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Prevalence of Dyslipidemia in Patients with Type 1 Diabetes

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Abstract

Introduction: Patients with Type 1 Diabetes tend to present premature cardiovascular disease and dyslipidemia is a relevant risk factor in this cases.

Objective: To determine the prevalence of dyslipidemia and its association with glycemic control, insulin therapy, nutritional therapy of carbohydrate counting, body mass index and physical activity level in children, adolescents and adults with Type 1 diabetes.

Methodology: Cross-sectional study with 87 children, adolescents and adults with Type 1 Diabetes assisted in a public hospital in Brazil. The variables studied were: age, sex, education level, blood lipid levels, glycated hemoglobin, fasting glucose, body mass index, physical activity level, insulin therapy, and the nutrition therapy of carbohydrate counting. Data were collected from medical records and analyzed in their distribution, frequency, and association with the Person's exct chi-squared test and Fisher's exact test ($p<0,05$).

Results: The patients of the study were mostly adults (54%), females (64%) and, 40% concluded high school. The predominant insulin therapy was based in multiple daily injections with basal and rapid-acting analogs of insulin. The minority followed the nutrition therapy of carbohydrate counting. The prevalence of elevated glycated hemoglobin and fasting glucose was high (80,5% and 73,3%, respectively). Obesity was observed in 4,6% of adults. Regarding the blood lipid levels, hypercholesterolemia and low levels of HDL-c were observed in all age categories. Dyslipidemia was not associated with the variables of the study.

Conclusion: There was observed dyslipidemia in all age categories of the patients of the study. Most of them were not following the nutrition therapy of carbohydrate counting and presented poor glycemic control. These two last caracteristics are modifiable and more educational activities should be developed to encourage self-care and prevent premature diabetes complications like cardiovascular diseases.

Keywords: Diabetes Mellitus; Type 1; Dyslipidemias; Blood Glucose; Nutrition Therapy

Introduction

Individuals with Type 1 diabetes (T1D) are classified as at high risk for CVD, with variable morbidity outcomes. Mortality from CVD is two to 20 times higher in these patients when compared to individuals without diabetes [1]. It is estimated that with each 1% rise in glycated hemoglobin (A1C), the chance of a cardiovascular event increases from 11% to 16% [2] and that the decrease in blood glucose is beneficially reflected in the lipid profile preventing dyslipidemia [3].

Dyslipidemia is characterized by changes in normal levels of blood lipids and lipoproteins, which can be influenced by environmental and genetic factors. Elevated levels of Total Cholesterol (TC) or Low-density Lipoprotein Cholesterol (LDL-c), and low levels of High-density Lipoprotein Cholesterol (HDL-c) are associated with a higher incidence of atherosclerotic disease and high blood pressure, among other cardiovascular diseases (CVD) [4,5].

Sedentary lifestyle and change in the dietary pattern have favored weight gain and the development of a more atherogenic lipid profile, with the elevation of LDL-c, triglycerides (TGs), and reduction of HDL-c. Therefore, for a progressive improvement in risk factors in individuals with diabetes, glycemic control is essential [6].

Once it is demonstrated the close relationship between T1D and macronutrient metabolism, nutrition therapy is important to reduce A1C; fasting blood glucose (FBG), healthy weight; plasma lipids and lipoproteins; and the reduction of metabolic stress. Therefore, the objective of the present study was to verify the prevalence of dyslipidemia and its association with glycemic control, insulin therapy, nutrition therapy of carbohydrate counting, anthropometry, and physical activity level in children, adolescents and adults with T1D.

Methods

It is a cross-sectional Institutional-based study. Data were collected from medical records of patients from a public hospital in the center-west of Brazil. The participants were 87 patients of both sexes with the diagnose of T1D for more than a year including children (from 3 to 9 years and 11 months), adolescents (from 10 to 17 years and 11 months), and adults (older than 18 years). It was excluded from the study patients diagnosed with other syndromes related to diabetes such as Mauriac Syndrome and Down Syndrome and pregnant women.

The following data were collected from the medical records: age, sex, education level, plasma lipid profile, A1C, FBG, Body Mass Index (BMI), physical activity level, insulin therapy, and whether the patient underwent nutrition therapy of carbohydrates counting (CC). Data were collected from June 2018 to June 2019.

Dyslipidemias were classified according to the Guideline of the Brazilian Society of Cardiology from 2019 [7] for TC, TGs, LDL-c and HDL-c. The glycemic control was evaluated by A1C and FBG. The cut points for adequacy were obtained from the Guideline of the Brazilian Society of Diabetes [8]. The results included were those whose tests were performed using methods certified by the National Glycohemoglobin Standardization Program (NGSP) [9]. The BMI was classified according to the World Health Organization [10] and the physical activity level was based on a population study in Brazil, the VIGITEL [11]. Nutrition therapy was determined by prescriptions and food consumption records.

