia and hypercholesterolemia in childhood. In a study from Delhi, where 3076 normal school children (3-17 years) were assessed, the prevalence of hypercholesterolemia and abnormal LDL was 1.5% and 3.6%, respectively, which is very low as compared to prevalence of 12.3% and 34.9%, respectively, in our study.[30] Similarly, in studies conducted by Gupta et al and Joshi et al on normal school children in Jaipur and Pune, respectively, the overall prevalence of hypercholesterolemia and hypertriglyceridemia was lower as compared to the prevalence in our study.[31,32] Thus, the overall prevalence of dyslipidemia in poorly controlled children with type 1 diabetes included in our study was considerably higher as compared to the prevalence found in healthy Indian children.

An interesting finding of our study was the number of children with dyslipidemia being missed (11.9%) if we had followed the American Diabetic Association guideline for screening for dyslipidemia in children

with type 1 diabetes after 10 years of age.[6] Similar findings have been reported by other studies where, as high as 22.9% children with type 1 diabetes having dyslipidemia would have been missed if only children above 10 years would have been screened.[28] On the other hand, International Society for Pediatric and Adolescent Diabetes (ISPAD) guidelines state that if there is family history of hypercholesterolemia, premature cardiovascular disease or if family history is unknown, children with type 1 diabetes may be screened as early as at 2 years of age.[7] Childhood dyslipidemia is known to track into adulthood and increase the risk of cardiovascular disease and thus morbidity and mortality.[33] In addition to this, with cardiovascular disease being the most frequent cause of death in Indian adults and premature mortality in terms of years lost in India has gone up by 59% from 1993 to 2010, there may be a need to screen children with type 1 diabetes early.[34] Hence, in accordance with the ISPAD guidelines, which are followed in Indian children with type 1 diabetes, these children particularly those with poor control, may need to be screened earlier for dyslipidemia.

Our results suggest that glycemic control is an important modifiable risk factor that is associated with the development of dyslipidemia as a whole as well as in the development of hypertriglyceridemia. These findings are consistent with many cross sectional and longitudinal studies in children and adults with type 1 diabetes.[28,35,36] Lipid abnormalities are more prevalent in youth with poor or suboptimal glycemic control as demonstrated by the SEARCH for diabetes in youth (SEARCH) study.[37] The SEARCH study also reported that total and LDL cholesterol, TG and non-HDL cholesterol concentrations as also dense LDL and apolipoprotein B concentrations increased with increasing A1C. Similar findings were also seen in studies done by Marcovecchio et al and Reh et al.[38,39] Interestingly, TSH concentration was the other important modifiable risk factor associated with the development of dyslipidemia. This is consistent with the findings of other studies where increasing cholesterol was associated with increased TSH concentrations. In a study conducted by Denzer et al, when children with type 1 diabetes were grouped according to TSH specific quartiles, a stepwise increase was noticed in TC and LDL-C concentrations.[40]

Another important modifiable risk factor identified in our study was the body fat percentage. In a longitudinal analysis by Lipsky et al, body fat percentage was associated with higher TG and LDL-C and trunk fat mass was inversely associated with HDL.[41] Similar finding of fat mass percentage being an important predictor of non-HDL cholesterol was reported by Maffeis et al.[42] In our study, though body fat percentage was an important predictor of hypercholesterolemia and abnormal HDL cholesterol, BMI of the children did not show any association with lipid parameters. Thus, in our study, in addition to poor glycemic control and higher TSH, our results underline the significance of adiposity, rather than overall physical size, in the development of dyslipidemia and cardiovascular disease. Finally, gender was an important non-modifiable predictor for low HDL in our study. In a study, performed by Homma et al significant differences were observed between boys and girls in terms of overall dyslipidemia and abnormal LDL.[11]

Our study was limited by the lack of family history of early cardiovascular disease and dyslipidemia and also a lack of assessment of the various apolipoprotein concentrations and carotid artery intima media thickness, which are both important predictors of CVD risk. Dietary history and measurement of waist circumference could not be elicited in all the patients in our study and hence was not included in the final analysis. Due to the cross-sectional nature of the study, lipid assessment was performed only once during the study. More frequent assessments are required to understand the trend or natural history of lipid profile in these children. Also, as this was the first time lipids were assessed in these children, we do not know if they previously had dyslipidemia or developed it recently and whether dietary counseling would have helped these children. In addition, as this was not a multi-centric study, the clinic population may not be an overall representative of youth with type 1 diabetes in India, but may very well portray a representation of the underprivileged youth with type 1 diabetes in India. The strengths of our study are; ours is one of the very few Indian/Asian studies to report dyslipidemia in poorly controlled children with type 1 diabetes. Further, the inclusion of data on physical activity, pubertal status, and TSH levels, which are all known to influence lipid concentrations is also strength of the study.

