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ORIGINAL RESEARCH

Lack of correlation between body mass index and ultrasound grade of hepatic steatosis in children and adolescents: a single-center study.

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Abstract

Introduction: Nonalcoholic fatty liver disease is characterized by fat infiltration greater than 5%, and in the pediatric population, it is associated with acquired or congenital metabolic alterations, with a high prevalence in the Hispanic population. The aim of the present study was to establish the correlation between the body mass index and the ultrasound grade of hepatic steatosis in children and adolescents attending a health check-up.

Methods: The present observational, analytical, cross-sectional, retrospective study was carried out with patients from 2 to 17 years of age with hepatic steatosis treated in the outpatient area of the "Dr. Roberto Gilbert Elizalde" Children´s Hospital, Guayaquil, Ecuador, between the years 2015 and 2019. Weight, height, body mass index, degree of steatosis and AST and ALT levels were measured. A correlation analysis was established between steatosis as a dependent variable.

Results: 77 cases with an average age of 11 years entered the study, and females represented 39% of the sample. There was no association between the ultrasound grade of hepatic steatosis vs. age, gender, weight, height, or body mass index. In the analysis between transaminase levels in patients with mild to severe ultrasound grade, a significant rise in AST (P = 0.003) and a moderately significant rise in ALT (P = 0.0583) were observed.

Conclusions: This study demonstrated the absence of correlation of the ultrasound grade of steatosis with the body mass index. Early detection of hepatic steatosis with the appropriate tools should be a priority in the care of pediatric patients to avoid its progression to liver cirrhosis, for which the use of transaminases as a screening method is recommended for patients with risk factors.

Key words: Non-alcoholic Fatty Liver Disease; Ultrasonography; Obesity; Child; Alanine Transaminase.

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Introduction

Nonalcoholic fatty liver disease (NAFLD) is defined as a form of chronic liver disease characterized by fatty infiltration greater than 5% or steatosis that is not attributed to alcohol consumption and not secondary to genetic or metabolic diseases, infections, or the use of steatogenic medication [1]. In the pediatric population, NAFLD is associated with insulin resistance, central or generalized obesity, dyslipidemia characterized by hypertriglyceridemia, and a low level of high-density lipoprotein. The prevalence varies according to local epidemiology [1] and is particularly high in Hispanics [2]. In North American studies, the prevalence of NAFLD ranges from 0.7% in children 2 to 4 years of age (confirmed at autopsy) to 29% to 38% in obese children (based on ALT elevation studies and an autopsy study) [3]. In addition, the prevalence has increased by 2.7 times from the late 1980s to the 2007-2010 and at a faster rate than childhood obesity [4].

Within its diagnostic approach, complementary tests should be requested to carry out a general assessment of a patient's metabolic status. One of the main markers (although not specific for this pathology) is an increase in aminotransferase (ALT), which serves as a sign of liver involvement [1]. Other non-invasive methods are abdominal ultrasound, abdominal tomography, and magnetic resonance imaging, which vary in sensitivity and specificity for the detection of steatosis.

The approach to a patient with NAFLD is multidisciplinary, and its treatment is comprehensive. It is necessary to intervene in individual risk factors and make changes in lifestyle (such as an adequate and balanced diet in combination with moderate to high physical activity). In some cases, the administration of drug therapy is justified as part of the management to prevent disease progression [5].

Pediatric nonalcoholic fatty liver disease is a worldwide public health problem, and the incidence is not entirely clear [1]. Some authors and organizations attribute it to the difficulty that arises when making the diagnosis. This question becomes vitally important when observing its direct relationship with childhood obesity [6], which is being an entity that affected approximately 41 million children under 5 years of age globally by 2016 [7].

In available studies, the Hispanic population is projected as the one with the highest risk of presenting this disease. The outcome and complications in the medium and long term can be prevented with timely diagnosis and treatment, so it is imperative to know the true impact of the disease on pediatric patient health. Therefore, the present study established the present research question: what is the correlation between the body mass index and the ultrasound grade of hepatic steatosis in children and adolescents attending a health check-up consultation? Thus, we established an observational study to answer this question.