The study was approved by the Research Ethics Committee CAAE: 62108616.1.3001.5078. Patients and those responsible for participants under the age of 18 were consulted regarding their interest in participating in the study. They received information about the research objectives, data collection procedures, publication of results and the guarantee of confidentiality and anonymity. Those who voluntarily agreed to participate signed the consent form.

Data were analyzed using the Statistical Package of Social Sciences (SPSS) version 18.0. Descriptive statistics were used (frequencies, averages, medians, standard deviations, percentiles and minimum and maximum values). The exact chi-squared test and Fisher's exact test were applied to assess the association ($p < 0.05$).

Results

The participants were predominantly of adults, females and less than half concluded high school (Table 1). The insulin therapy most adopted was the combination of ultra-rapid and basal analogs of insulin, but with low adherence to carbohydrate counting, especially among children. A little more than half of the participants performed moderate physical activity (Table 2).

The prevalence of hyperglycemic was elevated for both A1C and FBG. Regarding BMI, overweight was observed in adolescents and adults, but obesity, only among adults (Table 2). About lipid profile, increased levels of TGs and LDL-c were not found among children. However, increased CT and low HDL-c levels were observed in all age groups (Table 2). The clinical, anthropometric, glycemic control and nutrition therapy of CC variables did not influence the prevalence of dyslipidemia in the patients of the study.

Characteristics	n	%
Age range		
Children	12	13.8
Adolescents	28	32.2
Adults	47	54.0
Sex		
Male	31	35.6
Female	56	64.4
Education level		
Not declared/Illiterate	11	12.6
Elementary school (1st phase) – incomplete	12	13.8
Elementary school (2nd phase) – incomplete	14	16.1
High school – incomplete	15	17.2
High school – complete	21	24.1
Higher education – incomplete	6	6.9
Higher education – complete	8	9.2
Total	87	100

Table 1: Sociodemografic characteristics of pacientes with Type 1 diabetes (N = 87).

Caracteristics	Children (12)		Adolescents (28)		Adults (47)		Total	
	N	%	N	%	N	%	N	%
Insulin								
NPH e RA	0	0	1	3.6	6	12.7	7	8.0
NPH e R	0	0	0	0	7	14.9	7	8.0
LA e RA	11	91.7	26	92.8	30	63.8	67	77.0
RA	1	8.3	0	0	1	2.1	2	2.3
LA	0	0	0	0	3	6.4	3	3.5
LA e R	0	0	1	3.6	0	0	1	1.1
CC								
Yes	0	0	8	28.6	11	23.4	19	21.8
No	12	100	20	71.4	36	76.6	68	78.2
A1C								
Adequated	2	16.7	7	25.0	8	17.0	17	19.5
Inadequated	10	83.3	21	75.0	39	83.0	70	80.5
FBG								
Adequated	2	16.7	6	22.2	15	31.9	23	26.7
Inadequated	10	83.3	21	77.8	32	68.1	63	73.3
BMI								
Underweight	0	0	2	7.1	2	4.3	4	4.6
Eutrophic	12	100	20	71.4	30	63.8	62	71.4
Overweight	0	0	6	21.4	11	23.4	17	19.5

Obesity	0	0	0	0	4	8.5	4	4.6
Physical Activity								
Sedentary	5	41.7	10	35.7	23	48.9	38	43.7
Moderate	7	58.3	16	57.1	21	44.7	44	50.6
Intense	0	0	2	7.1	3	6.4	5	5.7
HDL-c								
Adequated	9	75.0	21	75.0	35	74.5	65	74.7
Inadequated	3	25.0	7	25.0	12	25.5	22	25.3
LDL-c								
Adequated	12	100	24	85.7	42	89.4	78	87.7
Inadequated	0	0	4	14.3	5	10.6	9	10.3
TGs								
Adequated	12	100	21	75.0	40	85.1	73	83.9
Inadequated	0	0	7	25.0	7	14.9	14	16.1
TC								
Adequated	10	83.3	18	64.3	36	76.6	64	73.6
Inadequated	2	16.7	10	35.7	11	23.4	23	26.4

Table 2: Distribution of patients by age group, insulin therapy, nutrition therapy, glycemic control, body composition, physical activity and plasma lipid.

NPH: Neutral protamine Hagedorn insulin; R: Regular insulin; RA: rapid-acting insulin analogs; LA: long-acting insulin analogs; CC: Nutrition therapy of carbohydrates counting; A1C: Glycated hemoglobin; FBG: Fasting blood glucose; BMI: Body mass index; HDL-c: High-density Lipoprotein Cholesterol; LDL-c: Low-density Lipoprotein Cholesterol; TGs: Triglycerides; TC: Total cholesterol.

Discussion

It is well established that intensive insulin replacement with multiple daily injections or continuous subcutaneous administration is the best therapy to achieve good glycemic control. People with T1D, treated with analog insulins are associated with less hypoglycemia, less weight gain, lower A1C, and less macro and microvascular complications when compared with those using human insulins [12]. But, in our study, despite the majority is in the multiple daily injections therapy, almost all had inadequate levels of A1C and FG.

