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DYSLIPIDEMIA IN CHILDREN WITH TYPE 1 DIABETES MELLITUS: CROSS SECTIONAL STUDY

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ABSTRACT

Background: Type 1 diabetes mellitus (T1DM) and dyslipidemia (DLP) are serious metabolic disorders, and their coexistence has been associated with dangerous outcomes. Objective: The purpose of the present study is to investigate dyslipidemia and its association with glycosylated hemoglobin (HbA1c) in Type 1 diabetes mellitus children. Methods: In a cross-sectional study design included 118 patients with Type 1 diabetes mellitus aged between 5-13 years. Serum glycosylated hemoglobin (HbA1C), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL), and triglyceride (TG) were measured. Results: The results showed that there was a significant relationship between all lipid profiles expects HDL-C with glycosylated hemoglobin (p=0.0001). Conclusion: The current study concludes that Poor glycemic control plays a role as a risk factor for the development of dyslipidemia in children with Type 1 diabetes mellitus.

KEYWORDS: Dyslipidemia (DLP), Type 1 diabetes mellitus (T1DM), glycemic control.

INTRODUCTION

Type 1 diabetes mellitus (T1DM) is the most common childhood endocrine-metabolic disorder. It results from the marked and progressive inability of the pancreas to secrete insulin because of the autoimmune destruction of the beta cells.[1] In recent years, Diabetes rates are increasing epidemiologically by 2-5% per year in Europe, the Middle East, and Australia whereas some central and eastern European countries demonstrate an even more rapid increase up to 9%.[2] In patients with type 1 diabetes mellitus (T1DM), chronic complications including nephropathy, neuropathy, retinopathy, peripheral vascular and cardiovascular diseases (CVD) directly affect the expectancy and long term quality of the life.[3] The presence of dyslipidemia increases the frequency and severity of these complications.[4]

Diabetic dyslipidemia is defined as low levels of high-density lipoprotein cholesterol (HDL-C) and increased low-density lipoprotein cholesterol (LDL-C), triglyceride (TG), and total cholesterol (TC).[5] Diabetic dyslipidemia is a preventable major risk factor for CVD. Several studies have evaluated dyslipidemia in patients with type 2 diabetes mellitus, but dyslipidemia in T1DM especially young children remains largely undiagnosed and undertreated.[6-7] There is no research on dyslipidemia in T1DM children in Syria. The study aimed to determine the lipid profile and its relationship to glycemic control in Syrian T1DM children.

METHODS

A cross-sectional retrospective study included 118 children who had referred to the outpatient pediatric clinic of endocrinology at Tishreen University Hospital and the Diabetic Center of Latakia, Syria over 1 year period from October 2018 to November 2019. The patients who had other chronic illnesses, hypothyroidism, familial dyslipidemia, or taking other medications than insulin were excluded clinical data include age, gender, duration of diabetes since diagnosis was obtained from the patients and their parents. Physical examination was performed to measure weight(Kg), length (cm), and age-specific body mass index (BMI; Kg/m²). BMI scores were calculated as weight(kg)/ square of length (m²) and expressed in Z

score, based on the standards assessed by the CDC growth charts.[8]

Laboratory data were obtained after 8-12 hours fasting including Glycosylated hemoglobin (HbA1C), TC, TG, LDL-C, HDL-C.

Lipid profile was analyzed and classified according to American Heart Association Guidelines 2019 as TC ≥ 200 mg/dl, LDL ≥ 130 mg/dl, HDL-C <40 mg/dl, TG ≥ 100 mg/dL for children younger than 10 years and ≥ 130 mg/dL for older than 10 years. Dyslipidemia was defined by the presence of one or more abnormal serum lipid concentrations.[9]

HbA1C was determined by using an I-Chroma HbA1C kit based on the immunofluorescence assay method. the normal range was 4.5 -6.5%.

Diabetic children classified as optimal glycemic control (OGC) and poor glycemic control (PGC) according to the recommendation from the American Diabetes Association (ADA) that contains the HbA1C values in T1DM children according to age; up to 6 years 7.5 - 8.5%, 6-12 years <8%, 13-19 years <7.5%.[10]

All data were analyzed using the Statistical Package for Social Sciences (SPSS Version 20). Data were presented in simple measures of frequency, percentage, mean, standard deviation. The significance of the difference between different means (quantitative data) was tested using the Student-t-test for the difference between two independent means, while different percentages (qualitative data) were tested using the Pearson Chi-square test. Results were considered statistically significant with a p-value<5%.

This study was reviewed and approved by the ethical Committee of the Tishreen University Hospital, all participants provide informed consent and /or assent.