In conclusion, nearly half of the underprivileged children and youth with type 1 diabetes in our study were found to have lipid abnormalities; one-tenth of the study participants who developed dyslipidemia were under 10 years. Risk factors that lead to the development of dyslipidemia include poor glycemic control, increased TSH levels, and increased adiposity. Further longitudinal and large-scale studies are required in underprivileged Indian children with type 1 diabetes to provide early identification and to assess the efficacy of better glycemic control, dietary habits, and effect of lipid lowering agents on the lipid profile in these children.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

AUTHOR CONTRIBUTIONS

Nikhil Shah conceptualized and designed the study; contributed to acquisition of data; and analysis and interpretation of data. Anuradha Khadilkar, Ketan Gondhalekar, and Vaman Khadilkar conceptualized, contributed to analysis and interpretation of data. All the authors contributed in manuscript writing and checking. All authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

COMPLIANCE WITH ETHICAL STANDARDS

Yes.

Peer Review

The peer review history for this article is available at https://publons.com/publon/10.1111/pedi.13063.

ORCID

Nikhil Shah https://orcid.org/0000-0002-7808-2662

REFERENCES

1. International Diabetes Federation. *IDF Diabetes Atlas*. 9th ed. Brussels, Belgium: International Diabetes Federation; 2019.