Hyperglycemia appears to have a more profound effect on cardiovascular risk in T1D than Type 2 Diabetes. It has been demonstrated that individuals with T1D who have an A1C of 52 mmol/mol or lower still have a risk of death from cardiovascular causes twice as high as the risk in the general population. The risks are several times higher among patients with higher A1C concentrations. A1C may also relate more strongly to fatal rather than nonfatal CVD events [13].

Regarding the BMI the prevalence of obesity in children and adolescents of our study was below the prevalence presented by a meta-analysis which was 14.1% in children and adolescents without T1D [14], and between 12.5% to 33.3% in those with T1D [15]. About the adults, our results were lower than those demonstrated by Szadkowska, et al. [16] (35.5% and 13.2% for overweight and obesity, respectively). Even though the prevalence is lower, the presence of obesity, alone, is a classical risk factor for CVD [7], even more, when associated with diabetes and hyperglycemia [17].

Known risk factors seem to operate differently in T1D, suggesting a difference in the pathophysiology of CVD. The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Research Group [18] presented mean A1C over time as a strong risk factor for clinical CVD (events) in T1D followed by age. The onset of T1D before 10 years of age is associated with a 30-fold increased risk of CVD in early adulthood [13]. That is an important point as the children of our study presented low levels of HDL-c and elevated levels of TC.

The acceleration of atherosclerosis in T1D is likely to result from many pathways, including effects from inflammation and dyslipidemia [13]. The prevalence of dyslipidemia in individuals with T1D vary in the studies [19,20], but it is shown that the A1C levels are significantly

higher in patients with dyslipidemia [21]. In our study, no association was found, but this can be explained by the number of participants, considering that it is an institutional-based study.

Defects in insulin action and hyperglycemia could lead to changes in plasma lipoproteins in patients with diabetes. In poorly controlled type 1 diabetes hypertriglyceridemia and reduced HDL-c commonly occur. Replacement of insulin in these patients may correct these abnormalities, and well controlled diabetics may have increased HDL-c and lower than average TGs levels [22].

In risk prediction models for patients with T1D, TC and HDL-c are more important than LDL-c in predicting adverse cardiovascular outcomes [23]. A study enrolled in the SEARCH for Diabetes in Youth (SEARCH) Study reported the natural evolution of dyslipidemia over 7 years in a large cohort of youth with T1D. After adjusting for covariates, it was identified two modifiable risk factors, waist-to-height ratio and A1C burden over time, that were independent predictors of unfavorable changes in lipids or of stable abnormal levels over time [24].

The nutritional therapy of CC is the cornerstone of diabetes care in T1D. Carbohydrates are the primary macronutrient that affects the postprandial glycaemic response. Their dietary intake should not be limited to ensure proper growth in children and adolescents with T1D and energy to adults. The adjustment of the insulin dose to carbohydrate intake produces improvements in glycaemic control [25].

Our patients, despite the importance of the nutrition therapy, were not following the prescription to count carbohydrates, principally children and adolescents, which responsibility rebound on their parents and caregivers. The CC can be difficult for some patients as it demands the knowledge of the total of carbohydrates of the meals, how to calculate the insulin-to-carb ratio, even in physical activities, how carbohydrates will raise blood glucose and the insulin-sensitive factor [25]. The low educational level of our patients or their parents can be the reason why the goal of CC therapy is not achieved.

This scenario highlights the important point of the management of T1D that is a planned and adequated meal, good insulin therapy, and self-monitoring glucose, which means adherence to diabetes care recommendations. In a study in which children and adolescents had 37% of adherence to the treatment when evaluated the specific treatment parameters showed that 52%, 76.5%, and 29.5% of the children and adolescents adhered to insulin, blood glucose monitoring, and dietary recommendations, respectively [26]. Regarding adults with T1D, a multicentric study from Brazil demonstrated adherence to therapy of 45.8% [27].

It seems that our patients with T1D are following this tendency resulting in overweight, obesity, hyperglycemia, dyslipidemia and untimely CVD. Education of patients on how to adjust prandial insulin to account for carbohydrate intake, premeal glucose levels, and anticipated activity can be effective [12], and should be offered more frequently to ameliorate the modifiable risk factors and achieve the goals of good metabolic control and quality of life.

The limitations of the study are the number of participants that influence the statistical analyses, we did not analyze the waist circumference and the blood pressure, that are known risk factors for CVD, the pharmacological therapy for dyslipidemia.

Conclusion

We conclude that despite our patients are mostly eutrophic, practicing physical activities and with the best insulin therapy, they are not following the nutritional therapy of CC and achieving good metabolic control demonstrated by fasting glucose and A1C, which may be leading to dyslipidemia and CVD. These results highlight the need for educational interventions to modify this behavior and improve de self-management of diabetes.

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