RESULTS

The study included 118 children with T1DM, 60(50.8%) were female and 58(49.20%) were male with a mean age of 10±2.3 years (5-13 years). The patient's characteristics are described in table I.

Table (I): Characteristics of the patients with T1DM.

Group characteristics	Total (n = 118)
Gender, n (%)	60 Females (50.8); 58 Males (49.20)
Actual age – years (SD)	10 (2.3)
Disease duration – years (SD)	3.4 (2.3)
HbA1C - %(SD)	8.4(1.9)

HbA1C: Glycosylated hemoglobin

The frequency of dyslipidemia was 48.3%. overall, 57 patients had dyslipidemia which included: 27(22.9%) patients with a low level of HDL-C, 25(21.2%) patients with hypertriglyceridemia, 22(18.6%) patients with hypercholesterolemia, 19(16.1%) patients with a high level of LDL-C (Figure 1).

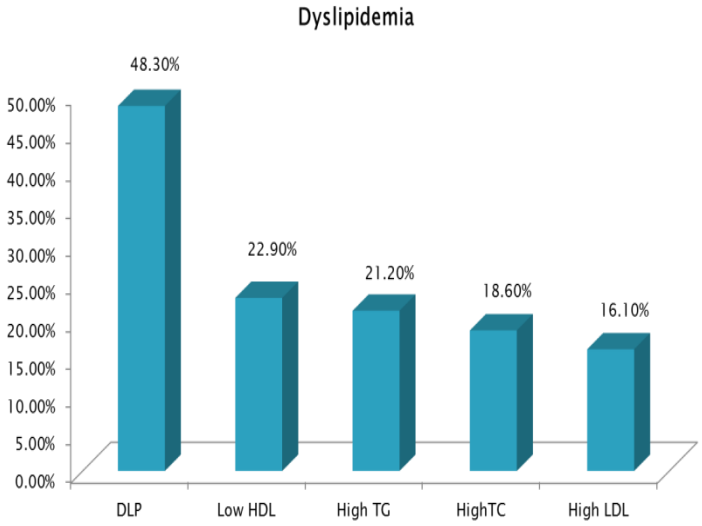

Figure (1): Different type of dyslipidemia.

Comparison between dyslipidemic and normolipidemic groups, There were no significant differences between the two groups regarding age, sex, BMI, duration of diabetes (Table II). HbA1c was significantly higher in the dyslipidemic group (P = 0.0001) (Table III).

Table (II): Characterizes of the patients with and without dyslipidemia.

Variables	Dyslipidemia	Normolipidemia	P
Age – years (SD)	10.3(2.5)	9.8(2.3)	0.2
Gender (female), n(%)	31(54.4)	29(47.5)	0.4
BMI			
Underweight, n(%)	19(33.3)	13(21.3)	0.2
Normal weight, n(%)	36(63.2)	44(72.1)	
Overweight, n(%)	2(3.5)	2(3.3)	
Increase weight, n(%)	0(0)	2(3.3)	
Duration Disease- years (SD)	3.3(2.4)	3.4(2.2)	0.7
HBA1C - % (SD)	9.2(2.03)	7.6(1.5)	0.0001

HBA1C: Glycosylated hemoglobin, **BMI**: Body mass index

Table (III): Comparison of dyslipidemia with PGC and OGC.

Normolipidemia	Dyslipidemia	Glycemic control	P
20(31.7)	43(68.3)	**PGC, n (%)**	0.0001
41(74.5)	14(25.5)	**OGC, n (%)**	

OCG: optimal glycemic control, **PCG:** poor glycemic control

To evaluate the association between lipid values and glycemic control, we categorized patients into two groups according to the values of HbA1C recommended by ADA**[10].** There was 46.7%(55) of patients with OGC, and 53.3%(63) with PGC. When comparing the OGC group with the PGC group, Hypercholesterolemia, hypertriglyceridemia, and high LDL-C were statistically significant. There was no statistically significant difference in low HDL-C between the OGC group and the PGC group. **(Table IV)**.

Table (IV): Comparison of different types dyslipidemia with PGC and OGC.

Dyslipidemia	OGC	PGC	P
TC, n(%)	1(1.8)	21(33.3)	0.0001
TG, n(%)	5(9.1)	20(31.7)	0.003
LDL-C, n(%)	3(5.5)	16(25.4)	0.007
HDL-C, n(%)	9(16.4)	18(28.6)	0.1

OCG: optimal glycemic control, **PCG:** poor glycemic control, **TC**: total cholesterol, **TG**: triglyceride, **LDL-C**: low-density lipoprotein cholesterol, **HDL-C:** high-density lipoprotein cholesterol.

