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Hepatic Function in Obese Adolescents and the Relationship with Hepatic Steatosis

ORIGINAL

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Abstract

Introduction: The prevalence of obesity has increased at an impressive rate over the past years, especially among children and adolescents. Many are the alterations that may be found in obese individuals; hepatic steatosis is one of them. The aim of this study was to analyze biochemical and radiographic parameters in overweight and obese adolescents and relate these parameters to anthropometric data so that the hepatic dysfunction could be characterized.

Methods: Anthropometric and laboratory data, as well as the nutritional status of the patients, were evaluated. Besides laboratory exams, a liver ultrasound scan was performed to confirm hepatic alterations.

Results: A total of 41 patients were recruited and 6 out of that total were excluded due to the fact they were eutrophic. The remaining group was compared with a control group of 12 patients. The overweight/obese group had higher values of AST and ALT in relation to the control group. There were no alterations associated with biochemical parameters regarding anthropometric variables. A significant difference between the BMI of patients with and without steatosis could be observed.

Conclusions: There was a predominance of hepatic steatosis in the overweight/obese group, which was associated with the increase in GGT and ALT levels.

Keywords
Obesity, adolescents, hepatic steatosis

Introduction

Epidemiology

Over the past years the prevalence of obesity has increased at an impressive rate both in developed and developing countries. This fact has been alarming health professionals owing to its epidemic proportions in certain areas along with its clinical repercussions, turning obesity into one of the major public health issues.

In the United States over one-third of the adult population and nearly 17% of the young population are classified as obese [1]. In Brazil around one million children aged 10 years or under were obese in 1989, with prevalence of 2.5% of this total in low-income families and 8% in families with better socioeconomic status. In 1996 the obesity rate in the country was of 4.5% in children and 23% in adolescents. Today a great amount of studies on the prevalence of obesity can be found in the literature with astounding numbers [2].

The increase in the incidence of obesity can be observed not only among adults, but also among children and adolescents [3, 4, 5]. The highest risk for the establishment of obesity occurs during the first years of life of a child and during adolescence [6].

Hepatic steatosis is one of the many alterations that can be found in obese individuals. It is related to the body mass index (BMI), waist circumference, hypertriglyceridemia, hyperinsulinemia, glucose intolerance and diabetes [7]. Nonalcoholic steatohepatitis (NASH) is another obesity-related disease frequently associated with visceral fat accumulation. It is closely associated with hepatic fat and markers of insulin resistance syndrome [8, 9].

The prevalence of nonalcoholic steatohepatitis is around 3% in the general population, reaching rates of 20-40% in obese patients. The focus on this pathology is due to the fact it is a progressive fibrotic disease which may evolve to cirrhosis in 25% of the cases and lead 10% of the cases to death within a period of 10 years [10].

Considering the lack of data in the literature, this study proposes to investigate the hepatic repercussions of obesity in adolescents by analyzing biochemical and radiographic parameters in overweight and obese adolescents and relate these parameters to anthropometric data so that the hepatic dysfunction can be characterized.

Patients and methods

Study Design

This is a retrospective study which included obese adolescents aged between 10 and 19 years and 11 months from the ABC Medical School (FMABC) Healthcare Outpatient Clinic. All medical records between 1998 and 2003 were evaluated.

Inclusion Criteria:

- Adolescents of both sexes aged between 10 and 19 years and 11 months;
- adolescents with BMI between 85 and 95 (overweight) and above the 95th percentile (obese).

Exclusion Criteria:

- Chronic diseases: cardiopathies, endocrinopathies, nephropathies or neuropathies;
- status of morbidity;
- use of immunosuppressants six months prior to the beginning of the study.

Variables of Interest and Establishment of Groups

In order to identify obesity, the criteria of Must et al (1991) was used [20]:

- low weight: below the 5^{th} percentile;
- eutrophic: between the 5^{th} and 85^{th} percentile;
- overweight: between the 85^{th} and 95^{th} percentile;
- obese: above the 95^{th} percentile.

Control group was constituted of eutrophic patients.

The current study was previously submitted to the Local Research Ethics Committee approval under the number 094/2003.

The following variables were analyzed

1) Anthropometry: All patients were weighed in underwear and in bare feet on a portable Plenna MEA-08608 150 X 0.1 kg electronic scale. Height was obtained through an Alturexata stadiometer in centimeters. When measured, patients were barefoot, in the upright position and, in case of female patients, without hair accessories.

