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Research Article

Hepatic Steatosis in a Population of Overweight and Obese Children and Adolescents

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Abstract

Objective: To identify the presence of fatty liver in a group of overweight and obese children and adolescents.

Methods: An exploratory-descriptive cross-sectional study of overweight and obese children and adolescents with no history of alcoholism, infectious or hereditary liver diseases, or use of any medications who were treated in a pediatric outpatient clinic from March 2017 to October 2018. The following variables were analyzed: sex, age, weight, height, waist circumference, blood pressure; lipid profile, alanine aminotransferase, aspartate aminotransferase, and fasting blood glucose. Fatty liver was diagnosed by Doppler ultrasound.

Results: The sample consisted of 55 participants aged 4 to 18 years. Of these, 33 (60%) were male and 22 (40%), female. Fatty liver was found in 26 (47.2%) patients: five (19.3%) overweight, 21 (80.7%) obese; 12 (46.1%) female, 14 (53.8%) male. Total cholesterol was elevated in eight (30.8%) patients, LDL-c in two (7.7%), triglycerides in 11 (42.3%), and fasting blood glucose in five (19.2%). Of 26 patients with a diagnosis of fatty liver, 12 (46.2%) had HDL-c concentrations below recommended targets, and 11 (42.3%) had metabolic syndrome. Seventeen (65.3%) patients with fatty liver had increased waist circumference ($p < 0.001$).

Conclusion: There was an association between total cholesterol, waist circumference, and fatty liver, suggesting that waist circumference may be used as a screening tool to predict fatty liver.

Keywords: *Fatty Liver; Obesity; Overweight; Child; Waist Circumference*

Introduction

Nonalcoholic fatty liver disease (NAFLD) is currently a leading cause of chronic disease in children [1], affecting 10 to 20% of the pediatric population [2,3]. NAFLD is defined as the infiltration of liver fat into more than 5% of hepatocytes, detected by liver biopsy, in the absence of excessive alcohol intake, use of medications and drugs, or hereditary diseases [1-3]. The spectrum of liver diseases ranges from simple fat accumulation in the liver (steatosis) to varying degrees of necrotic inflammation, fibrosis (steatohepatitis), and cirrhosis [1-4]. NAFLD is considered a hepatic manifestation of metabolic syndrome (central obesity, hypertension, dyslipidemia, hyperglycemia, and insulin resistance) [1-3]. Obesity is the main risk factor for pediatric NAFLD, with a prevalence of 50 to 80% in overweight and obese children compared with normal-weight children (2 to 7%) [1].

The gold standard for NAFLD diagnosis is liver biopsy, which is able to differentiate between nonalcoholic steatohepatitis (NASH) and simple steatosis [1,3,4]. Because liver biopsy is an invasive procedure, it is reserved for cases with findings of NASH. Abdominal ultrasound (US) is a low-cost, noninvasive method that has been the imaging modality of choice for the diagnosis and screening of NAFLD in children [4].

NAFLD has become a public health problem due to the worldwide increase in obesity, and it is currently an indication for liver transplantation in children [1,5]. Early diagnosis and prompt intervention reduce the likelihood of developing liver fibrosis and cirrhosis. The pediatric NAFLD fibrosis index can be obtained from 3 simple parameters: age, waist circumference, and triglyceride levels [1,2].

Aim of the Study

The present study aimed to identify NAFLD in overweight and obese children and adolescents.

Methods

This was an exploratory-descriptive study with a cross-sectional design. The sample consisted of 55 overweight or obese participants, aged 4 to 18 years, with no history of alcoholism, infectious or hereditary liver diseases, or use of any medications who were treated in the general pediatrics and pediatric gastroenterology outpatient clinic at Hospital Universitário do Oeste do Paraná, in Cascavel, Brazil, from March 2017 to October 2018. Written informed consent was obtained from the parents or legal guardians for enrollment in the study, while informed assent was obtained from children/adolescents aged 12 years or over.

Children and adolescents were included in the study if they had age- and sex-specific body mass index (BMI) ≥ z-score +1 ≤ z-score +2 for overweight and ≥ z-score +2 for obesity, according to the 2006 World Health Organization (WHO) Child Growth Standards [6]. Exclusion criteria were presence of any infectious liver disease or of other confirmed etiology unrelated to NAFLD, drug therapy, and alcohol consumption.

