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ORIGINAL ARTICLE

## Hepatic steatosis in overweight and obese children and adolescents

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Fatty Liver,  
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### Abstract

**Objective:** To identify the presence of hepatic steatosis in a group of overweight and obese children and adolescents. **Methods:** This descriptive, exploratory, cross-sectional study included 30 patients aged between 5 and 18 years and was conducted between January 2016 and January 2017. Overweight and obesity were defined as body mass index  $\geq$  p85 and  $\geq$  p97 for age and sex, respectively. Further, the following variables were analyzed: sex, age, weight, height, waist circumference, and blood pressure. Biochemical evaluation involved assessment of lipid profile (total cholesterol, low-density lipoprotein [LDL c], high-density lipoprotein [HDL c], and triglycerides), alanine aminotransferase (ALT) level, and fasting glycemia. Hepatic steatosis evaluated using ultrasonography was classified as normal, mild, moderate, or severe. **Results:** Hepatic steatosis was diagnosed in 53.4% of the patients; a higher frequency of mild steatosis (46.7%) was observed, followed by that of moderate steatosis (6.7%). Of those with hepatic steatosis, 56.3% were male and 43.7% were female, and 62.5% were aged 12 years or older. Hepatic steatosis was detected in 18.7% of overweight patients and 81.3% of obese patients. Arterial hypertension was observed in 10% of the patients, whereas borderline high blood pressure was observed in 60%. A total of 90% of the patients had increased abdominal circumference. Biochemical evaluation revealed elevated ALT level in 6.7% of the patients, hypercholesterolemia in 30%, elevated LDL c level in 6.7%, hypertriglyceridemia in 43.3%, low HDL c level in 46.7%, and fasting hyperglycemia in 6.7%. **Conclusion:** The frequency of hepatic steatosis was found to be elevated in overweight and obese patients. Therefore, patients with the risk factors for hepatic steatosis should be screened.

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## INTRODUCTION

Over the past three decades, the incidence of childhood obesity has considerably increased worldwide, and it has become a major public health concern<sup>1</sup>. Among its various consequences, hepatic steatosis, which is the initial stage of non-alcoholic fatty liver disease (NAFLD), is considered remarkable<sup>2</sup>. NAFLD is defined as hepatic fatty infiltration of more than 5% in hepatocytes on liver biopsy without excessive alcohol consumption or evidence of viral infection, autoimmune disease, or drug-induced liver disease<sup>3,4</sup>. Initially, hepatic fatty infiltration (hepatic steatosis) is observed, but the disease can progress to advanced fibrosis and cirrhosis<sup>5</sup>.

For the diagnosis of NAFLD, histological examination of a liver fragment is considered the gold standard method; however, it is not frequently performed in the pediatric population owing to its invasiveness<sup>5</sup>. Therefore, in this population, the diagnosis of hepatic steatosis is done using clinical and biochemical methods or ultrasonography<sup>6</sup>.

Pediatric NAFLD is a problem that remains underdiagnosed; thus, this study aimed to identify the presence of hepatic steatosis in a group of overweight and obese children and adolescents.

## MATERIALS AND METHODS

This was a descriptive, exploratory, cross-sectional study, and it included 30 overweight and obese children and adolescents aged 5–18 years who were the patients of the general pediatrics outpatient clinic of Western Paraná University Hospital from January 2016 to January 2017.

All children and adolescents observed at the clinic during this period who had body mass index (BMI)  $\geq$  p85 for age and sex (overweight) and BMI  $\geq$  p97 (obese), as defined by the World Health Organization charts (2007), were included.

The following variables were analyzed: sex, age, weight, height, waist circumference, and blood pressure. The assessed laboratory variables were serum alanine aminotransferase (ALT), total cholesterol (TC), low-density lipoprotein (LDLc), high-density lipoprotein (HDLc), triglycerides (TG), and fasting glycemia. Dyslipidemia was classified in accordance with the I Brazilian Guidelines for Prevention of Atherosclerosis in Childhood and Adolescence, which has established the following cut-off values: desirable values: TC < 150 mg/dL, LDLc < 100 mg/dL, HDLc  $\geq$  45 mg/dL, and TG < 100 mg/dL; borderline values: TC = 150–169 mg/dL, LDLc = 100–129 mg/dL, and TG = 100–129 mg/dL; and altered values: TC > 170 mg/dL, LDLc > 130 mg/dL, TG > 130 mg/dL, and HDLc < 45 mg/dL. Fasting blood glucose level was considered elevated when above 100 mg/dL.

