

ORIGINAL ARTICLE

Association of Dyslipidemia and Type-I Diabetes Mellitus Among Children Up to 16 Years of Age

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ABSTRACT

Introduction: Diabetes is associated with a high risk of cardiovascular disease (CVD). Hypertriglyceridemia & low HDL-C values are the most common symptoms of diabetic dyslipidemia. Elevated LDL-C is a well-known CVD risk factor.

Objective: To determine the association of dyslipidemia and type 1 diabetes mellitus among children up to 16 years of age.

Material & Method

Study design: Case-control study

Settings: Outpatient department, National Institute of Child Health (NICH)

Duration: Six months from 26th February 2018 to 28th August 2018

Data Collection procedure: All patients age 9 to 16 years of either gender were included. Cases were defined as presence of fasting plasma glucose of > 126.0 mg/dL (7.0 mmol/L) for more than one year whereas all patients with fasting plasma glucose of less than 126 mg/dL (7.0 mmol/L) were defined as controls. The blood sample was collected in a sterile manner after an overnight fasting of 8 hours and was sent to hospital laboratory and verified by pathologist.

Results: Out of total 60 patients, the mean age of the patients was 11.23 ± 1.76 years. Dyslipidemia was found to be significantly higher (n=26, 86.7%) among diabetic patients as compared to non-diabetic patients (n=18, 60%). (p-value 0.020) Moreover, the risk of dyslipidemia was 4.33 times higher among diabetic patients than that of non-diabetics (OR 4.33). Patients having >10 years of age and diabetes were 8.01 times more likely (OR 8.01, p-value 0.042) and diabetic males were 8.40 times more likely (OR 8.40, p-value 0.008) to have dyslipidemia.

Conclusion: Highly significant association of dyslipidemia and type 1 diabetes mellitus was found among children up to 16 years of age.

Keywords: Dyslipidemia, diabetes mellitus, children

INTRODUCTION

Children with type 1 diabetes mellitus (T1DM) are at an increased risk of developing subclinical & clinical cardiovascular disease early in life¹⁻³. Children with type 1 diabetes are classified as having the highest cardiovascular risk, according to the American Heart Association, which recommends both lifestyle & pharmacological treatment for patients with high level of cholesterol⁴.

When diabetes is controlled in children over the age of ten years, the Global ISPAD Guideline for Childhood & Adolescence diabetes of 2014 advised screening for fasting blood lipids. Furthermore, screening should begin at age of two years if there's a history of hypercholesterolemia or early CVD, or if there is no family history. Screening should be repeated every five years if normal results are found^{5,6}.

In a study, out of 60 children with T1DM, dyslipidemia was observed in 65% of the patients⁷. Another study has also reported dyslipidemia in 66% of the children with T1DM⁸.

Therefore, lipid & lipoprotein related health with its effects on micro & macrovascular disease will continue to be a main aspect of the health care in people with T1DM. Although advances in care, adolescents & children with type 1 diabetes continue to have high rate of vascular disease, with dyslipidemia being a prominent risk factor^{9, 10}.

There are several international studies which demonstrate association between dyslipidemia and T1DM. The present study is designed in order to ascertain the local perspective as there is scarcity of local data. The local condition varies widely with respect to education level and economic status and the difference in awareness regarding the two modalities. This study generates local data and the same was disseminated to other health care providers for timely diagnosis and treatment may minimize morbidity related issues and lead to good quality of life.

MATERIAL AND METHODS

This case control study was conducted 26th February to 28th August 2018 from outpatient department, National Institute of Child Health. Total sample 60, 30 case and 30 control with 95% confidence interval and 90% power of test with percent of cases exposed 65% and control exposed 28.2%.

Patients present with age 9-16 years with fasting plasma glucose of greater than or equal to 126 mg/dl (7.0 mmol/L) for more than one year (cases) and fasting plasma glucose of less than 126 mg/dl (7.0 mmol/L) (controls) were included from the study. Patients were excluded if they had hypothyroidism or were on thyroxine or lipid-lowering medicines.

