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# Perfil lipidico de crianças e adolescentes com Diabetes Mellitus tipo 1

## Lipid profile of children and adolescents with type 1 Diabetes Mellitus

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## RESUMO

**Introdução:** Em pacientes com Diabetes Mellitus tipo 1 (DM1), os fatores de risco para o desenvolvimento de doença cardiovascular começam na infância, aumentando o risco de desenvolvimento precoce de lesões de aterosclerose e aceleração da progressão de doenças cardiovasculares na idade adulta.

**Métodos:** Trata-se de um estudo transversal. Todos os pacientes atendidos na clínica até novembro/2011 foram incluídos no estudo. As variáveis dependentes foram colesterol total, HDL, LDL e triglicerídeos. As variáveis independentes foram sexo, idade, duração da doença, índice de massa corporal, hemoglobina glicada e tipo de planejamento dietético. Um modelo de regressão logística para cada desfecho foi construído e essas associações foram consideradas significativas com p <0,05.

**Resultados:** Foram incluídos 195 pacientes, com idade média de 11,01 anos (± 3,78) e 55,9% do sexo masculino. A frequência de sobrepeso foi de 36,7%. O colesterol elevado foi encontrado em 42,8% da amostra, 15,8% apresentaram HDL inadequado, 7,9% LDL aumentado e 12,5% triglicerídeos elevados. As crianças do sexo masculino tiveram maior chance de ter colesterol total elevado (OR 2,21, IC 95%: 1,16-4,20) e 54% menos chance (OR 0,46, IC 95%: 0,23-0,92) de LDL elevado. Quanto aos triglicerídeos, aqueles com idade mais avançada e com pior hemoglobina glicada apresentaram maior chance de hipertrigliceridemia (OR 1,53, IC 95%: 1,23-1,90 e OR 4,89, IC 95%: 1,45-16,52, respectivamente).

**Conclusão:** Foi encontrada alta prevalência de dislipidemia em crianças e adolescentes com DM1, o que indica a necessidade de definir medidas e estratégias para promover hábitos e estilo de vida saudáveis.

## PALAVRAS-CHAVE

Perfil lipídico; crianças; Adolescentes; Diabetes mellitus tipo 1; nutrição.

## ABSTRACT

**Background:** In Type 1 Diabetes Mellitus (T1DM) patients, the risk factors for developing cardiovascular disease begin in childhood, rising the risk of early development of atherosclerosis lesions and accelerated progression of cardiovascular diseases throughout adulthood.

**Methods:** This was a cross-sectional study. All the patients who registered at the clinic until November/2011 were included in the study. The dependent variables were total cholesterol, HDL, LDL and triglycerides. The independent vari-

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ables were gender, age, disease duration, body mass index, glycated hemoglobin and type of prescribed meal plan. A model of logistic regression for each outcome was built and those associations were considered significant with p <0.05.

**Results:** 195 patients were included in the study, mean age 11.01 years (± 3.78), and 55.9% were males. The frequency of overweight was 36.7%. High cholesterol was found in 42.8% of the sample, 15.8% had inadequate HDL, 7.9% increased LDL, and 12.5% increased triglyceride. Male children were more likely to have elevated total cholesterol (OR 2.21, 95% CI: 1.16-4.20) and 54% less likely (OR 0.46, 95% CI: 0.23-0.92) to have high LDL. Regarding triglyceride, those with older age and with high glycated hemoglobin had a greater chance of hypertriglyceridemia (OR 1.53, 95% CI: 1.23-1.90 and OR 4.89, 95% CI: 1.45-16,52, respectively).

**Conclusion:** A high prevalence of dyslipidemia was found among children and adolescents with T1DM, indicating the need to defining define measures and strategies to promote healthy eating habits and lifestyle.

## KEYWORDS

Lipid profile; children; adolescents; type 1 diabetes mellitus; nutrition.

## INTRODUCTION

Diabetes is characterized by abnormal glucose metabolism, however, changes in serum lipids and arterial[1] pressure are very common. The incidence of type 1 diabetes mellitus (T1DM) has increased, particularly in children under 5 years old. The incidence rate per 100 000 individuals under 15 years old varies geographically, with rates of 38.4 in Finland, 7.6 in Brazil and 0.5 in Korea, for example[2].