Ultrasonographic evaluation was performed by a single radiologist who was blinded to the clinical data and results of the laboratory tests. For the diagnosis of hepatic steatosis, the Toshiba Medical Aplio 300 ultrasound device was used. When hepatic steatosis was observed, it was classified as

normal, mild, moderate, or severe. This classification uses hepatic echogenicity as a parameter, compared with the renal cortex; the echo penetration intensity of the hepatic parenchyma; diaphragmatic visibility; and the echogenicity of the hepatic vascular structures<sup>6,31,32</sup>.

Metabolic syndrome was diagnosed using the International Federation of Diabetes criteria: triglyceridemia  $\geq$  150 mg/dL, blood glucose > 100 mg/dL, HDLc  $\leq$  40 mg/dL, systolic or diastolic blood pressure  $\geq$  p90, and abdominal circumference  $\geq$  p90 for age and sex. For adolescents aged over 16 years, the criteria for adults were used, which indicate metabolic syndrome in the presence of a combination of three or more of the following conditions: central obesity (abdominal circumference > 88 cm in female and > 102 cm in male), low HDL levels (female  $\leq$  50 mg/dL and male  $\leq$  40 mg/dL), triglycerides  $\geq$  150 mg/dL, fasting glycemia  $\geq$  100 mg/dL, and high blood pressure (systolic  $\geq$  130 mmHg and/or diastolic  $\geq$  85 mmHg). Although metabolic syndrome cannot be diagnosed before the age of 10 years, the same criteria as those for the children aged between 10 and 16 years were adopted for this age group.

Weight was measured with an individual wearing light clothing using a Líder® scale (model P300C, series 31403, year of manufacture: 2014, Brazil), whereas height was measured using a wall anthropometer (model E150 A, Tonelli Equipamentos Médicos Ltda., Brazil) while patients were barefoot. BMI was calculated using the Quetelet's method (BMI = weight / height<sup>2</sup>). Stature and BMI were classified according to the growth curves for children aged 5–19 years (WHO, 2007).

Abdominal circumference was measured using a non-extensible measuring tape with a patient placed in the orthostatic position, and the circumference at the midpoint between the last rib and iliac crest was measured and noted in centimeters. Abdominal circumference was classified in accordance with Freedman's classification for sex and age (1999)<sup>7</sup>.

Blood pressure was measured in the right arm after a minimum rest of 20 min with the arm supported at the level of the precordium using a Welch Allyn® mercury sphygmomanometer equipped with a cuff adapted to a child's size. The categorization of systolic or diastolic hypertension followed the parameters describes by the VII Brazilian Guidelines for Hypertension.

Patients with any confirmed hepatopathy unrelated to non-alcoholic hepatic steatosis and those using corticosteroid therapy, estrogen, or alcohol were excluded from the study.

Data analysis was performed using the IBM SPSS Statistics® v. 20 software. Frequencies and percentages are used to describe quantitative variables. For the assessment of dichotomous qualitative variables, Fisher's exact test was used. *P*-values < 0.05 were considered statistically significance.

The parents or guardians of the children and adolescents participating in the study signed an informed consent, and the patients aged over 12 years signed an informed assent.

This study was approved by the Research Ethics Committee of Western Paraná State University under opinion No. 1.545.286/2016.

## RESULTS

In total, 30 patients aged 5–18 years were assessed. Equivalence between sexes (50%) was observed with a predominance of children aged below 12 years (53.3%) compared with those aged 12 years or older (46.7%). Of the patients studied, 86.7% were obese and 13.3% were overweight.

Hepatic steatosis was diagnosed in 53.4% of the patients; a higher frequency of mild steatosis (46.7%) was observed, followed by that of moderate steatosis (6.7%). Notably, no cases of severe steatosis were observed. Of the patients with hepatic steatosis, 56.3% were male and 43.7% female, and 62.5% were aged 12 years or older. Hepatic steatosis was detected in 18.7% of the overweight patients and 81.3% of the obese patients (Table 1).

Table 2 presents the clinical, anthropometric, and biochemical data of the patients.

Arterial hypertension was observed in three (10%) patients, whereas borderline blood pressure was noted in 60%.

A total of 90% of the patients had increased abdominal circumference, and 51.9% of those with hepatic steatosis had an altered value for this parameter.

Elevated ALT was observed in 6.7% of the patients, and only 12.5% of the patients with hepatic steatosis presented an altered value for this parameter.

In this study, 30% of the patients had elevated TC level, 6.7% presented elevated LDLc level, 43.3% presented triglyceride alterations, and 46.7% had low HDLc level. Regarding fasting glycemia, two patients (6.7%) presented alterations (Table 3).

Metabolic syndrome was diagnosed in 26.7% of the patients, of whom 75% had hepatic steatosis.