The following variables were analyzed: sex, age, weight, height, waist circumference, and blood pressure. Laboratory variables were as follows: serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), total cholesterol (TC), low-density lipoprotein (LDL-c), high-density lipoprotein (HDL-c), triglycerides (TG), and fasting blood glucose. Abdominal US was performed for the diagnosis of NAFLD, which was classified as mild, moderate, or severe. All US examinations were performed by the same sonographer.

Dyslipidemia was classified based on the first Brazilian Guideline for Preventing Atherosclerosis in Childhood and Adolescence [7], which establishes the following cutoff points for desirable values: TC: 150 mg/dL, LDL-c: < 100 mg/dL, HDL-c: ≥ 45 mg/dL, and TG: < 100 mg/dL; for borderline values: TC: 150 - 169 mg/dL, LDL-c: 100 - 129 mg/dL, and TG: 100 - 129 mg/dL; and for altered values: TC: > 170 mg/dL, LDL-c: > 130 mg/dL, HDL-c: < 45 mg/dL, and TG: > 130 mg/dL. Blood glucose was considered elevated if ≥ 99 mg/dL [7].

Currently, there are no diagnostic criteria for metabolic syndrome in children aged 6 to 10 years. Therefore, in the present study, the International Diabetes Federation (IDF) criteria [8,9] were used to define metabolic syndrome in patients younger than 10 years: TG ≥ 150 mg/dL, blood glucose ≥ 99 mg/dL, HDL-c ≤ 40 mg/dL, and blood pressure > p95 for age and sex. Adult criteria were used for patients older than 16 years.

Body weight was measured using an electronic scale (Líder®, model P-300C, series 31403, year of manufacture 2014, Brazil) with the participant wearing light clothing. Height was measured using a wall-mounted stadiometer (Tonelli Equipamentos Médicos Ltda., model E150 A, year of manufacture 2014, Brazil) with the participant wearing no shoes. BMI was calculated using the Quetelet index (weight/height^2). Height and BMI were calculated based on the growth charts of the 2006 WHO Child Growth Standards [6].

With the participant standing erect, waist circumference was measured using a non-stretchable tape measure at the midpoint between the last rib and the iliac crest and was recorded in centimeters. Waist circumference was evaluated according to age- and sex-specific cutoff points suggested by Freedman., *et al* [10].

Blood pressure was measured on the right arm after a 20-min rest, with the forearm resting at the level of the precordium, using a Welch-Allyn® mercury sphygmomanometer with an appropriate cuff size for children. The classification of systolic and diastolic hypertension followed the parameters of the VII Brazilian Guidelines on Hypertension [11].

Data analysis was performed using SPSS, version 20 (IBM SPSS Statistics, Armonk, NY). Qualitative variables were expressed as frequencies and percentages. Fisher's exact test was used to compare dichotomous qualitative variables. A p-value < 0.05 was considered statistically significant.

This study was approved by the Research Ethics Committee of Universidade Estadual do Oeste do Paraná, Cascavel, Brazil (approval number 1.545.286/2016).

Results

The sample consisted of 55 participants aged 4 to 18 years (mean: 10.6 years), of whom 33 (60.0%) were male and 22 (40.0%) were female. Thirty-one (56.4%) participants were younger than 12 years of age, and 24 (43.6%) were 12 years or older.

Analysis of biochemical parameters showed that TC was elevated in 10 (18.1%) patients; of these, 7 (12.5%) were younger than 12 years. Regarding sex, TC was elevated in 5 female (22.7%) and 5 male (15.2%) patients. LDL-c was elevated in 2 (3.6%) girls aged < 12 years. Low HDL-c levels were found in 13 (23.6%) patients aged < 12 years and in 9 (16.3%) aged ≥ 12 years; of these, 10 (18.1%) were female and 12 (21.8%) were male. TG levels were elevated in 19 (34.5%) patients aged < 12 years and in 8 (14.5%) aged ≥ 12 years; of these, 13 (23.6%) were female and 14 (25.4%) were male. Altered blood glucose levels were observed in 6 (10.9%) patients aged < 12 years and in 2 (3.6%) aged ≥ 12 years, but the values were below the level for the diagnosis of diabetes. Hyperglycemia was more frequent in males, accounting for 6 (10.9%) cases (Table 1).