Population and methods

Design research

This was an observational, analytical, cross-sectional, retrospective recovery study.

Venue and study period

The study was carried out in the external consultation area of the "Dr. Roberto Gilbert Elizalde" Children's Hospital, entity of the Board of Charity of Guayaquil, Ecuador, between the dates of January 1, 2015, and December 31, 2019.

Sample size

The sample was a non-probabilistic, census-type sample of all possible cases that attended the institution.

Participants

Patients from 2 to 17 years of age were included if they attended a health check-up and had a diagnosis with the following codes of the international classification of diseases (ICD-10): Z00.1 Routine health check of the child, Z00.2 Examination during the period of rapid growth in infancy, and Z00.3 Examination of the developmental status of adolescents with obesity or overweight (E66.0 Obesity due to excess calories, E66.9 Simple obesity). Furthermore, at the discretion of the treating physician, an abdominal ultrasound was requested to estimate the presence and ultrasound grade of hepatic steatosis. Cases were excluded if there was a history of endocrine or metabolic diseases such as diabetes mellitus, hypothyroidism, galactosemia, tyrosinemia, Wilson's disease, or hemochromatosis were excluded; viral infections such as hepatitis

type A, B, C, or D; systemic diseases such as collagen diseases; metabolic diseases such as defects in the urea cycle; use of hepatotoxic mediation such as anticonvulsants; or reported alcohol consumption.

Variables

Sociodemographic variables such as age, education, sex, weight, height, and body mass index were recorded. Serum values of AST and ALT were recorded (UI / L). Additionally, the patients underwent ultrasound for the diagnosis of hepatic steatosis.

Data sources and measurements

The statistics department was requested to list patients seen by outpatient consultation with the ICD-10 mentioned during the proposed research period. Through a manual review, the definitive list of cases was finally determined. Information related to demography (age, sex), anthropometry (weight, height), presence and grading of hepatic steatosis by abdominal ultrasound, and transaminases (AST and ALT) were recovered.

Avoidance of bias

The protocol for this investigation with all methodological filters was approved. The information was always taken by the same person (the main researcher), and he data were curated and validated by the director of the study. Supervision was carried out by the study director.

Statistical methods

Statistical analysis was performed with the statistical package R v.3.6.3 (R Foundation for Statistical Computing; Vienna, Austria).

Descriptive statistics

The numerical variables are described as mean (standard deviation) or median (interquartile range), depending on their statistical distribution (Kolmogórov-Smirnov test). The descriptive variables are described in frequencies (percentages).

Inferential statistics

The association between the ultrasound grade of hepatic steatosis and the numerical variables was contrasted using ANOVA or the Kruskal-Wallis test (depending on their statistical distribution). Qualitative variables were compared using Pearson's chi-squared test. The association between the BMI classification and the ultrasound grade of hepatic steatosis was made using Kendall's correlation coefficient (tau), both in the total sample and stratified according to age group and sex. The diagnostic sufficiency of AST and ALT was calculated for the presence of steatosis.

Ethical criteria

A commission of the Graduate System of the Graduate School of Health Sciences of the Universidad Católica Santiago de Guayaquil approved this investigation.

Results

77 cases entered the study with a mean age of 11 (9-13) years, of which 1/77 (1.3%) were preschool age, 25/77 (32.5%) were school age, 17/77 (22.1%) were preadolescents, and 34/77 (44.2%) were adolescents. Females represented 39% of the sample. Table 1 summarizes the demographic and clinical characteristics of the study population.