DISCUSSION

There is no detailed information about the prevalence of T1DM and its association with dyslipidemia in Syria, but according to evidence predicate globally increasing of T1DM and its complications.[11] To the best of our knowledge, most results that investigate the relationship between DLP and glycemic control in T1D patients were done on studies with the adult population.[12-13-14] The current study supports the importance of clinical and research interest in blood samples and T1DM children.

The majority(48.3%) of the T1DM patients had dyslipidemia. Besides, 68.3% were PGC since treatment was provided at a free public health center, most patients were from a lower socioeconomic level.

Dyslipidemia frequency in diabetic children varies between 3.8% and 74.8% in different studies.[15-16] Redondo et al. found a dyslipidemia prevalence of 3.8% in the USA with 11,348 T1D patients aged 2–18 years. The authors attributed this low ratio of dyslipidemia to the fact that the patients included in the study were mostly younger and highly active children and that the number of obese subjects was low.[15] In a study from Iran, the ratio of dyslipidemia among 274 T1DM patients was 74.8% and it was shown that the majority dyslipidemia developed was hypercholesterolemia and hypertriglyceridemia was less frequently. Possible cause high-frequency dyslipidemia due to the board age range, different reference values used for DLP diagnosis, and possibly genetic variation.[16] In a study from Turkey, the rate of dyslipidemia in patients with T1D was found to be 26.2% with a high prevalence of hypercholesterolemia and hypertriglyceridemia.[17] A possible explanation of variation reports includes multiple genetic factors in different ethnic groups, the diet and physical activity of the general population, and different laboratory methods.[18-19]

The current study showed that there was a relationship between dyslipidemia and glycemic control. This result is in concordance, Bulut et al found that glycemic control in T1DM had a direct effect on DLP,[17] This can be explained by insulin deficiency that leads to increase the release of lipoprotein lipase from adipose tissue, besides, increased very-low-density lipoprotein (VLDL) and free fatty acid.[20] On the contrary, Hasan et al found that dyslipidemia in T1DM children not related to glycemic control. The author attributed this to the fact that most of the patients included in the study had normal or near-normal HbA1C values.[21]

It was observed that abnormal TG, TC, and LDL-C were higher in PGC patients compared to OGC patients participants with a significant association (p=0.003, p=0.0001, and p=0.007, respectively). whereas, abnormal HDL-C was found in PCG patients than OGC patients but with no significant association (p=0.1). The same finding in the study of Bangladesh,[22] which can be explained that HDL-C disorder affected by many factors included genetic, dietary habits, lifestyle, and physical activity.[23] Zabeen et al showed that there is a significant relationship between levels of HbA1C in patients and abnormal HDL-C,[24] this modification has been attributed to an increase cholesterol ester transfer between lipoproteins which increases the transfer of TG to HDL-C, resulting in an increase in HDL-C content from TG, thus increasing its susceptibility to breakage.[25] Mostofizadeh et al study showed that LDL-C was higher in PGC patients and this corresponds to the result of the current study.[16] This can be explained by insulin deficiency in PGC patients reduces the activity of LDL-C and the number of available receptors that lead to its concentration.[26]

Poor information and Awareness of nutrition content of local food and calories spent were limitations of data collected for this study. Repeated measurement of fasting lipids was not made over time in individual subjects that may be also a limitation.

CONCLUSION

We conclude that poor glycemic control is a modifiable red flag marker that causes dyslipidemia among children with T1DM. More studies with larger samples and the possibility of following up with patients after improving glycemic control are recommended.

List of Abbreviations

T1DM: Type 1 diabetes mellitus.
HbA1c: glycated hemoglobin.
BMI: body mass index
HDL-C: high-density lipoprotein cholesterol.
LDL-C: low-density lipoprotein cholesterol.
TG: triglyceride.
TC: total cholesterol.
DLP: dyslipidemia.
PGC: poor glycemic control.
OGC: optimal glycemic control.
VLDL-C: very-low-density lipoprotein cholesterol.
CVD: cardiovascular disease.

Declaration

✓ Ethics approval and consent to participate

All parents whose children were studied gave informed consent for the sharing of this research. Ethical clearance for this study was obtained from the Ethical Committee of the University of Tishreen Hospital.

✓ Availability of data and materials

We can't share patient data due to our hospital's privacy policy, which concerns with maintaining patient confidentiality and refuses to publish or share data. Also, the informed consent signed by the parents to participate in the study prevents the sharing of information with the unknown researchers.

✓ Author Contributions

Both authors developed and carried out sample collection. A Literature review was done by Dr.Leen Doya, and both authors did the data analysis and read through the final data.

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