Total cholesterol	**Age**				**P-value**
	< 12 years		**≥ 12 years**		
	n	**%**	**n**	**%**	
Desirable/borderline	24	77.4%	21	87.5%	
Elevated	7	22.6%	3	12.5%	0.119
Total	31	100.0%	24	100.0%	
LDL	**Age**				
	< 12 years		**≥ 12 years**		
	n	**%**	**n**	**%**	
Desirable/borderline	29	93.5%	24	100.0%	
Elevated	2	6.5%	0	0.0%	0.499
Total	31	100.0%	24	100.0%	
HDL	**Age**				
	< 12 years		**≥ 12 years**		
	n	**%**	**n**	**%**	

Desirable	18	58.1%	15	62.5%	
Low	13	41.9%	9	37.5%	0.787
Total	31	100.0%	24	100.0%	
Triglycerides	**Age**				
	< 12 years		**≥ 12 years**		
	n	**%**	**n**	**%**	
Desirable/borderline	12	38.7%	16	66.7%	
Elevated	19	61.3%	8	33.3%	0.058
Total	31	100.0%	24	100.0%	
Blood glucose	**Age**				
	< 12 years		**≥ 12 years**		
	n	**%**	**n**	**%**	
< 99 mg/dL	25	80.6%	22	91.7%	
≥ 99 mg/dL	6	19.4%	2	8.3%	0.443
Total	31	100.0%	24	100.0%	
Total cholesterol	**Sex**				
	Female		**Male**		
	n	**%**	**n**	**%**	
Desirable/borderline	17	77.3%	28	84.8%	
Elevated	5	22.7%	5	15.2%	0.498
Total	22	100.0%	33	100.0%	
LDL*	**Waist circumference**				
	Adequate		**Increased**		
	n	**%**	**n**	**%**	
Desirable/borderline	32	100.0%	21	91.3%	
Elevated	0	0.0%	2	8.7%	0.156
Total	32	100.0%	23	100.0%	
HDL*	**Sex**				
	Female		**Male**		
	n	**%**	**n**	**%**	
Desirable	12	54.5%	21	63.6%	
Low	10	45.5%	12	36.4%	0.580
Total	22	100.0%	33	100.0%	
Triglycerides	**Sex**				
	Female		**Male**		
	n	**%**	**n**	**%**	0.277
Desirable/borderline	9	40.9%	19	57.6%	
Elevated	13	59.1%	14	42.4%	
Total	22	100.0%	33	100.0%	

Blood glucose	Sex				
	Female		Male		
	n	%	n	%	
< 99 mg/dL	20	90.9%	27	81.8%	
≥ 99 mg/dL	2	9.1%	6	18.2%	0.454
Total	22	100.0%	33	100.0%	
Total cholesterol	**Waist circumference**				
	Adequate		**Increased**		
	n	**%**	**n**	**%**	
Desirable/borderline	25	78.1%	20	87.0%	
Elevated	7	21.9%	3	13.0%	0.170
Total	32	100.0%	23	100.0%	
LDL*	**Waist circumference**				
	Adequate		**Increased**		
	n	**%**	**n**	**%**	
Desirable/borderline	32	100.0%	21	91.3%	
Elevated	0	0.0%	2	8.7%	0.170
Total	32	100.0%	23	100.0%	
HDL*	**Waist circumference**				
	Adequate		**Increased**		
	n	**%**	**n**	**%**	
Desirable	21	65.6%	12	52.2%	
Low	11	34.4%	11	47.8%	0.405
Total	32	100.0%	23	100.0%	
Triglycerides	**Waist circumference**				
	Adequate		**Increased**		
	n	**%**	**n**	**%**	
Desirable/borderline	17	53.1%	11	47.8%	
Elevated	15	46.9%	12	52.2%	0.787
Total	32	100.0%	23	100.0%	
Blood glucose	**Waist circumference**				
	Adequate		**Increased**		
	n	**%**	**n**	**%**	0,446
< 99 mg/dL	26	81.3%	21	91.3%	
≥ 99 mg/dL	6	18.8%	2	8.7%	
Total	32	100.0%	23	100.0%	

Table 1: *Correlation between age, sex, waist circumference, and laboratory findings.*

**HDL: High-Density Lipoprotein; LDL: Low-Density Lipoprotein.*

NAFLD was found in 26 (47.2%) patients. Of these, 5 (19.3%) were overweight and 21 (80.7%) were obese; 12 (46.1%) were female and 14 (53.8%) were male.