The ultrasound grade of hepatic steatosis in the analyzed sample was normal in 29/77 (37.6%) cases, mild in 14/77 (18.2%), moderate in 28/77 (36.4%), and severe

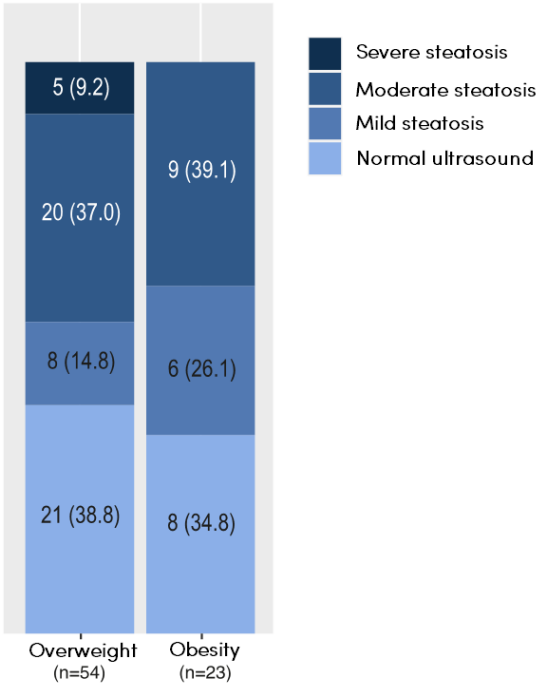

Fig. 1 Association between body mass index vs. ultrasound grade of hepatic steatosis.

in 5/77 (6.5 %). There was no association between the ultrasound grade of hepatic steatosis vs. age, gender, weight, height, or body mass index (Figure 1). Similarly, in the subanalysis between transaminase levels in patients with mild to severe ultrasound grade, a significant rise in AST (P <0.001) and ALT (P <0.001) was observed. Table 2 illustrates the correlation between body mass index and ultrasound grade of hepatic steatosis with stratification according to age groups and sex. Both in general and in each age group or gender, there was no statistical association between both variables (Figure 2).

Table 3 describes the diagnostic adequacy of transaminases for the presence of ultrasound hepatic steatosis (any grade). Both AST and ALT have a high positive predictive value but a low negative predictive value. In other words, an elevated AST/ALT value is highly suggestive of following the patient with further studies in order to confirm hepatic steatosis, whereas it is not possible to rule out said pathology with an AST/ALT value below the normal range.

Discussion

The present study looks at the relationship between the body mass index and the ultrasound grade of hepatic steatosis, specifically in overweight or obese patients. It was possible to recover 77 cases that met the inclusion criteria. Most were adolescent male patients, which is comparable to the world statistics published by the United States expert committee (NASPGHAN) in 2017 [1]. These data indicate that despite being different populations with different cultures and diets, the presence of some degree of steatosis is predominant in this age and gender worldwide.

Recent population analyses relate obesity to the presence of steatosis. For example, a study published by Anderson et al. in 2015 [8] indicated that the prevalence of children with obesity and some degree of steatosis is 34%. However, in the case of our patients, it was not possible to find an association between the presence of steatosis and body mass index or between the degree of steatosis in the patients who presented it with the body mass index. It is important to highlight that the technique used for the detection of hepatic steatosis was abdominal ultrasound. This technique is not being indicated for the diagnosis or follow-up of this pathology due to its low sensitivity and specificity [1], but it is widely used in the study center and is currently used as an important part of the approach to patients with suspected hepatic steatosis.

Table 1. Demographic and clinical characteristics of the study population.

