Cystic Fibrosis

Dyslipidemia in Brazilian Children

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BACKGROUND

Cystic fibrosis (CF) is an inherited disease of the secretory glands. The CF is an autosomal recessive genetic disorder that affects most critically the lungs, and also the pancreas, liver and intestine.[1] It is characterized by abnormal transport of chloride and sodium across an epithelium, leading to thick, viscous secretions.[2]

The CF gene codes for the CFTR (cystic fibrosis transmembrane regulator) protein, which is 1,480 amino acids. The most prevalent mutation of CFTR is the deletion of a single phenylalanine residue at amino acid 508 (ΔF508). Cystic fibrosis occurs most frequently in Caucasians of northern European descent, in whom the CF gene is most common — although people of other heritages can have the disease, too.[1,2,3]

The life expectancy of these patients are increasing and new complications have been observed, among them are the repercussions on the endocrine system, such as changes in carbohydrate metabolism, lipid metabolism, bone metabolism, pubertal development, impaired growth and disease thyroid.

OBJECTIVES AND HYPOTHESIS

Cystic fibrosis is associated with abnormal lipid metabolism and this abnormality is commonly characterized by low cholesterol and hypertriglyceridemia. The increase in life expectancy of cystic fibrosis patients has been enhancing the interest to prevent the risk factors for cardiovascular diseases like dyslipidemias[5,6,7]. Hyperlipidemia is common in the general population and is associated with significant morbidity and mortality.[5,8,9]

The aim of this study is to determine whether concentrations of cholesterol and triacylglycerol are related to nutritional status and fasting glucose in pediatric patients with cystic fibrosis.

METHOD

This is a cross sectional study by record review of patients with cystic Fibrosis treated in the pediatric pulmonology department at Hospital da Criança de Brasília. Sixty four patients were selected for our study and 52 patients had information on lipid profile for the last 6 months. Patients without such medical records were excluded from the study. Fasting lipid profiles and fasting glucose were measured in 52 pediatric patients with cystic fibrosis (10,5 ± 5,0y - 23F/29M). Data were analyzed with the use of Sigma Stat 3.5 and are presented as means ± SDs.

RESULTS

Twenty patients (38,4%) presented hypertriglyceridemia (143,437,8mg/dL), and 9 patients (17,3%) hypercholesterolemia (16215mg/dL). In most cases, hypertriglyceridemia was isolated; only 3 subjects had elevation of both cholesterol and hypertriglyceridemia. Twenty-eight patients (53,8%) had low HDL-cholesterol (34,86,5mg/dL).

Table 1 – Results of CF patients of Hospital da Criança de Brasília

	CF population (23F/29M)
Age (y)	10,5 ±5,0
Triacylglycerol (mg/dL)	20 (38,4%) 143,4 ±37,8mg/dL
Cholesterol (mg/dL)	9 (17,3%) 162 ±15mg/dL
HDL Cholesterol (mg/dL)	28 (53,8%) 34,8 ±6,5mg/dL

Fourty patients (76,9%) were healthy weight (normal range), six patients were overweigth (11,5%), four (7,6%) underweight and one was obesity and another severe underweight (table 2).

In this study, four patients (7,6%) presented altered carbohydrate metabolism: altered oral glucose tolerance test (OGTT) and elevated A1C test measure.

Table 2 – Results of body mass index in CF patients of Hospital da Criança de Brasília

BMI (Zescore) WHO	CF population (23F/29M)
Underweight (⩾ z-3 e < z -2)	-0,99 ±2,8
Healthy weight (normal range) (⩾ z-2 e < z +1)	+0,44 ±0,77
Overweight (⩾ z +1 e <z +2)	+1,45 ±0,28

Lipid concentrations were not related to body mass index, gender or age or fasting glucose (table 3).

Table 3 – Correlation between lipid profile and fasting glucose and the Z escore of BMI

CF population (n=52)	Zescore BMI
Cholesterol (mg/dL)	0,143 (p=0,316)
HDL Cholesterol (mg/dL)	-0,537 (p<0,001)
Triglycerides (mg/dL)	0,252 (p=0,0739)
Fasting glucose (mg/dL)	0,0493 (p=0,740)

Table 4 – Correlation between lipid profile and gender

CF population (n=52)	Total Cholesterol (TC)	Triglycerides (TG)
Female (n=23)	128,00 ± 24,03	90,27 ± 55,66
Male (n=29)	120,35 ± 24,13	95,86 ± 44,48
	1,124 (p=0,266)	-0,399 (p=0,692)

These results have shown a group with higher triacylglycerol, lower cholesterol and lower HDL-cholesterol concentrations than the general Brazilian pediatric population. There is a study of lipid profile among schoolchildren in Brazil that corroborates these results, which is shown in table 3.

Table 5 – Comparison between CF group and Pediatrics Brazilian average[12]

	Cholesterol (mg/dL)	HDL Cholesterol (mg/dL)	Triglycerides (mg/dL)
CF Group	162±15	34,8±6,5	143,4±37,8
Mean for Pediatrics Brazilian population[12]	160±30	49±12	79±39

It is speculated that hypertriglyceridemia in CF may be related to inflammation. CF patients experience chronic inflammation exacerbated by frequent bouts of acute infection.[5] Pro-inflammatory cytokines such as tumor necrosis factor a (TNF-a) are known to be mediators of hyperlipidemia in infection and in severe stress because they both inhibit lipoprotein lipase activity (thereby decreasing triacylglycerol clearance) and stimulate hepatic lipogenesis.

Table 6 – Lipid profile references in population under 20 years old - V Brazilian Guideline for Dyslipidemia and Prevention of Atherosclerosis of BSC - 2013.[16]

	Desirable (mg/dL)	Borderline (mg/dL)	High (mg/dL)
TC	< 150	150-169	⩾ 170
LDL-C	< 100	100-129	⩾ 130
HDL-C	⩾ 45		
TG	< 100	100-129	⩾ 130

*BSC: Brazilian Society of Cardiology; TC: total cholesterol; LDL: low -density lipoprotein; HDL: high -density lipoprotein; e TG: triglycerides.

Fasting hypertriglyceridemia can occur in individuals who chronically consume a high-carbohydrate, low-fat diet.[15]

CONCLUSION

Isolated hypertriglyceridemia appears to be common in cystic fibrosis, whereas cholesterol concentrations are generally low. Abnormal lipid metabolism is associated with a high risk of cardiovascular disease in the general population, like elevation in cholesterol and triacylclycerol and low HDL-cholesterol, these findings arouse an importance to understand the abnormalities in lipid metabolism in this special group of children with cystic fibrosis in order to prevent the risk factors of cardiovascular diseases and to improve their survival.

We speculate that the hypertriglyceridemia was related to chronic, low-grade inflammation. Alternatively, dietary fat malabsorption, together with enhanced glucose absorption from the gut, may lead to hypertriglyceridemia as is seen in individuals who consume high-carbohydrate, low-fat diets. Dietary absorption and lipid turnover studies will be needed to further explore these hypotheses.

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