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Hepatic steatosis in overweight and obese children and adolescents

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ABSTRACT:

Objective: Toidentifythepresence of non-alcoholichepatic steatosis in a group of overweight and obese children and adolescents.

Method: Descriptive, observational, and cross-sectional study, with children and adolescents from a general pediatrics outpatient clinic assisted at a university hospital, carried out from September/2021 to September/2023. Body mass index (BMI) was classified according to the World Health Organization (WHO, 2006) into overweight, percentile between 85 and 97; obesity, percentile between 97 and 99.9; and severe obesity if percentile greater than 99.9. The following variables were analyzed: sex, age, weight, height, BMI, waist circumference, and blood pressure, in addition to the following biochemical tests: total cholesterol, LDL, HDL, triglycerides, alanine aminotransferase, and fasting plasma glucose. Hepatic steatosis, assessed by ultrasound examination, was classified as mild, moderate, and severe.

Results: Hepatic steatosis was diagnosed in 21 (30.4%) subjects. A higher frequency of mild steatosis was observed, with 13 (61.9%) subjects, followed by moderate, with six (28.5%) subjects and two (9.5%) cases of severe steatosis. Of the children with hepatic steatosis 12(57.1%) were male and nine (42.8%) were female. Hepatic steatosis was detected in three (14.2%) of the overweight subjects and 18(85.7%) of the obese subjects. Arterial hypertension was identified in six (28.5%) of the participants diagnosed with steatosis. Waist circumference was increased in 21 (100%) of the participants. Elevated alanine aminotransferase occurred in five (23.8%), hypercholesterolemia in 12 (57.1%), elevated LDL in nine (42.8%), hypertriglyceridemia in 16 (76.2%), low HDL in 15 (71.4%) and fasting hyperglycemia was found in seven (33.4%) of the participants. There was relation between hepatic steatosis, age, weight, triglycerides, alanine aminotransferase, and abdominal circumference.

Conclusion:the frequency of hepatic steatosis in overweight children was high in this research, making early diagnosis of this condition important.

Key-Words: Pediatricobesity, Non-alcoholicfattyliverdisease, Ultrasonography, Alanine aminotransferase, Waist circumference.

I.INTRODUCTION

Obesity is a condition characterized by the excessive accumulation of body fat[1]. Over the last four decades, the prevalence of obesity in children aged between 5 and 19 has increased in most countries[2]. Weight gain is associated with numerous complications, including hepatic steatosis.

Non-alcoholic fatty liver disease (NAFLD) is defined as an abnormal accumulation of fat in the absence of other etiologies, affecting at least 5% of hepatocytes, associated with hepatocellular damage[3]. Diagnosis is made using liver ultrasound, although the gold standard is liver biopsy.

In this sense, due to the increasing incidence and prevalence of childhood obesity, the diagnosis of NAFLD is important to prevent the early onset of chronic diseases such as type 2 diabetes and liver cirrhosis[2].

This study aimed to assess the presence of non-alcoholic fatty liver disease in overweight children and adolescents assisted to a general pediatric outpatient clinic.

II.METHODS

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This was a descriptive, observational, cross-sectional study of children and adolescents with excess weight (overweight or obese), carried out in a general pediatrics outpatient clinic at a university hospital, from September 2021 to September 2023.

Before the research began, parents and/or guardians signed the Parental Written Informed ConsentForm for the children and adolescents, and the latter also signed the Adolescent Written Informed Assentwhen they were over 12 years old.

All children and adolescents seen during this period who had a body mass index (BMI) of overweight, obesity, or severe obesity were voluntarily included. Children were considered overweight when BMI values were between the 85th and 97th percentiles, obese when values were between the 97th and 99.9th percentiles, and severely obese when BMI values were above the 99.9th percentile (WHO, 2006). Weight was measured with the research participant wearing light clothing on a Líder® scale (model P-300C, series 31403, year of manufacture: 2014, Brazil) and height was measured on a wall anthropometer with the patients barefoot. Body mass index (BMI) was calculated using the formula: BMI = weight/height².

The other variables analyzed were: age, gender, weight, height, waist circumference, and blood pressure. The laboratory variables analyzed were: serum levels of alanine aminotransferase (ALT), total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TG), and fasting glucose.