Regarding biochemical markers in patients with NAFLD, TC was elevated in 8 (30.8%) and LDL-c was elevated in 2 (7.7%), but the values were below 160 mg/dL. TG levels were elevated in 11 (42.3%) patients, and blood glucose in 5 (19.2%). Low HDL-c levels were found in 12 (46.2%) patients with a diagnosis of NAFLD, and metabolic syndrome was confirmed in 11 (42.3%). As for liver biochemical markers, ALT levels were elevated in 5 (19.2%) patients with NAFLD, and in 8 (17.02%) obese participants. Seventeen (65.3%) patients with a diagnosis of NAFLD had increased waist circumference. TC and waist circumference were associated with the presence of NAFLD (Table 2).

Total cholesterol	**Fatty liver**				**P-value**
	Normal		**Mild or moderate**		
	n	**%**	**n**	**%**	
Desirable/borderline	27	93.1%	18	69.2%	0.035
Elevated	2	6.9%	8	30.8%	
Total	29	100.0%	26	100.0%	
***LDL**	**Fatty liver**				
	Normal		**Mild or moderate**		
	n	**%**	**n**	**%**	
Desirable/borderline	29	100.0%	24	92.3%	0.219
Elevated	0	0.0%	2	7.7%	
Total	29	100.0%	26	100.0%	
***HDL**	**Fatty liver**				
	Normal		**Mild or moderate**		
	n	**%**	**n**	**%**	
Desirable	19	65.5%	14	53.8%	0.420
Low	10	34.5%	12	46.2%	
Total	29	100.0%	26	100.0%	
Triglycerides	**Fatty liver**				
	Normal		**Mild or moderate**		
	n	**%**	**n**	**%**	
Desirable/borderline	13	44.8%	15	57.7%	0.422
Elevated	16	55.2%	11	42.3%	
Total	29	100.0%	26	100.0%	
Blood glucose	**Fatty liver**				
	Normal		**Mild or moderate**		
	n	**%**	**n**	**%**	
< 99 mg/dL	26	89.7%	21	80.8%	0.455
≥ 99 mg/dL	3	10.3%	5	19.2%	
Total	29	100.0%	26	100.0%	

Fatty liver	Metabolic syndrome				
	Yes		No		
	n	%	n	%	
Normal	11	50.0%	18	54.5%	0.788
Mild or Moderate	11	50.0%	15	45.5%	
Total	22	100.0%	33	100.0%	
Total cholesterol	**BMI**				
	Overweight		**Obesity**		
	n	**%**	**n**	**%**	
Desirable/borderline	6	75.0%	39	83.0%	0.627
Elevated	2	25.0%	8	17.0%	
Total	8	100.0%	47	100.0%	
***LDL**	**BMI**				
	Overweight		**Obesity**		
	n	**%**	**n**	**%**	
Desirable/borderline	8	100.0%	45	95.7%	1.00
Elevated	0	0.0%	2	4.3%	
Total	8	100.0%	47	100.0%	
***HDL**	**BMI**				
	Overweight		**Obesity**		
	n	**%**	**n**	**%**	
Desirable	6	75.0%	27	57.4%	0.454
Low	2	25.0%	20	42.6%	
Total	8	100.0%	47	100.0%	
Triglycerides	**BMI**				
	Overweight		**Obesity**		
	n	**%**	**n**	**%**	
Desirable/borderline	6	75.0%	22	46.8%	0.252
Elevated	2	25.0%	25	53.2%	
Total	8	100.0%	47	100.0%	
Blood glucose	**BMI**				
	Overweight		**Obesity**		
	n	**%**	**n**	**%**	
< 99 mg/dL	6	75.0%	41	87.2%	0.328
≥ 99 mg/dL	2	25.0%	6	12.8%	
Total	8	100.0%	47	100.0%	
***ALT**	**Fatty liver**				
	Normal		**Mild or moderate**		
	n	**%**	**n**	**%**	
Adequate	25	86.21%	21	80.77%	0.721

