PREVALENCE, CONTRIBUTING FACTORS AND CLINICAL CHARACTERISTICS OF DYSLIPIDEMIA IN CHILDREN WITH TYPE 1 DIABETES

Shaimaa Salah[1*], Dina Khedr[2], Amera Hasnoon[3]

[1] Pediatric Department, Faculty of Medicine, Kafrelsheikh University, Kafr Elsheikh, Egypt.
[2]Pediatric Endocrinology Units, Faculty of Medicine, Cairo University, Egypt.
[3]Pediatric Gastroenterology Unit, Faculty of Medicine, Cairo University, Egypt.

ABSTRACT

Background: Achieving ideal goals of glycemic control in children and adolescents with type 1 diabetes (T1D) is challenging. One of the commonest adverse effects of poor control is dyslipedemia with the subsequent cardiovascular events in young adulthood.
Aim: This study investigates the prevalence of lipoprotein disorders in children with T1D and studies its possible causes.
Materials and Methods: We recruited 80 type 1 diabetic child, took full history and assessed them clinically for their status of growth and puberty. Biochemical analysis including glycated hemoglobin (HbA1c) and lipoprotein profiles was done.
Results: Abnormal lipid profiles were detected in 33% and poor glycemic control in 85% of our studied patients.The group of patients with better glycemiccontrol had a significant elevation of HDL-c and a significant reduction of TG levels than those with poor control. Moreover the group of patients who did not have dyslipdemia had a significant reduction in HbA1c level.
Conclusion: Dyslipedemia is highly prevalent in diabetic children. Poor glycemic control is a strong contributing factor. Early recognition and intervention is fundamental for the prevention of its harmful sequences. Further studies are warranted to asses the effect of improving glycemic control on the status of dyslipedemia in diabetic children.

Keywords: Dyslipedemia, T1D, children

Introduction

Improper glycemic control has its adverse consequences in children with type 1 diabetes (T1D), of these poor growth rates, the development of insulin resistance and dyslipidemia are frequently noticed.

According to ISPAD guidelines, screening for dyslipidemia should be performed soon after diagnosis in all children with T1D from age of 11 years. Cholesterol plays an important role in the initiation and progression of atherosclerosis.[1]In addition, dyslipidemia was associated with microalbuminuria and retinopathy development in the DCCT/EDIC [2] and some other studies.[3,4]

The prevalence of hypocholesteremia approached 50% of young adults in one study [5], while elevated non-HDL cholesterol approached 25% in another study of individuals younger than 21 years of age.[6]

This study aimed at observing the prevalence of dyslipidemia in children with T1Dand studying the clinical characters of those patients.

Materials and Methods

Study population:

We studied 80 children diagnosed with T1D following in the pediatric diabetes clinic, Cairo University Children Hospital over 12 months period from November 2016 to November 2017.

Patients were diagnosed according to the ADA consensus guidelines[7] that includes clinical symptoms and the laboratory findings. Patients with a minimum of 3 years diabetes duration were

Shaimaa Salah
Pediatric Department, Faculty of Medicine, Kafrelsheikh University, Kafr Elsheikh, Egypt.
Email. mysarah552012@yahoo.com

included. T1D Patients with known cardiovascular, hepatic, renal, systemic disease, chronic inflammatory disorder or receiving any medication other than insulin were excluded.

The protocol was approved by the local research ethics committee of the Pediatric department at Cairo University and all the participants or their guardians gave informed consent. The study complied with the World Medical Association Declaration of Helsinki regarding ethical conduct of research involving human subjects.

Clinical Measurements:

Complete clinical examination was applied to all studied patients including, blood pressure was measured on 3 different occasions and were compared to percentile curves for same age and sex. Patients lying on or higher than the 95th percentile for their height were considered hypertensive.[8]

The height was measured using Harpenden stadiometer and recorded to the nearest 0.1 cm and the weight was measured using self-calibrating electronic SECA scale that records to the nearest 0.1 kg. BMI (body mass index) was calculated as weight in kg/height in m2. We used Growth vision computer software provided by Novo Nordisk, Denmark to assess height SDS (standard deviation score), weight SDS and BMI SDS. Pubertal assessment was done following Tanner pubertal stages in girls[9] and in boys[10]. The waist circumference (WC) was measured in centimeters with a tape measure, at the narrowest circumference between the lower costal margin and the iliac crest[11] and was plotted on WC centiles.[12]

Biochemical Measurements

The most recent results of fasting lipid profile including; serum Cholesterol (TC), Triglycerides (TG), High density lipoproteins (HDL) and Low density lipoproteins (LDL) were obtained from the medical records. To define abnormal lipid profile (dyslipidemia), we followed the cut-offs of the National Heart Lung and Blood Institute. [8] Mean HbA1C levels over the preceding year presented in percentage were calculated, poor glycemic control was defined by HbA1C<7.5%.[13]TC, HDL, LDL, TG were performed by the use of standard methods on Cobas MIRA automated analyzer (Roche Diagnostics, Basel, Switzerland).