	Total (*n*=77)	Nomal Ultrasound (*n*=29)	Mild steatosis (*n*=14)	Moderate steatosis (*n*=29)	Severe steatosis (*n*=5)	*P*
Age (years) *	11 (9 – 13)	12 (9 – 14)	11 (11 – 13)	10 (9 – 12)	12 (9 – 12)	0.4596[a]
Preschool	1 (1.3)	1 (3.4)	-	-	-	
School	25 (32.5)	7 (24.1)	3 (21.4)	13 (44.8)	2 (40.0)	
Pre-adolescent	17 (22.1)	5 (17.2)	5 (35.7)	7 (24.1)	-	
Adolescent	34 (44.2)	16 (55.2)	6 (42.9)	9 (31.0)	3 (60.0)	
Sex (Female), n (%)	30 (39.0)	11 (37.9)	3 (21.4)	13 (44.8)	3 (60.0)	0.3657[b]
Weight (kg),	59.0 (48.0 -	60.0 (51.0 -	63.0 (54.4 - 71.8)	58.0 (46.0 -	50.0 (47.0 -	0.3190[a]
Height (m), *	1.46 (1.31 - 1.54)	1.50 (1.42 - 1.57)	1.47 (1.42 - 1.52)	1.38 (1.31 - 1.52)	1.37 (1.28 - 1.39)	0.1416[a]
BMI (kg/m2),	27.4 (26.0 -	26.8(25.9 - 31.2)	28.6 (27.4 - 31.0)	27.4 (26.0 - 33.4)	27.2 (27.1 - 28.7)	0.4718[a]
Overweight	54 (70.1)	21 (72.4)	8 (57.1)	20 (69.0)	5 (100.0)	
Obesity	23 (29.9)	8 (27.6)	6 (42.9)	9 (31.0)	-	
AST (UI/L), *	31 (19 - 61)	17 (12 - 24)	29 (24 - 45)	61 (37 - 78)	87 (72 - 106)	<0.001[a]
0 – 32	42 (54.5)	29 (100)	8 (57.1)	5 (17.2)	-	
≥33	35 (45.5)	-	6 (42.9)	24 (82.8)	5 (100)	
ALT (UI/L), *	29 (17 - 35)	17(12 - 23)	27 (23 - 32)	34 (27 - 44)	39 (35 - 47)	<0.001
0 – 33	43 (55.8)	29 (100)	8 (57.1)	6 (20.7)	-	
≥34	34 (44.2)	-	6 (42.9)	23 (79.3)	5 (100)	

* The median and interquartile range are presented; a. Kruskal-Wallis test; b. Pearson's chi-square test. IQR: Interquartile range

Table 2 Correlation between body mass index and ultrasound grade of hepatic steatosis: stratification according to age groups and sex.

	n (%)	tau (CI 95%)	*P*
Total	77 (100.0)	0.023 (-0.121; 0.168)	0.76
	Groups by age		
School age	25 (32.5)	0.073 (-0.213; 0.359)	0.59
Pre-adolescent	17 (22.1)	0.139 (-0.243; 0.523)	0.40
Teen	34 (44.2)	-0.026 (-0.252; 0.198)	0.81
	Sex		
Female	30 (39.0)	0.009 (-0.222; 0.241)	0.94
Male	47 (61.0)	0.043 (-0.161; 0.248)	0.65

tau: Kendall's tau correlation coefficient; CI: confidence interval.

Table 3 Diagnostic sufficiency of transaminases for the presence of ultrasound hepatic steatosis (any grade).

	AST	ALT
Sensitivity	35/48; 73% (58 – 85)	23/48; 39% (33 – 63)
Specificity	29/29; 100% (88 – 100)	29/29; 100% (88 – 100)
PPV	35/35; 100% (90 – 100)	23/23; 100% (85 – 100)
NPV	29/42; 69% (53 – 92)	29/54; 54% (40 – 67)
OM	64/77; 83% (72 – 91)	52/77; 68 (56 – 78)

AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; PPV: positive predictive value; NPV: negative predictive value. OM: Observed match.

Regarding the association between hepatic steatosis and transaminase levels, patients with ultrasound evidence presented an increase in both aspartate aminotransferase (AST) and alanine aminotransferase (ALT), with a higher level in patients with higher hepatic commitment. Regarding ALT levels, the sensitivity was 80% with a positive predictive value of 87%. That is, if this parameter is altered, we can suspect hepatic steatosis and start the approach according to medical criteria. This finding is similar to that published in clinical practice guidelines such as NASPGHAN in 2017 [1], in which transaminases, specifically ALT, are indicated as a useful marker of liver compromise.

The limitations of the present study stem from the collection of the study population since demographic data, measurement of abdominal girth, and other diagnostic methods such as abdominal tomography or magnetic resonance imaging were not available. Ideally, future studies would be prospective, include all patients seen in outpatient consultation, and request for laboratory tests and images for the identification of fatty liver. Moreover, it would be interesting to follow up patients with pathological results to know the outcome in both those with successful interventions through lifestyle changes and/or support medication and in those who did not achieve good control for specific reasons.