Increased	4	13.79%	5	19.23%	
Total	29	100.00%	26	100.00%	
***ALT**	**BMI**				
	Overweight		**Obesity**		
	n	**%**	**n**	**%**	
Adequate	7	87.50%	39	82.98%	1.00
Increased	1	12.50%	8	17.02%	
Total	8	100.00%	47	100.00%	
Fatty liver	**BMI**				
	Overweight		**Obesity**		
	n	**%**	**n**	**%**	
Normal	3	37.50%	26	55.32%	0.455
Mild or moderate	5	62.50%	21	44.68%	
Total	8	100.00%	47	100.00%	
Fatty liver	**Sex**				
	Female		**Male**		
	n	**%**	**n**	**%**	
Normal	10	45.45%	19	57.58%	0.420
Mild or moderate	12	54.55%	14	42.42%	
Total	22	100.00%	33	100.00%	
Fatty liver	**Age**				
	< 12 years		**≥ 12 years**		
	n	**%**	**n**	**%**	
Normal	19	61.29%	10	41.67%	0.180
Mild or moderate	12	38.71%	14	58.33%	
Total	31	100.00%	24	100.00%	
Fatty liver	**Waist circumference**				
	Adequate		**Increased**		
	n	**%**	**n**	**%**	
Normal	23	71.88%	6	26.09%	0.001
Mild or moderate	9	28.13%	17	73.91%	

***Table 2:** Correlation between fatty liver, laboratory findings, BMI, metabolic syndrome, age and sex.*

**ALT: Alanine Aminotransferase; BMI: Body Mass Index; HDL: High-Density Lipoprotein; LDL: Low-Density Lipoprotein.*

Discussion and Conclusion

The prevalence of NAFLD has increased alongside the growing prevalence of obesity. In children, obesity has already been recognized as a major risk factor for metabolic disorders [12]. The role of dyslipidemia in the development and progression of NAFLD remains to be established. However, in the pathophysiology of NAFLD, it is clear that there is a cascade of molecular events related to obesity and insulin resistance [13]. In the present study, prevalence of hypertriglyceridemia was higher in obese patients, a result similar to that observed in previous studies in the same age group, with elevated TC and TG levels being a risk factor for NAFLD [13-19].

NAFLD was more frequent in adolescents, occurring predominantly in overweight adolescent boys, a finding consistent with the literature [19]. NAFLD is the most common cause of chronic liver disease in children and adolescents [20] and the number of cases during childhood has increased owing to the increasing prevalence of obesity. In children with a diagnosis of NAFLD, the disease has been reported to progress more rapidly to NASH with increasing BMI, with a risk of cirrhosis in young adults [18], although this association was not found in the present study.

NAFLD has been studied in pediatrics because of the growth in the number of cases of liver diseases requiring transplantation and the increased risk of hepatocellular carcinoma. Anthropometric data, such as BMI and waist circumference, are predictors of NAFLD [22], with a correlation between larger waist circumference and greater accumulation of lipids in hepatocytes. This occurs because adipose tissue functions as an endocrine organ releasing pro-inflammatory cells and suppressing adipokines, which leads to insulin resistance and hyperinsulinemia, causing accumulation of fatty acids in adipocytes, thus resulting in central obesity with accumulation of intra-abdominal fat that predisposes to NAFLD [19,21,22]. In the present study, a positive relationship was observed between increased waist circumference and US diagnosis of NAFLD, which is consistent with previous studies [21,23,24], demonstrating that a simple measurement of waist circumference during the physical examination of children and adolescents may be an effective screening tool and an important predictor of NAFLD.

Childhood obesity is a serious public health problem, which is associated with the risk of complications in childhood and an increased risk of chronic diseases in adulthood. In this context, pediatricians should always consider the possibility of NAFLD when evaluating overweight and obese patients. It can be concluded that altered TC levels and waist circumference may be used as a screening tool for NAFLD, providing a simple and inexpensive method to screen for NAFLD.

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