In DM1 patients, the risk factors for developing cardiovascular disease begin in childhood and can persist throughout adulthood, with the early development of atherosclerosis lesions and accelerated progression of cardiovascular diseases[3]. Studies showed early onset of severe atherosclerosis in children with T1DM compared to healthy children[4,5], due to the damage caused by high blood glucose to the heart and blood vessels[6]. Van Vliet et al.[7], in a cohort of children and adolescents with type 1 diabetes, elevated triglyceride levels were found in 17.3%, high LDL-cholesterol in 28.6%, low HDL-cholesterol in 21.2% and hypertension in 13 1% of the sample. In the same study, 38.5% of the patients were overweight, demonstrating that the prevalence of overweight and obesity in children and adolescents with type 1 diabetes has also been increasing just like in the general population.

Identifying patients at high cardiovascular risk is essential for adopting preventive measures[8]. Factors associated with dyslipidemia in patients with DM1 are sex, glycemic control and age[7,9-12]. Intensive glycemic control dramatically reduces the chance of dislipidemia[13-15]. Females have an independent risk factor for poor glycemic control and therefore for the DM1-related complications such as obesity, vascular complications and dislipidemia[16-20].

According to the American Diabetes Association (ADA), individuals with diabetes should receive appropriate nutritional therapy in order to achieve the goals of the treatment[21]. The Carbohydrate Count Method is a meal planning technique that focuses on the carbohydrates, allowing flexibility in the food choice[22,23]. Despite being used since 1935 in Europe and since 1997 in Brazil, not a single study has investigated the effects of the prescribed dietary planning type and the occurrence of dyslipidemia.

Due to the high prevalence of dyslipidemia in pediatric patients with type 1 diabetes, the aim of this study was to describe the lipid profile and associated factors in children and adolescents with T1DM treated at a pediatric clinic of a university hospital in Rio de Janeiro.

## MATERIALS AND METHODS

This is a cross-sectional study involving medical records of children and adolescents attending a Pediatric University Hospital in the city of Rio de Janeiro. The clinic is a reference center for the treatment of children and adolescents with diabetes in the city of Rio de Janeiro and is composed of a multidisciplinary team of pediatric endocrinologists, nutritionists, nurses and psychologists. Upon admission to the service, patients participate of an integrated medical appointment with a physician and a nutritionist. They should also take part of a monthly educational meeting with the whole healthcare team. All the patients registered at the clinic until November 2011, excluding those who used medications with side-effects on weight gain and those with genetic syndromes, celiac disease or other chronic diseases were included in the study.

The dependent variables were: total cholesterol (desirable <150 mg/dL, borderline between 150-169 mg/dL; increased ≥ 170 mg/dL); HDL (desirable[3] 45 mg/dL; inadequate <45 mg / dL); LDL (desirable <100 mg/dL, borderline between 100-129 mg/dL; increased ≥ 130 mg/dL); and triglycerides (desirable <100 mg/dL; borderline 100-129 mg/dL and increased ≥ 130 mg/dL)[24]. The independent variables were gender; age (years old); disease duration (years); nutritional status (Thinness, if BMI <-2 EZ; Normal, if BMI between -2 and 1 EZ; Overweight, if BMI between 1 and 2, and Obesity, if BMI > +2EZ)[25], glycated hemoglobin (HbA1c)[26], type of meal plan prescribed (traditional method or carbohydrate count method).

Descriptive statistical procedures were performed and bivariate logistic regression was used to examine the isolated effect of independent variables on the lipid profile. In the regression models, the three categories of total cholesterol, LDL and triglyceride (desirable, borderline and increased) were

grouped into two categories (adequate for "desirable" and inadequate for "borderline" or "increased"). The variables with p value ≤ 0.20 were included in multivariate logistic regression. Results are presented as odds ratios (OR) and confidence interval of 95%. All analyzes were performed using the Statistical Package for Social Sciences (SPSS) version 19.

The study was designed respecting the ethical guidelines and was approved by the Ethics in Research Committee, under number 59/11 protocol.

## RESULTS

There were 195 children and adolescents in the study, 44.1% (n = 86) were females and 55.9% (n = 109) were males. The average age was 11.01 (± 3.78) years old, the age at diagnosis of DM1 was 5.54 (± 2.8) years old, and the average length of illness was 5.59 (± 3.37) years. The average insulin dose was 1.04 (± 0.48) units / kg of ideal body weight, the average weight was 44.73 (± 16.89) kg and the average height was 1.47 (± 0, 19) meters. The dietary plan based on carbohydrate counting was followed by 44.7% of the sample (n = 85) and the traditional method by 55.3% (n = 105). Approximately 39.2% (n = 69) showed poor HbA1c.

It was observed that 36.7% of the sample were overweight (overweight and obesity). Regarding the changes in lipid profile, 42.8% of the sample had elevated total cholesterol, 15.8% had inappropriate HDL, 7,9% presented increased LDL, and 12.5% increased triglyceride (Table 1).