2.4 Statistical Analysis

Statistical analysis was performed using SPSS version 25 (IBM Co., Armonk, NY, USA). Student *t* tests or chi-square tests were used to compare the baseline characteristics between patient groups. All *P*-values were two-tailed, and $P<0.05$ was considered statistically significant.

Results

A number of 80 children with T1D with an age range of (11.1 to 18.1 years) were enrolled in the study. Table (1) shows the baseline clinical characteristics and biochemical parameters in those subjects.

Table (1): Clinical and biochemical data of the studied patients (n=80):

		Range
Age(yrs)	14.51±1.76	11.1- 18.1
Duration of diabetes(yrs)	5.15*	2.8-15.7
Insulin dose (IU/Kg/day)	1.25*	0.3-2.8
Weight SDS	0.2*	-4-3.1
Height SDS	-1.1*	-5.8-1.8
BMI SDSs	0.95*	-2.7-2.4
Waist circumference (cm)	79.27±6.54	64-94
SBP (MmHg)	117.56±16.27	70-160
DBP (MmHg)	78.1±11.96	50-109
Total cholesterol (mg/dl)*	170.5	133-285
Triglycerides (mg/dl)*	88	16-235
LDL-c (mg/dl)*	110	65-191
HDL-c (mg/dl)*	48.5	39-65
HbA1C (%)	10.11±2.43	5-14

Data are represented as mean and standard deviation. * median, BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure

46 Females were included in the study. Only 5% of T1D patients were considered obese with BMI SDS more than 2 and only 4 of them had their WC more than 90th centile. Hypertension was recognized in 33% of them and all of them were pubertal. Poor glycaemic control defined by HbA1C > 7.5 gm% was detected in 85%with a mean HbA1C 10.11±2.43 gm%. Regular insulin and NPH (Neutral Protamine Hagedorn; intermediate acting insulin) in a basal-bolus regimen was the most commonly used regimen with a total daily insulin dose range (0.3 to 2.8 IU/kg/day).

Dyslipidaemia was the most frequent complication detected in our T1D patients (33%), we compared between two groups of patients according to the presence of dyslipidaemias and a statistically significant elevation of HbA1C (P = 0.031) in the group with dyslipidaemia was recognized. No significant difference in BMI, insulin dose or blood pressure between the two groups.

When comparing two groups of our patients according to glycaemic control (HbA1C %), showed a statistically significant elevation of serum HDL-c levels, in addition to a statistically significant reduction in TG level in the group with good glycaemic control (HbA1C<7.5%).

Table (2): Comparison between two groups of patients according to the presence of dyslipidemia (n=80):

	Dyslipidemia (n=27)	No dyslipidemia (n=53)	P value
Age (Yrs)	14.53±1.9	14.42±1.71	0.736
Diabetes Duration (Yrs)*	5.2(4.2-8.4)	5(3.7-7.5)	0.728
Insulin Dose (IU/KG/Day)*	1.1(1-1.4)	1.3(1.2-1.5)	0.209
Weight SDS*	-0.1(-0.7-1.1)	0.3(-0.5-0.8)	0.630
Height SDS*	-1.7(-2.4- -0.2)	-1(-1.6- -0.2)	0.243
BMI SDS*	0.9(0.3-2)	1(0.1-1.5)	0.545
WC (cm)	79.24±6.49	79.29±6.67	0.979
SBP (mmhg)	115.82±15.19	118.41±16.92	0.593
DBP (mmhg)	79.53±13.24	77.32±11.4	0.550
HbA1C (%)	11.5±1.88	9.93±2.53	**0.031**

Data are represented as mean ± SD, or * median and interquartile range (IQR). P-value <0.05 is considered significant. BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; LDL-c: low density lipoprotein cholesterol; HDL-c: high density lipoprotein cholesterol; HbA1C: glycated hemoglobin.