All of the patients signed informed consent forms before being assigned to a sample and having their data used in research. The blood sample was collected in a sterile manner after an overnight fasting of 8 hours for serum cholesterol, triglycerides, LDL, VLDL, HDL and fasting plasma glucose levels sent to hospital laboratory and verified by pathologist. The findings of variables as mentioned above along with demographic of the patients was entered in proforma.

Data were analyzed on SPSS Version 20. Age, height, weight and BMI were presented as mean & SD. Gender & dyslipidemia was presented as percentage & frequency. Cross-tabulation was done to see the association of dyslipidemia in patients with T1DM. Chi-square test was applied between cases & controls, P-value less than 0.05 considered as significant. To see the strength of association Odds ratio was calculated with 95% CI. To see the effect of effect modifiers on the outcome variable, stratification of age, BMI & gender was used. Post stratification chi-square test was also applied. Odds ratio was also computed.

RESULTS

Out of total 60 patients, the mean age was 11.23 ±1.76 years. There were 33 (55%) patients with >10 years and 27 (45%) patients with ≤10 years of age. Majority of the patients (n=38, 63.3%) patients were males while 22 (36.7%) patients were females. The average height, weight & BMI was 1.40 ±0.92 m, 29.72 ±3.94 Kg and 15.12 ±1.53 kg/m2. Table: 1

Table 1: Descriptive Statistics of Age, Gender

		Frequency %
age	Mean + SD	11.23 ±1.76
	<10 years	27(45%)
	>10 years	33(55%)
Gender	Male	38(63.30%)
	Female	22(36.70%)

Overall frequency of dyslipidemia was observed in 44 (73.3%) patients. Table: 2 The comparison of diabetic status with dyslipidemia showed that dyslipidemia was found to be significantly higher (n=26, 86.7%) among diabetic patients as compared to non-diabetic patients (n=18, 60%). (p-value 0.020) The odds ratio also showed that risk of dyslipidemia is 4.33 times higher among diabetic patients than that of non-diabetics (OR 4.33). Table: 3

Table 2: Frequency of Dyslipidemia

	Frequency (%)
Yes	44(73.30%)
No	16(26.70%)

Table 3: Comparison of dyslipidemia with respect to diabetic status of the patients

		Diabetes	Non Diabetes
Dyslipidemia	Yes	26(86.70%)	18(60%)
	No	4(13.30%)	12(40%)

The comparison of dyslipidemia with baseline characteristics showed that patients having ≤10 years of age and diabetes were 3.11 times insignificantly more likely

(OR 3.11, p-value 0.201), >10 years of age and diabetes were 8.01 times significantly more likely (OR 8.01, p-value 0.042), diabetic males were 8.40 times significantly more likely (OR 8.40, p-value 0.008), and ≤15 kg/m2 BMI were 3.01 times insignificantly more likely to have dyslipidemia. Table: 4.

Table 4: Comparison of dyslipidemia with baseline characteristics of the patients.

	Yes	No	P value	OR
Age< 10 years				
Diabetic	14(82.4%)	3(17.6%)	0.201	3.11
Non- diabetic	6(60%)	4(40%)		
Age > 10 years				
Diabetic	12(92.3%)	1(7.7%)	0.042	8.01
Non- diabetic	12(60%)	8(40%)		
Male Gender				
Diabetic	14(87.5%)	2(12.5%)	0.008	8.40
Non- diabetic	10(45.5%)	12(54.5%)		
Female Gender				
Diabetic	12(85.7%)	2(14.3%)	0.262	
Non- diabetic	8(100%)	0		
BMI <15 kg/m2				
Diabetic	12(75%)	4(25%)	0.126	3.01
Non- diabetic	10(50%)	10(50%)		
BMI > 5 kg/m2				
Diabetic	14(100%)	0	0.081	
Non- diabetic	8(80%)	2(20%)		

DISCUSSION

Diabetes mellitus is a collection of carbohydrate metabolism disorders that have the common symptom of chronic hyperglycemia caused by production of insulin, insulin action. Insulin is a critical anabolic hormone that causes a variety of metabolic irregularities in proteins, lipids & carbs^{11,12}. Reduced levels of high-density lipoprotein cholesterol & increase levels of low-density lipoprotein cholesterol or tri-glycerides explain diabetic dyslipidemia^{13, 14}.