2. Das AK. Type 1 diabetes in India: overall insights. *Indian J Endocrinol Metab*. 2015;19(1):31-33.
3. Garg A. *Dyslipidemias: Pathophysiology, Evaluation and Management*. Totowa, NJ: Humana Press Inc.; 2015:1-525.
4. Kavey REW, Allada V, Daniels SR, et al. Cardiovascular risk reduction in high-risk pediatric patients: a scientific statement from the American Heart Association expert panel on population and prevention science; the councils on cardiovascular disease in the young, epidemiology and prevention. *Circulation*. 2006;114(24):2710-2738.
5. Harrington J, Peña AS, Gent R, Hirte C, Couper J. Aortic intima media thickness is an early marker of atherosclerosis in children with type 1 diabetes mellitus. *J Pediatr*. 2010;156(2):237-241.
6. Chiang JL, Maahs DM, Garvey KC, et al. Type 1 diabetes in children and adolescents: a position statement by the American Diabetes Association. *Diabetes Care*. 2018;41(9):2026-2044.
7. Donaghue KC, Marcovecchio ML, Wadwa RP, et al. ISPAD clinical practice consensus guidelines 2018: microvascular and macrovascular complications in children and adolescents. *Pediatr Diabetes*. 2018;19 (27):262-274.
8. Bulut T, Demirel F, Metin A. The prevalence of dyslipidemia and associated factors in children and adolescents with type 1 diabetes. *J Pediatr Endocrinol Metab*. 2017;30(2):181-187.
9. Abed E, Labarbera B, Dvorak J, Zhang Y, Beck J, Talsania M. Prevalence of dyslipidemia and factors affecting dyslipidemia in young adults with type 1 diabetes: evaluation of statin prescribing. *J Pediatr Endocrinol Metab*. 2019;32(4):327-334.
10. Mostofizadeh N, Hashemipour M, Roostazadeh M, Hashemi-Dehkordi E, Shahsanai A, Reisi M. The impact of poor glycemic control on lipid profile variables in children with type 1 diabetes mellitus. *J Educ Health Promot*. 2019;8:6.
11. Homma TK, Endo CM, Saruhashi T, et al. Dyslipidemia in young patients with type 1 diabetes mellitus. *Arch Endocrinol Metab*. 2015; 59(3):215-219.
12. Andrade CJ d N, Alves C d AD. Influence of socioeconomic and psychological factors in glycemic control in young children with type 1 diabetes mellitus. *J Pediatr*. 2019;95(1):48-53.
13. Couper JJ, Haller MJ, Ziegler AG, Knip M, Ludvigsson J, Craig ME. Phases of type 1 diabetes in children and adolescents. *Pediatr Diabetes*. 2014;15(20):18-25.
14. Daniel WW, Cross CL. *Biostatisics: A Foundation for Analysis in the Health Sciences*. 10th ed. USA: John Wiley & Sons; 2013.
15. Barbosa N, Sanchez CE, Vera JA, Perez W, Thalabard JC, Rieu M. A physical activity questionnaire: reproducibility and validity. *J Sport Sci Med*. 2007;6(4):505-518.
16. Marshall WA, Tanner JM. Variations in the pattern of pubertal changes in boys. *Arch Dis Child*. 1970;45(239):13-23.
17. Marshall WA, Tanner JM. Variations in pattern of pubertal changes in girls. *Arch Dis Child*. 1969;44(235):291-303.
18. Falkner B, Daniels SR. Summary of the fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Hypertension*. 2004;44(4):387-388.
19. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *Hypertension*. 2018;71(6):1269-1324.
20. Flynn JT, Kaelber DC, Baker-Smith CM, et al. Clinical practice guideline for screening and management of high blood pressure in children and adolescents. *Pediatrics*. 2017;140(3):e20171904.
21. Khadilkar VV, Khadilkar AV. Revised Indian academy of pediatrics 2015 growth charts for height, weight and body mass index for 5-18-year-old Indian children. *Indian J Endocrinol Metab*. 2015;19(4):470-476.
22. Warnick GR, Knopp RH, Fitzpatrick V, Branson L. Estimating low-density lipoprotein cholesterol by the Friedewald equation is adequate for classifying patients on the basis of nationally recommended cutpoints. *Clin Chem*. 1990;36(1):15-19.
23. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. *Pediatrics*. 2011;128(5):213-256.
24. Kyle UG, Bosaeus I, De Lorenzo AD, et al. Bioelectrical impedance analysis-part II: utilization in clinical practice. *Clin Nutr*. 2004;23(6): 1430-1453.
25. Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult treatment panel III). *JAMA*. 2001;285:2486-2497.
26. Schwab KO, Doerfer J, Hecker W, et al. DPV initiative of the German working Group for Pediatric Diabetology. Spectrum and prevalence of atherogenic risk factors in 27,358 children, adolescents, and young adults with type 1 diabetes: cross-sectional data from the German diabetes documentation and quality management system (DPV). *Diabetes Care*. 2006;29:218-225.
27. Zabeen B, Balsa AM, Islam N, Parveen M, Nahar J, Azad K. Lipid profile in relation to glycemic control in type 1 diabetes children and adolescents in Bangladesh. *Indian J Endocrinol Metab*. 2018;22(1):89-92.
28. Stankute I, Dobrovolskiene R, Danyte E, et al. Factors affecting cardiovascular risk in children, adolescents, and young adults with type 1 diabetes. *J Diabetes Res*. 2019;2019:9134280.
29. Nadeau KJ, Regensteiner JG, Bauer TA, et al. Insulin resistance in adolescents with type 1 diabetes and its relationship to cardiovascular function. *J Clin Endocrinol Metab*. 2010;95(2):513-521.
30. Marwaha RK, Khadgawat R, Tandon N, et al. Reference intervals of serum lipid profile in healthy Indian school children and adolescents. *Clin Biochem*. 2011;44:760-766.
31. Gupta R, Goyle A, Kashyap S, Agarwal M, Consul B, Jain BK. Prevalence of atherosclerosis risk factors in adolescent school children. *Indian Heart J*. 1998;50:511-515.
32. Joshi SM, Katre PA, Kumaran K, et al. Tracking of cardiovascular risk factors from childhood to young adulthood: the Pune Children's study. *Int J Cardiol*. 2014;175:176-178.
33. Nielsen TRH, Lausten-Thomsen U, Fonvig CE, et al. Dyslipidemia and reference values for fasting plasma lipid concentrations in Danish/north-European white children and adolescents. *BMC Pediatr*. 2017;17(1):1-11.
34. Prabhakaran D, Jeemon P, Roy A. Cardiovascular diseases in India: current epidemiology and future directions. *Circulation*. 2016;133(16): 1605-1620.
35. Shah AS, Maahs DM, Stafford JM, et al. Predictors of dyslipidemia over time in youth with type 1 diabetes: for the SEARCH for diabetes in youth study. *Diabetes Care*. 2017;40(4):607-613.
36. Parthasarathy L, Chiplonkar S, Khadilkar V, Khadilkar A. Association between metabolic control and lipid parameters in Indian children with type 1 diabetes. *Indian Pediatr*. 2016;53(1):39-41.
37. Hamman RF, Bell RA, Dabelea D, et al. The SEARCH for diabetes in youth study: rationale, findings, and future directions. *Diabetes Care*. 2014;37(12):3336-3344.
38. Marcovecchio ML, Dalton RN, Prevost AT, Acerini CL, Barrett TG, et al. Prevalence of abnormal lipid profiles and the relationship with the development of microalbuminuria in adolescents with type 1 diabetes. *Diabetes Care*. 2009;32:658-663.
39. Reh CM, Mittelman SD, Wee CP, Shah AC, Kaufman FR, Wood JR. A longitudinal assessment of lipids in youth with type 1 diabetes. *Pediatr Diabetes*. 2011;12:365-371.
40. Denzer C, Karges B, Näke A, et al. Subclinical hypothyroidism and dyslipidemia in children and adolescents with type 1 diabetes mellitus. *Eur J Endocrinol*. 2013;168(4):601-608.
41. Lipsky LM, Gee B, Liu A, Nansel TR. Body mass index and adiposity indicators associated with cardiovascular biomarkers in youth with

type 1 diabetes followed prospectively. *Pediatr Obes*. 2017;12(6): 468-476.
42. Maffeis C, Fornari E, Morandi A, et al. Glucose-independent association of adiposity and diet composition with cardiovascular risk in children and adolescents with type 1 diabetes. *Acta Diabetol*. 2017;54(6): 599-605.

How to cite this article: Shah N, Khadilkar A, Gondhalekar K, Khadilkar V. Prevalence of dyslipidemia in Indian children with poorly controlled type 1 diabetes mellitus. *Pediatr Diabetes*. 2020;1–8. https://doi.org/10.1111/pedi.13063