The logistic regression models adjusted values for total cholesterol, HLD, LDL and triglyceride are shown in Tables 2. Male children have 2.21 times (95% CI: 1.16 - 4.20) the chance of presenting high total cholesterol levels compared with female. Regarding LDL, boys had a chance 54% lower (OR 0.46, 95% CI: 0.23-0.92) to present high levels of LDL than girls. None of the variables studied was associated significantly with HDL results. Each one-year increase in the patient's age rises 1.53 (95% CI: 1.23 -1.90) times the chance of hypertriglyceridemia; and those with high levels of glycated hemoglobin raised in 4.89 the chances for hypertriglyceridemia compared with normal glycated hemoglobin (95% CI: 1.45 - 16.52). The variables BMI, type of diet and disease duration were not associated with any changes in the lipid profile.

## DISCUSSION

In the present study, the high frequency of dyslipidemia is consistent with that described in the literature. The frequency of high LDL (> 100 mg/dL) in other studies ranges from 20% to 50%[27-28]. A study of 500 Polish patients with 4-18 years old presenting T1DM, conducted in 2010, demonstrated a prevalence of high total cholesterol in 43.2%, low HDL levels in 6.4% and high triglycerides in 6.2% of the participants[28].

**Table 1.** Nutritional status and lipid profile in children and adolescents with Type 1 Diabetes Mellitus attended in a public health service in Rio de Janeiro / RJ, 2012 (n = 195).

| Lipid profile and nutritional status | n (%) |
|---|---|
| **Nutritional Status** | |
| Underweight | 7 (4.1) |
| Normal | 100 (59.2) |
| Overweight | 59 (34.9) |
| Obesity | 3 (1.8) |
| **Total cholesterol** | |
| Desirable (< 150 mg/dL) | 55 (33.1) |
| Borderline (150 – 169 mg/dL) | 40 (24.1) |
| Increased (≥ 170 mg/dL) | 71 (42.8) |
| **HDL cholesterol** | |
| Adequate (≥ 45 mg/dL) | 139 (84.2) |
| Inadequate (< 45 mg/dL) | 26 (15.8) |
| **LDL cholesterol** | |
| Desirable (< 100 mg/dL) | 118 (71.5) |
| Borderline (100 – 129 mg/dL) | 34 (20.6) |
| Increased (≥ 130 mg/dL) | 13 (7.9) |
| **Triglycerides** | |
| Desirable (< 100 mg/dL) | 129 (80.6) |
| Borderline (100 – 129 mg/dL) | 11 (6.9) |
| Increased (≥ 130 mg/dL) | 20 (12.5) |

The prevalence of overweight found in this study is consistent with data from national and international studies. The U.S. SEARCH study, with 3953 young people with T1DM, showed a 34.6% prevalence of overweight in this group (22.1% overweight and 12.6% obesity) and 33% of overweight in the group control (without diabetes)[27]. In Brazil, Marques et al.[30] and Liberatore et al.[30] found a prevalence of overweight among children and adolescents with T1DM of 14.1% and 16%, respectively. The Household Budget Survey (HBS, 2009) found that 33.5% of children aged 5-10 years old were overweight, while the prevalence among adolescents was 21.5%[31]. Thus, it is observed that children and adolescents with T1DM are following the epidemiological profile of overweight shown by children and adolescents without diabetes.

**Table 2.** Unadjusted and adjusted odds ratio for total cholesterol, HDL-cholesterol, LDL-cholesterol and triglyceride of children and adolescents with Type 1 Diabetes Mellitus treated at a Pediatric University Hospital - Rio de Janeiro / RJ, 2012 (n = 195).