The findings of this study showed that dyslipidemia was found to be significantly higher (n=26, 86.7%) among diabetic patients as compared to non-diabetic patients (n=18, 60%). Somewhat similar findings were observed in other studies as well. In a new study, dyslipidemia was observed in 72.5% type 1 children.¹⁰ In another study, out of 60 children with T1DM, dyslipidemia was observed in 65% of the patients⁷.

One study has also reported dyslipidemia in 66% of the children with T1DM.⁸ Another study has reported that the load of dyslipidemia is high in people with diabetes. A cross-sectional study of 2,473 patients with type 2 diabetes found that 55.0 percent of those with diabetes for more than two years had dyslipidemia. In individuals who had diabetes for 15 years, the percentage increased to 66.0%¹⁵.

In our study, it was found that the risk of dyslipidemia was 4.33 times higher among diabetic patients than that of non-diabetics (OR 4.33). Patients having >10 years of age and diabetes were 8.01 times more likely (OR 8.01, p-value 0.042) and diabetic males were 8.40 times more likely (OR 8.40, p-value 0.008) to have dyslipidemia.

The finding of this showed that the mean cholesterol level, triglyceride level, LDL, and HDL levels were found to

be 139.7 ±36.26 mg/dL, 112.05 ±56.41 mg/dL, 80.13 ±29.75 mg/dL, and 37.83 ±9.56 mg/dL respectively. In particular, high cholesterol level was found in 96.7%, triglyceride level ≥150mg/dL in 25%, LDL ≥100mg/dL in 20%, and HDL in 16.7% patients. Somewhat similar observations were observed in a study of Homma et al as well. According to their study finding, high-CT was observed in 56.7%, low-HDL 21.7%, high LDL 44.0%, high-TG 11.8%.⁹ Another study reported 18.6% of children with type 1 diabetes had abnormal TC (>200 mg/dl) or high density lipoprotein cholesterol (HDL-c) (<35 mg/dl) levels in a retrospective cross sectional analysis¹⁶.

In contrast to our results, 3.0% of type 1 diabetes patients had LDL-c levels above 160.0 mg / dl, 14.0% had LDL-c levels above 130.0 mg / dl, and nearly half (48.0%) had LDL - c levels above the recommended LDL - c level of 100 mg / dl.¹⁷ In one study, the frequency of DLP among young Patients with type 1 diabetes, especially females. In order to prevent/delay chronic problems and heart disease, programs designed to prevent dyslipidemia should be implemented, particularly for this population^{9,10}.

In past few decades, diabetes-related vascular problems have shifted away from a "glucocentric" approach to include multiple risk factors which contribute to the development & progression of atherosclerosis. Dyslipidemia is a metabolic condition linked with diabetes that is defined by a range of quantitative, qualitative variations in lipids & lipoproteins. Hypertriglyceridemia, a decrease in HDL cholesterol content, and move toward a small dense LDL cholesterol are all symptoms of diabetic dyslipidemia, a frequent pattern of lipid abnormalities^{18,19}.

CONCLUSION

Highly significant association of dyslipidemia and type-1 diabetes mellitus was found among children up to 16 years of age. A higher prevalence of dyslipidemia raises a concern in type-1 diabetes mellitus children. Early dietary modification and pharmacological therapy intervention is also required for type-1 children.