2) Body Composition: The brachial circumference was measured with a measuring tape in centimeters, and the triceps skinfold thickness (TS) was measured using a Lange skinfold caliper (Figure 2), with a 0-60 mm scale, halfway between the olecranon process of the elbow the acromial process of the scapula. The parameters found were analyzed with percentile calculations and classified, according to Frisancho's classification criteria (1990) (11), as follows: patients who had brachial circumference and triceps skinfold thickness values between the 90th and the 95th percentile (p90<TS<p95) were considered overweight; those with values above the 95th percentile (TS>95) were considered obese [11].

3) Nutritional State Classification: BMI was calculated according to the height and weight data supplied (weight in kilograms/height in square meters). As cut-off point reference standards, the criteria of Must el al (1991) were applied. The cut-off points used were: p85 < BMI<p95 for overweight patients and BMI > p95 for obese patients [12].

4) Laboratory Evaluation: Laboratory evaluation included blood biochemical tests carried out at the Clinical Analyses Laboratory of FMABC.

- Complete blood count, coagulogram, ALT, AST, gamma-glutamyl transferase, alkaline phosphatase, total bilirubin and fractions, total proteins and fractions, total cholesterol and fractions, triglycerides, insulin, fast glycemia, ferritin;
- Liver ultrasound scan, performed with an HDI 1500 ultrasound system, using a 3.5-5.0 MHz multifrequency convex transducer. All tests were carried out by the same professional. The parameter for the diagnosis of hepatic steatosis was the comparison with the renal cortex [13].

Statistical Analysis

At first all variables were analyzed descriptively. For quantitative variables the analysis was made through the observation of minimum and maximum values and the calculation of means, standard deviations and median. For qualitative variables absolute and relative frequencies were calculated.

Student's t test was used for the sake of comparison of means between both groups; the non-parametric Mann-Whitney test was applied whenever the supposition of data normality was rejected.

When the supposition of data normality was rejected, the non-parametric Kruskal-Wallis test was used followed by Dunn's pair wise comparison.

In order to test the homogeneity between the proportions, the chi-square test was used, or the Fisher exact test when the expected frequencies were less than 5.

The multivariate logistic regression model was used to obtain factors associated with events. The significance level was set at p=0.05.

All tests were conducted using SPSS-10 software. Student's t test was applied to compare parametric variables; Mann-Whitney test was used to compare non-parametric variables. The significance level was established as p=0.05.

Results

At first a total of 41 patients were included in the overweight/obese group. From this amount, 6 patients were excluded due to the fact they were eutrophic, leaving a total of 35 individuals in the study -14 males and 21 females. Control group was composed of 12 patients- 5 males and 7 females.

Table 1 shows the demographic characteristics of overweight/obese and control groups. A significant difference can be observed regarding the parameters that characterize weight excess, such as BMI, weight in kilograms, brachial circumference and triceps skinfold thickness.

In **Table 2** a significant difference in glycemia, insulin and triglyceride values, higher in the overweight/obese group than in the eutrophic group, can be observed.

Table 3 separates patients with and without hepatic steatosis. ALT and GGT values are higher in the steatosis group. On the other hand, this group had a mean BMI of 28.26 whereas this value in the non-steatosis group was of 23.34 kg, with significance level of 0.014.

Table 1. Demographic characteristics of overweight/obese and control groups.

Variable	BMI > 25 (n=35)	BMI < 25 (n=12)	p
Age (years)	14.86 (2.56)	14.75 (2.18)	0.897
Sex: Female (%)	-22,6	± 41,3	0,55
Ethnic Group Caucasian (%)	23 (65.7)	7 (58.3)	0.650
Weight (kg)	77.47 (15.75)	51.39 (7.69)	<0.001
Height	1.63 (9.59)	1.64 (0.11)	0.918
BMI	28.58(4.17)	19.15(1.70)	<0.001
Brachial circumference (cm)	34.04(3.25)	25.54(2.62)	<0.001
Triceps skinfold thickness (cm)	29.12(4.91)	15.17(6.89)	<0.001

Table 2. Laboratory variables found in overweight/obese group and control.