Dyslipidemia was classified according to the Brazilian Society of Pediatrics`s Guidelines[4], which establishes the following cut-offs for desirable values: TC < 150 mg/dL, LDL < 100 mg/dL, HDL ≥ 45 mg/dL and TG < 100 mg/dL; for borderline values: TC 150-169 mg/dL, LDL100-129 mg/dL and TG 100-129 mg/dL; and altered values: TC ≥ 170 mg/dL, LDL ≥ 130 mg/dL and TG ≥ 130 mg/dL. Fasting glucose was considered altered if it was above 100 mg/dL and ALT values were considered altered if they were above 40 U/L.

The ultrasound evaluation was always carried out by the same radiologist, without prior knowledge of the clinical data and laboratory test results. The equipment used was the Aplio 300 - brand Toshiba® - model TUS-A 300, USA, 2017, for the diagnosis of hepatic steatosis, which was classified as mild, moderate, or severe. This classification uses hepatic echogenicity compared to the renal cortex as a parameters.

The waist circumference was measured using a tape measure with the patient in an orthostatic position, taking as a reference the midpoint between the last rib and the iliac crests, and measuring it in centimeters. The subjects were classified according to the proposal by Freedman et al.[5] , with an increased risk when the circumference was greater than or equal to p90.

Blood pressure was measured after the subject had been at rest for 20 minutes, with the arm resting on the right arm at the level of the precordium, using a Welch-Allyn® brand aneroid sphygmomanometer (Mexico, 2014) with a cuff suitable for the size of the child or adolescent. The categorization of systolic or diastolic hypertension followed the parameters of the VII Brazilian Hypertension Guidelines (2016)[6] .

Mean, median, minimum, and maximum values, 1st and 3rd quartiles, and standard deviation were used to describe the quantitative variables. Frequencies and percentages were used to summarize the qualitative variables. Student's t-test for independent samples was used to compare two classifications of quantitative variables. The Chi-square and Fisher's exact tests were used to assess the association between qualitative variables. The Jarque-Béra test was used to assess the normality of the results. A p-value < 0.05 indicated statistical significance.

This research was approved by the Committee Research Ethics of the Western Paraná State University under protocol number 4.899.979/2021.

III.RESULTS

In this study, 69 children and adolescents aged between 5 and 17 were assessed. There was a predominance of males, with 42 (60.8%), and 50 (72.5%) under 12 years old and 19 (27.5%) over 12 years old.

Of the subjects studied, 31(45%) were severely obese, 27(39.1%) obese and 11(15.9%) overweight. Hepatic steatosis was diagnosed in 21(30.4%) of the participants and there was a higher frequency of mild steatosis in 13(61.9%), followed by moderate steatosis in six(28.5%), with only two(9.5%) cases of severe steatosis. Of the patients with hepatic steatosis, 12(57.1%) were male and nine(42.8%) were female, of this, 12(57.1%) were under 12 years old. Hepatic steatosis was detected in seven (33.4%) of the overweight patients, six (28.5%) of the obese patients, and eight (38%) of the severely obese patients.

Table 1 shows the number (n) and percentage (%) of participants concerning being overweight.

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Table 1: Number (n) and percentage (%) of participants in relation to being overweight.

BMI*	Hepatic steatosis				TOTAL
	Yes		No		
	n	%	n	%	
Overweight	4	8.3	7	33.4	11
Obesity	21	43.7	6	28.5	27
Serious obesity	23	48	8	38	31
TOTAL	48	100%	21	100%	69

Mass Index.

Table 2 shows the correlation between hepatic steatosis and the participants' anthropometric and biochemical measurements.

Variable	HS#	n	Average	Minimum	1th quartil	Median	3bd quartil	Maximum	Standard-Deviation	p value*
Age (year)	No	48	9,09	5,00	6,71	8,88	10,77	15,50	2,80	0,021*
	Yes	21	10,88	5,50	8,75	11,33	13,07	17,00	3,16	
Height (meters)	No	48	1,39	1,06	1,25	1,40	1,52	1,70	0,16	0,016*
	Yes	21	1,50	1,22	1,32	1,54	1,64	1,84	0,19	
Weight (Kg)	No	48	50,72	22,30	33,20	47,70	61,10	131,40	20,90	0,012*
	Yes	21	70,38	28,00	45,10	63,40	97,00	142,90	30,44	
BMI	No	48	2,84	1,07	2,11	2,88	3,47	4,97	0,94	0,327
	Yes	21	3,09	1,45	2,50	3,06	3,48	5,59	0,98	
CT	No	48	158,21	90,00	139,25	155,00	176,25	223,00	29,66	0,059
	Yes	21	173,10	114,00	154,00	175,00	192,00	220,00	29,42	
HDL	No	48	44,83	13,00	37,00	46,00	53,00	72,00	12,98	0,431
	Yes	21	41,95	16,00	35,00	39,00	46,00	75,00	15,86	
LDL	No	48	94,15	39,00	78,00	91,50	108,00	144,00	25,85	0,053

Table 2: Correlation among Hepatic Steatosis (HS) and anthropometric measurements.