Table (3): Comparison between two groups of patients according to glycemic control (HbA1c% cut off 7.5%) (n=80):

	>7.5% (n= 68) Poor control	<=7.5% (n=12) Good control	
Age (Yrs)	14.32±1.71	15.83±1.91	0.101
Diabetes duration (Yrs)*	5.15(3.9-7.5)	6.65(4.6-9.2)	0.478
Insulin dose IU/Kg/Day)*	1.2(1-1.5)	1.5(1.35-1.8)	0.132
Wt SDS*	0.2(-0.6-0.8)	0.55(-0.45-2.3)	0.416
Ht SDS*	-1.1(-1.8-0.2-)	-1.45(-1.85-0.4-)	0.850
BMI SDS*	0.94(0.1-1.6)	1.4(0.05-2.15	0.569
WC (cm)	78.82±6.47	84.50±5.69	0.096
SBP (mmhg)	118.26±15.22	109.50±27.53	0.307
DBP (mmhg)	78.87±11.61	69.25±14.22	0.124
Total cholesterol (mg/dl)*	172.5(155-197)	169(152-170)	0.339
Triglycerides (mg/dl)*	94.5(70-140)	53(50-63)	**0.024**
LDL-c (mg/dl)*	111(98-124)	94.00(86.5-102.5)	0.097
HDL-c (mg/dl)*	48(43-53)	59(52.5-64)	**0.021**

Data are represented as mean ± SD, or * median and interquartile range (IQR). P-value <0.05 is considered significant. BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; LDL-c: low density lipoprotein cholesterol; HDL-c: high density lipoprotein cholesterol; HbA1C: glycated hemoglobin.

Discussion

This was a cross sectional study that studied the status of dyslipidaemia in children with T1D, our results point to the high prevalence of lipid disorders in this population, and that these disorders are mainly contributed to poor glycaemic control.

The main pattern of dyslipidaemia in our study was high TG levels, which is in agreement with Osawa and his colleagues[14] and with [8]who stated that the main dyslipidaemic pattern in childhood is moderate to severe elevation of TG level, normal to mild elevation of LDL-c and reduction of HDL-c, and low HDL levels in agreement with Pérez et al.[15]who announced that low HDL-c was the most frequent dyslipidaemic pattern in patients with poorly controlled T1D, that fortunately improved by optimization of glycaemic control through intensive insulin therapy.

In the previous literature, HDL-c levels were shown to be normal or high in T1D, a finding that was explained by the high activity of lipoprotein lipase(LPL) in adipocytes that avidly hydrolyses triacylglycerol rich particles, resulting in high HDL- c levels.[16]

Dyslipidaemia in itself has its adverse consequences on insulin sensitivity in diabetic patients as was reported by Krochick and colleagues[17],they stated that poorer sensitivity to insulin in children and adolescents with T1Dwas related to lipid disorders in those subjects.

In an attempt to understand the link between poor glycaemic control and dyslipidaemia, we searched the literature; Pang and Nardeen[18] postulated that chronic hyperglycaemia results in two metabolic pathways: accentuation of ectopic fat accretion with increased intramyocellular lipid content, interfering with insulin signaling pathways in skeletal muscles giving rise to insulin resistance, and promotes lipolysis. In the same context, Heptulla et al.[19]concluded that poor glycaemic control with the resultant glycation end products interfere with insulin action promoting lipolysis giving rise to non-esterified fatty acids which in turn impede with the insulin stimulated glucose uptake by substrate competition through the Randle cycle. These explanations point to a vicious circle of insulin resistance, poor glycaemic control and dyslipidaemia.

Another theory at hand is the reversed fat partitioning; as it is well known that insulin not only exerts its effects on glucose metabolism, but it also has profound effects on lipid metabolism via promotion of hepatic and peripheral fat storage and suppression of hepatic and peripheral fat oxidation. However in T1D, with absent pancreatic insulin

secretion and its exogenous replacement, contrasting lipid handling might be predicted.[20]

Unfortunately, dyslipidaemia predispose to atherosclerotic changes that, according to ISPAD [1], start in childhood and adolescence as shown by intima-media thickness of the aorta and carotids.[21,22] Moreover, some researchers detected silent coronary atherosclerosis by intravascular ultrasound in young adults with childhood onset of diabetes.[23]

In the same boat, Schofield and colleagues reviewed the pathophysiology and implications of the alterations in lipoproteins and reported a significant association between atherosclerotic changes and serum level of Tc, TG in T1D.[24]

Conclusion

Our results point to the high prevalence of dyslipidaemia in children with T1D, emphasizing on the strong link to poor glycaemic control. The expected deleterious complications urge all physicians caring for diabetic children to monitor lipoprotein profiles periodically, trying every effort in maintaining optimal glycaemic control.

Conflict of interest: none

Funding sources: No funding sources

Statement of human rights:

The study done was in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

Statement of informed consent

Informed consent was obtained from all subjects for being included in the study.

Ethical clearance:

Cleared by the ethical committee of the Pediatric department at Cairo University

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