REFERENCES

1. Babar G, Clements M, Dai H, Raghuvver G. Assessment of biomarkers of inflammation and premature atherosclerosis in adolescents with type-1 diabetes mellitus. *Journal of Pediatric Endocrinology and Metabolism*. 2019;32(2):109-13.
2. Abd El-Halim SS. Association between glycemic control and lipid profile in Children with type 1 diabetes mellitus. *Shawkia S. Abd El-Halim, Awatif M. Abd El-Maksoud 2, Hamdy El-Bassel 3 and Amal H. Abd El-Razek 4*.
3. Miller RG, Mahajan HD, Costacou T, Sekikawa A, Anderson SJ, Orchard TJ. A contemporary estimate of total mortality and cardiovascular disease risk in young adults with type 1 diabetes: the Pittsburgh Epidemiology of Diabetes Complications Study. *Diabetes care*. 2016;39(12):2296-303.
4. De Ferranti SD, Steinberger J, Ameduri R, Baker A, Gooding H, Kelly AS, et al. Cardiovascular risk reduction in high-risk pediatric patients: a scientific statement from the American Heart Association. *Circulation*. 2019;139(13):e603-e634.
5. Donaghue KC, Wadwa RP, Dimeglio LA, Wong TY, Chiarelli F, Marcovecchio ML, et al. Microvascular and macrovascular complications in children and adolescents. *Pediatric diabetes*. 2014;15(S20):257-69.
6. Donaghue KC, Marcovecchio ML, Wadwa RP, Chew EY, Wong TY, Calliari LE, et al. ISPAD Clinical Practice Consensus Guidelines 2018: Microvascular and macrovascular complications in children and adolescents. *Pediatric diabetes*. 2018;19(Suppl 27):262.
7. Mona HM, Sahar SA, Hend SM, Nanees A-WA. Dyslipidemia in type 1 diabetes mellitus: relation to diabetes duration, glycemic control, body habitus, dietary intake and other epidemiological risk factors. *Egyptian Pediatric Association Gazette*. 2015;63(2):63-8.
8. 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 journal of endocrinology and metabolism*. 2018;22(1):89.
9. Homma TK, Endo CM, Saruhashi T, Mori API, Noronha RMD, Monte O, et al. Dyslipidemia in young patients with type 1 diabetes mellitus. *Archives of endocrinology and metabolism*. 2015;59:215-9.
10. Bulut T, Demirel F, Metin A. The prevalence of dyslipidemia and associated factors in children and adolescents with type 1 diabetes. *Journal of Pediatric Endocrinology and Metabolism*. 2017;30(2):181-7.
11. Poznyak A, Grechko AV, Poggio P, Myasoedova VA, Alfieri V, Orekhov AN. The diabetes mellitus–atherosclerosis connection: The role of lipid and glucose metabolism and chronic inflammation. *International journal of molecular sciences*. 2020;21(5):1835.
12. Ortiz-Huidobro RI, Velasco M, Larqué C, Escalona R, Hiriart M. Molecular Insulin Actions Are Sexually Dimorphic in Lipid Metabolism. *Frontiers in Endocrinology*. 2021;12.
13. Gomes MB, Conte D, Drummond KRG, Mallmann F, Pinheiro AA, Leal FSL, et al. Overweight/obesity in adolescents with type 1 diabetes belonging to an admixed population. A Brazilian multicenter study. *Diabetology & Metabolic Syndrome*. 2022;14(1):1-10.
14. Hirano T. Pathophysiology of diabetic dyslipidemia. *Journal of atherosclerosis and thrombosis*. 2018;RV17023.
15. Harris SB, Ekoé J-M, Zdanowicz Y, Webster-Bogaert S. Glycemic control and morbidity in the Canadian primary care setting (results of the diabetes in Canada evaluation study). *Diabetes research and clinical practice*. 2005;70(1):90-7.
16. Shah AS, Maahs DM, Stafford JM, Dolan LM, Lang W, Imperatore G, 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):607-13.
17. Jaiswal M, Divers J, Dabelea D, Isom S, Bell RA, Martin CL, et al. Prevalence of and risk factors for diabetic peripheral neuropathy in youth with type 1 and type 2 diabetes: SEARCH for Diabetes in Youth Study. *Diabetes care*. 2017;40(9):1226-32.
18. Wolide AD, Zawdie B, Alemayehu T, Tadesse S. Association of trace metal elements with lipid profiles in type 2 diabetes mellitus patients: a cross sectional study. *BMC endocrine disorders*. 2017;17(1):1-7.
19. Jacob S, Krentz AJ, Deanfield J, Rydén L. Evolution of type 2 diabetes management from a glucocentric approach to cardio-renal risk reduction: the new paradigm of care. *Drugs*. 2021;81(12):1373-9.