(*) Significance was considered when p<0.05
(#) HS: Hepatic steatosis
(§)Waist circumference

It was identified 19 (27.5%) patients with hypertension, and only six (31.5%) of them had hepatic steatosis.

Waist circumference was increased in 63 (91.3%) of the participants, and all the subjects with hepatic steatosis on ultrasound had this parameter elevated.

Elevated ALT was found in six (8.7%) of the patients, and four (66.7%) of those with steatosis had this test altered.

In this analysis, high total cholesterol was found in 31 (45%) of the participants, high LDL in 21(30.4%), triglycerides in 43(62.3%) and low HDL in 38(55%). Concerning fasting glucose, 11(16%) had this test altered.

IV.DISCUSSION

According to the World Health Organization (WHO), overweight and obesity are defined as an abnormal or excessive accumulation of body fat that poses a risk to health[7] . Data from the Brazilian Ministry of Health (MS) shows that 12.9% of Brazilian children between the ages of 5 and 9 and 7% of adolescents between the ages of 12 and 17 are obese[8] .

Hepatic steatosis is the accumulation of fat in at least 5% of hepatocytes. Non-alcoholic fatty liver disease (NAFLD) is defined as a chronic liver disease not secondary to genetic, metabolic, infectious, or drug-related causes[9] . With the increase in the incidence of childhood obesity, there has been an increase in cases of chronic hepatic steatosis.

The average age of diagnosis of NAFLD is between 11 and 13 years[10,11]. In this study, cases of hepatic steatosis were more prevalent in children under 12. Benetoloet al.[12] found similar results, showing that the prevalence of NAFLD was higher in children under 10[10]. These findings differ from the literature, which shows that the prevalence of NAFLD is higher in adolescents[13].

In this research, the presence of hepatic steatosis was related to being overweight, as in a study carried out in Turkey[14]. In another study,

Weihe and Weirauch reported that 20% of obese children already have hepatic steatosis or NAFLD[15]. In addition, Anderson et al showed in a meta-analysis that the prevalence of NAFLD increased considerably with increasing BMI category, being present in 34.2% in a systematic review of 74 studies[16].

In this study, no relationship was found between gender and NAFLD, but there was a higher percentage of boys with NAFLD on ultrasound, which corroborates the findings in the literature that NAFLD is more common in males[10,11,12].

About triglycerides, it has been reported that 20 to 80% of children with fatty liver may have associated hypertriglyceridemia[17]. An Italian cohort of 120 children aged between 3 and 18 showed NAFLD on liver biopsy, and hypertriglyceridemia was present in 63% of patients with a positive biopsy[17]. Another study carried out in Turkey showed that participants who had hepatic steatosis confirmed by ultrasound had high triglyceride levels[18], results which are similar to this study which showed a relationship between hypertriglyceridemia and the presence of steatosis on ultrasound.

According to research by Pacifico et al.[19], the concentration of transaminases is positively correlated with an increase in liver fat fraction. In a study carried out in São Paulo, Benetoloet al.[12] showed that high ALT levels were associated with hepatic steatosis, a proximity result that found in this study. In addition, an observational cohort of pediatric patients in the United States showed that the prevalence of hepatic steatosis was three times more likely in children with high ALT levels[20].

The abdominal circumference is an important method for diagnosing central adiposity and correlates directly with NAFLD regardless of BMI[21,22]. In this study, increased abdominal circumference correlated with NAFLD, since all the subjects had some degree of hepatic steatosis on ultrasound, confirming the data in the literature showing that excess abdominal fat is associated with NAFLD[23,24].

This study had some limitations: the small number of participants, which could be attributed to the short period of the study and the lack of patient attendance at ultrasound examinations. Another limitation of this study was the low sensitivity of ultrasound in detecting steatosis, despite it being an easily accessible and low-cost method.

V. CONCLUSION

This study found a high percentage of children with fatty liver. Due to the significant increase in obesity in the pediatric population in recent decades, pediatricians should always be aware of the possibility of hepatic steatosis in overweight children, especially in cases where there is an increase in abdominal circumference. In these cases, whenever possible, it is suggested to carry out laboratory investigations, measuring alanine aminotransferase and performing liver ultrasound, to diagnose NAFLD at an early stage.

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