Variables			p
Hemoglobin (g/dl)	14.30 (1.35)	13.87(0.85)	0.305
Hematocrit (%)	43.46(4.24)	43.93(3.60)	0.731
Cholesterol	160.83(26.83)	148(19.55)	0.136
HDL	46.98(7.87)	44.59(11.19)	0.422
LDL	94.73(27.84)	87.51(14.52)	0.397
Triglycerides	100.97(45.45)	79.50(20.43)	0.032
Insulin	14.93(11.26)	7.83(2.88)	0.001
Glycemia	90.09(10.73)	79.75(5.55)	<0.001
Glycemia/Insulin	7.94(3.31)	11.39(3.76)	0.004

Table 3. Laboratory variables found in the groups with and without hepatic steatosis.

Variables	Hepatic Steatosis (n=22)	Non-hepatic steatosis (n=25)	p
Triglycerides	93.91 (45.85)	96.88 (7.6)	0.809
Cholesterol	159.05 (27.48)	156.24 (20.94)	0.712

HDL	47.28 (8.81)	45.57 (8.83)	0.510
LDL	94.70 (29.66)	91.30 (24.33)	0.649
Insulin (UI/ml)	16.13 (13.55)	10.46 (5.09)	0.076
Glycemia (mg/dl)	90.36 (12)	84.88 (8.73)	0.078
Glycemia/Insulin	8.27 (4.21)	9.31 (3.22)	0.345
Prothrombin (%)	96.82 (6.08)	96.20 (7.23)	0.880
TTPA	30.93 (4.66)	31.98 (6.52)	0.533
AST	21.95 (4.98)	19.68 (3.97)	0.080
ALT	18.82 (8.41)	13.96 (5.05)	0.024
GGT	20.41 (7.69)	15.44 (7.07)	0.026
Alkaline phosphatase	253.41 (156.51)	232.44 (114.31)	0.600
Albumin	4.15 (0.4)	4.40 (0.38)	0.030
Ferritin	43.79 (56.14)	31.21 (22.53)	0.308
HDL	46.98(7.87)	44.59(11.19)	0.422

Discussion

The current study found a higher frequency of overweight/obesity than in other studies. In Silva et al (14), which included 211 adolescents, there was a prevalence rate of 6.2% of overweight and of 5.7% of obesity [14]. Such numbers draw the attention of health professionals since overweight rates in this series were higher for both sexes with a greater number of obese male patients. In their study with school children, Huang et al [15] show a prevalence rate of obesity in 18.5% of the boys and in 15% of the girls [15].

In a study with obese children and adolescents ranging from 5 to 14 years of age, Asayama et al (16) found levels of insulin significantly higher in the obese group when obese and non-obese groups were compared [16]

Csábi et al, in a study with 180 obese children, found expressive differences in means of glycemia and insulin when compared with control group, a finding that complies with this study [17].

Concerning liver function tests, when overweight/obese group was compared with control group, substantial differences were found regarding the means of AST, ALT, albumin and globulin despite the fact individual levels were within the normal range.

When hepatic steatosis was investigated, 21 patients with steatosis were found in the overweight/obese group whereas only one in the control group, corroborating the literature on the subject [18].

A significant difference between the BMI of patients with and without steatosis could be noted. Studies with adults and children in the literature show a relation between higher rates of BMI and hepatic steatosis and higher levels of ALT with NASH [9, 18, 19, 20].

Such data lead to the assumption that patients from our sample are prone to develop NASH; therefore, multiprofessional guidance that includes medical, nutritional, psychological and physical activity advice should be supplied to these individuals.

When liver function tests of patients with steatosis were analyzed, values of alkaline phosphatase, which were within the normal range, were not higher than those found in other studied series [9, 19, 20].

In relation to aminotransferases, only ALT values were increased. However, there are studies in the literature that show increases in AST and ALT levels, with predominance of the latter. A study on children and adolescents which evaluate BMI parameters of patients with hepatic steatosis show the association of ALT elevation with BMI increase and hepatic steatosis, which suggest the presence of NASH [18].

In a case report, Moleston et al [21] highlighted the association of two NASH male patients, aged 10 and 12, with evolution to hepatic cirrhosis. They showed the presence of elevated aminotransferases in both boys, with prevalence of high levels of ALT. The liver ultrasound scan revealed steatosis and hepatomegalia [21].

When Sanyal [9] compared healthy patients with steatosis and NASH patients, he did not find substantial differences of albumin concentrations in none of the three groups. Other studies involving NASH patients with mean values of albumin slightly higher than the ones found in this study can be found in the literature [9, 19 ,21, 22, 23, 24].

In conclusion, the predominance of hepatic steatosis in the overweight/obese group of patients in this series could be observed. This presence was associated with the increase of GGT and ALT levels.

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