| Variables | Unadjusted model | | Adjusted model | |
|---|---|---|---|---|
| | OR | IC 95% | OR | IC 95% |
| **Model for inadequate total cholesterol** | | | | |
| BMI (kg/m$^2$) | 0.83 | 0.42 – 1.63 | 1.06 | 0.98 - 1.15 |
| Age (years) | 1.06 | 0.97 - 1.16 | - | - |
| Duration of disease (years) | 1.06 | 0.96 - 1.17 | - | - |
| High HbA1c [a] | 1.43 | 0.72 - 2.83 | - | - |
| Carbs Count Method [b] | 1.11 | 0.59 - 2.07 | - | - |
| Male [c] | 0.41 | 0.22 - 0.78 | **2.21** | 1.16 - 4.20 |
| **Model for inadequate HDL** | | | | |
| BMI (kg/m$^2$) | 1.04 | 0.95 - 1.15 | - | - |
| Age (years) | 1.13 | 1.00 - 1.28 | 1.04 | 0.87 - 1.24 |
| Duration of disease (years) | 1.15 | 1.01 - 1.30 | 1.15 | 0.95 - 1.39 |
| High HbA1c [a] | 1.94 | 0.69 - 5.50 | 1.84 | 0.61 - 5.56 |
| Carbs Count Method [b] | 1.75 | 0.73 - 4.21 | 0.54 | 0.21 - 1.41 |
| Male [c] | 1.29 | 0.55 - 3.04 | - | - |
| **Model for inadequate LDL** | | | | |
| BMI (kg/m$^2$) | 1.04 | 0.96 - 1.13 | - | - |
| Age (years) | 1.08 | 0.98 - 1.19 | 1.08 | 0.98 - 1.19 |
| Duration of disease (years) | 1.03 | 0.93 - 1.14 | - | - |
| High HbA1c [a] | 1.50 | 0.69 - 3.26 | - | - |
| Carbs Count Method [b] | 1.23 | 0.62 - 2.42 | - | - |
| Male [c] | 0.47 | 0.24 - 0.94 | 0.46 | 0.23 - 0.92 |
| **Model for inadequate triglyceride** | | | | |
| BMI (kg/m$^2$) | 1.12 | 1.03 - 1.23 | 0.95 | 0.83 - 1.08 |
| Age (years) | 1.42 | 1.22 - 1.66 | **1.53** | 1.23 - 1.90 |
| Duration of disease (years) | 1.21 | 1.07 - 1.37 | 0.99 | 0.83 - 1.18 |
| High HbA1c [a] | 3.38 | 1.11 - 10.26 | **4.89** | 1.45 - 16.52 |
| Carbs Count Method [b] | 0.62 | 0.27 - 1.39 | - | - |
| Male [c] | 0.59 | 0.27 - 1.31 | 0.46 | 0.17 - 1.22 |

Notes: Reference categories: Normal HbA1C [a], Tradidional diet [b] and Female [c].

It was observed in the sample that each one-year increase in the patient's age means an increase of 1.53 times in chance of presenting hypertriglyceridemia. This finding is consistent with Steigleder-Schweiger[11], who found levels of triglycerides increasing with age[11]. The variable duration of the disease was not associated with changes in the lipid profile. However, Jose et al.[32] was able to associate disease duration and insulin doses with worse control of T1DM according to the level of HbA1c.

In this sample, inadequate glycemic control was positively associated with total cholesterol, triglycerides and inadequate HDL. The relationship between glycemic control in patients with type 1 diabetes and dyslipidemia has been reported in some studies[28]. A possible explanation for this relation between blood glucose and cardiovascular disease mortality is associated with some mechanisms such as nonenzymatic glycation and oxidation of plasma arterial wall structural proteins, formation of advanced glycation end products, development of hypertriglyceridemia and hyperglycemia effect on aggregation of platelets, hemocoagulation and fibrinolysis[15]. This relationship could be explained because less active individuals are more likely to smoke, to present obesity, high levels of blood pressure, triglycerides, insulin and lower levels of HDL[24]. On the other hand, those who practice more physical activities have better control of glycemic levels (due to lower resistance to insulin action) and higher HDL levels.

Nutritional therapy is essential for the treatment of T1DM, contributing to glycemic control and providing the necessary nutrients for growth and adequate development[34]. Accordingly, the Carbs Count Method is the recommended dietary planning method in the Diabetes Control and Complications Trial[35]. A North American study with 35 young patients between 8 - 21 years old with type 1 diabetes showed that a program with a more flexible control of insulin and diet is associated, according to the parents and children, to a higher frequency of non-healthy meals, such as hypercaloric snacks with low content of fibers and micronutrientes[33]. The excessive consumption of these foods can lead to an accelerated weight gain and also to an increase in serum triglycerides and LDL. However, an important finding in this study was the lack of association between the type of prescribed dietary planning and dyslipidemia, which supports the use of this method, as a flexible dietary strategy. Nevertheless, specialized services should promote the conscious use of this method for the young patients with T1DM. In this study, no detailed dietary assessment was carried out based on dietary inquiries to quantify food consumption. However, the data found and the literature analysis lead to a reflection on the role of dietary intake in the frequency of dyslipidemia.

The limitations of the study were the absence of a control group, anthropometric measures such as waist circumference, measures of body composition and physical activity.

## CONCLUSION

It was found a high prevalence of dyslipidemia in children and adolescents with T1DM, glycemic control is an important variable in determining dyslipidemia and the method of carbohydrate counting was not associated with this problem. It is important to discuss strategies for promoting glycemic control in patients with T1DM, with a focus on lifestyle healthy eating habits and physical activity.

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