## DISCUSSION

In the present study, the percentage of patients with obesity and overweight was higher than that reported in other studies<sup>8,9</sup>. Obesity is believed to be the main risk factor for NAFLD. In obese children, the prevalence of NAFLD can range from 70% to 80%<sup>10</sup>. In the present study, hepatic steatosis was observed in 53.4% of the patients, which is below the rate reported in the literature<sup>8,22</sup>. Of the studied patients with hepatic steatosis, 81.3% were obese; this rate was higher than that reported in other studies, including the study by Navarro-Jarabo et al.<sup>11,33</sup> in which hepatic steatosis was diagnosed using ultrasonography in 34.7% of 144 patients aged 6–14 years. In necropsy studies<sup>3</sup>, NAFLD was verified in 38% of obese children. According to epidemiological data, NAFLD may affect 3%–10% of pediatric patients, with a male-to-female ratio of 2:1<sup>12</sup>. In agreement with the literature<sup>8,11,13,14</sup>,

a higher percentage of hepatic steatosis was observed in males in the present study. The incidence of NAFLD increases with age and can reach up to 17.3% in the age group of 15–19 years<sup>3</sup>. In this study, most patients with hepatic steatosis were aged 12 years or older. NAFLD has been well documented in children, but it is more prevalent in adolescents<sup>14</sup>. Its related factors include sex hormone levels, increased insulin resistance observed at puberty<sup>15,16</sup>, inadequate eating habits, and sedentary lifestyle<sup>17</sup>. Most children with NAFLD are asymptomatic, and this fact is of concern considering that liver cirrhosis secondary to NAFLD has been reported in obese children. Some physical examination findings may contribute to the suspicion of this disease, including arterial hypertension, increased abdominal circumference, and hepatomegaly<sup>18,19</sup>.

In the pediatric age range, the current prevalence of hypertension is approximately 3%–5%, and primary hypertension is observed in 10%–15% of children; these findings are primarily attributed to the large increase in childhood obesity<sup>20</sup>. In the present study, the percentage of patients with arterial hypertension was below that described in the literature, but 60% presented borderline arterial pressure for age and height. Moreover, an epidemiological study demonstrated that obesity increases the risk of hypertension in children by approximately three times<sup>21</sup>.

In the present study, 90% of the patients presented increased abdominal circumference, a value well above those reported in the literature. Furthermore, on physical examination, over half of the patients with hepatic steatosis had altered values for this parameter. In an Italian study on 197 children aged 3–19 years undergoing liver biopsy, abdominal circumference was the only component of metabolic syndrome associated with liver fibrosis<sup>22,23</sup>.

Literature data indicate that alterations in BMI and lipid profile are the predictors of NAFLD. In the present study, TC, LDLc, HDLc, and triglyceride levels did not present representative results, contrary to the findings reported in the literature<sup>24,25</sup>.

Compared with other reports, few patients had elevated ALT levels in the present study. ALT alterations would be related to some degree of hepatic inflammation, characterizing a more advanced stage of NAFLD<sup>25,26</sup>.

Insulin resistance, with or without hyperglycemia, is associated with NAFLD onset; however, in agreement with the results reported in the literature, the findings of the present study did not indicate a substantial number of fasting hyperglycemia cases<sup>27, 28</sup>.

The association between metabolic syndrome and NAFLD has been accepted<sup>29</sup>. Despite the lack of statistical significance, most patients with metabolic syndrome in this study had hepatic steatosis. A retrospective study including 43 American children with biopsy-proven NAFLD provided the first evidence of an association between these two conditions<sup>30</sup>. Accordingly, the study by Manco et al. demonstrated that 92% and 84% of 197 Caucasian children with NAFLD were

**Table 1.** Clinical and laboratory variables according to the presence of hepatic steatosis.

| Variables                  | Hepatic steatosis |                  | Total     | p     |
|----------------------------|-------------------|------------------|-----------|-------|
|                            | Absent<br>n (%)   | Present<br>n (%) |           |       |
| <b>Sex</b>                 |                   |                  |           | 0,715 |
| Male                       | 6 (42.8)          | 9 (56.3)         | 15 (50.0) |       |
| Female                     | 8 (57.2)          | 7 (43.7)         | 15 (50.0) |       |
| <b>Age</b>                 |                   |                  |           | 0.081 |
| < 12 years                 | 10 (71.4)         | 6 (37.5)         | 16 (53.3) |       |
| ≥ 12 years                 | 4 (28.6)          | 10 (62.5)        | 14 (46.7) |       |
| <b>Waist circumference</b> |                   |                  |           | 1.000 |
| Adequate                   | 1 (07.1)          | 2 (12.5)         | 3 (10.0)  |       |
| Increased                  | 13 (92.9)         | 14 (87.5)        | 27 (90.0) |       |
| <b>Cholesterol</b>         |                   |                  |           | 1.000 |
| Desired/Borderline         | 10 (71.4)         | 11 (68.8)        | 21 (70.0) |       |
| Elevado                    | 4 (28.6)          | 5 (31.3)         | 9 (30.0)  |       |
| <b>LDL</b>                 |                   |                  |           | 0.485 |
| Desejável/Limítrofe        | 14 (100)          | 14 (87.5)        | 28 (93.4) |       |
| Increased                  | 0 (0.0)           | 2 (12.5)         | 2 (6.7)   |       |
| <b>HDL</b>                 |                   |                  |           | 1.000 |
| Desired                    | 7 (50.0)          | 9 (56.2)         | 16 (53.3) |       |
| Low                        | 7 (50.0)          | 7 (43.8)         | 14 (46.7) |       |
| <b>Triglycerides</b>       |                   |                  |           | 0.484 |
| Desired/Borderline         | 9 (64.3)          | 8 (50.0)         | 17 (56.6) |       |
| Increased                  | 5 (35.7)          | 8 (50.0)         | 13 (43.3) |       |
| <b>Blood glucose</b>       |                   |                  |           | 1.000 |
| < 99                       | 13 (92.9)         | 15 (93.8)        | 28 (93.3) |       |
| > 99                       | 1 (7.1)           | 1 (6.2)          | 2 (6.7)   |       |
| <b>BMI</b>                 |                   |                  |           | 0.602 |
| Overweight                 | 1 (07.1)          | 3 (18.7)         | 4 (13.3)  |       |
| Obese                      | 13 (92.9)         | 13 (81.3)        | 26 (86.7) |       |
| <b>Metabolic syndrome</b>  |                   |                  |           | 0.225 |
| Yes                        | 2 (14.3)          | 6 (37.5)         | 8 (26.7)  |       |
| No                         | 12 (85.7)         | 10 (62.5)        | 22 (73.3) |       |
| <b>ALT</b>                 |                   |                  |           | 0.485 |
| Adequate                   | 14 (100)          | 14 (87.5)        | 28 (93.3) |       |
| Increased                  | 0 (0.0)           | 2 (12.5)         | 2 (6.7)   |       |

\*Statistical significance:  $p < 0,05$ .

overweight and had abdominal circumference  $\geq$  90th percentile, respectively<sup>23</sup>.

One limitation of the present study was the lack of willingness of the patients to undergo ultrasound, leading to a relatively small sample size for a NAFLD study.

## CONCLUSION

In the present study, the prevalence of hepatic steatosis was found to be high. These data were important to state that NAFLD is a frequent condition in childhood and adolescence. Owing to the substantial increase in obesity in the pediatric

**Table 2.** Participant clinical, anthropometric, and biochemical data.

| Variable            | n  | Mean  | Median | Minimum | Maximum | Standard Deviation |
|---------------------|----|-------|--------|---------|---------|--------------------|
| Age                 | 30 | 11.3  | 10.5   | 5       | 18      | 3.4                |
| Total cholesterol   | 30 | 158.2 | 161.5  | 114     | 226     | 25.9               |
| HDL                 | 30 | 45.9  | 45     | 25      | 79      | 12.0               |
| LDL                 | 30 | 91.6  | 95     | 45      | 144     | 23.7               |
| Triglycerides       | 30 | 125.5 | 93     | 49      | 567     | 97.6               |
| Fasting glucose     | 30 | 95.9  | 82     | 70      | 482     | 73.3               |
| Waist circumference | 30 | 89.2  | 84     | 62      | 140     | 17.2               |
| BMI                 | 30 | 27.2  | 24.8   | 19.8    | 39.6    | 5.1                |
| ALT                 | 30 | 24.5  | 23.5   | 12      | 44      | 8.2                |

**Table 3.** Distribution of occurrences of cholesterol, LDL, triglycerides, blood pressure, and hepatic steatosis among participants.

| Variable          | Desired/ Normal |       | Borderline/Mild |       | Increased/ Moderate |       | Total |
|-------------------|-----------------|-------|-----------------|-------|---------------------|-------|-------|
|                   | n               | %     | n               | %     | n                   | %     |       |
| Cholesterol       | 9               | 30.0% | 12              | 40.0% | 9                   | 30.0% | 30    |
| LDL               | 17              | 56.7% | 11              | 36.7% | 2                   | 6.7%  | 30    |
| Triglycerides     | 16              | 53.3% | 1               | 3.3%  | 13                  | 43.3% | 30    |
| Blood pressure    | 9               | 30.0% | 18              | 60%   | 3                   | 10%   | 30    |
| Hepatic steatosis | 14              | 46.7% | 14              | 46.7% | 2                   | 6.7%  | 30    |

population, pediatricians should always consider the possibility of NAFLD in their overweight or obese patients and, whenever possible, perform imaging examinations because early diagnosis leads to immediate intervention, preventing the onset of complications.

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