Conclusions

This study demonstrated the absence of correlation between the ultrasound grade of steatosis and the body mass index. Early detection of hepatic steatosis with the appropriate tools should be a priority in the care of pediatric patients to avoid its progression to liver cirrhosis. To this end, the use of transaminases as a screening method is recommended for patients with risk factors.

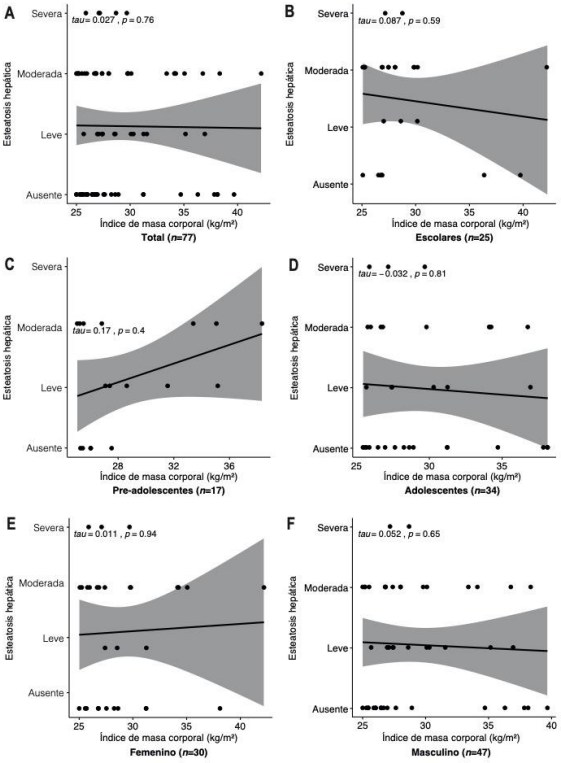

Fig. 2 Scatter diagram regarding the correlation (tau) between body mass index and ultrasound grade of hepatic steatosis: total (A), stratification according to age groups (B, schoolchildren; C, pre-adolescents; D, adolescents) and sex (E; male; F, female).

Abbreviations

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase. NAFLD: Nonalcoholic fatty liver disease. NPV: negative predictive value. PPV: positive predictive value.

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Authors' contributions

Maria Cecilia Massuh Coello: Data preservation, Formal analysis, Fund acquisition, Research, Resources, Software, Writing - original draft, Writing: review and edition.

Maria Isabel Sánchez Dávila: Conceptualization, Methodology, Project Management, Supervision, Validation, Visualization.

All authors read and approved the final version of the manuscript.

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Availability of data and materials

The data sets generated and / or analyzed during the current study are not publicly available due to the confidentiality of the participants, but are available through the corresponding author upon reasonable academic request.

Ethical statements

Protection of people

The authors declare that the procedures followed were in accordance with the ethical standards of the responsible human experimentation committee and in accordance with the World Medical Association and the Singapore Declaration.

Data confidentiality

The authors declare that they have followed the protocols of their work center on the publication of patient data without identification.

Publication consent

Informed written consent was obtained from the legal guardian of the patients for the publication of this research. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Conflicts of interest

The authors declare not to have any interest conflicts.

References

1. Vos MB, Abrams SH, Barlow SE, Caprio S, Daniels SR, Kohli R, et al.. NASPGHAN Clinical Practice Guideline for the Diagnosis and Treatment of Nonalcoholic Fatty Liver Disease in Children: Recommendations from the Expert Committee on NAFLD (ECON) and the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN). J Pediatr Gastroenterol Nutr. 2017 Feb;64(2):319-334. **doi**: 10.1097/MPG.0000000000001482. **PMID**: 28107283; **PMCID**: PMC5413933.

2. Bush H, Golabi P, Younossi ZM. Pediatric Non-Alcoholic Fatty Liver Disease. Children (Basel). 2017 Jun 9;4(6):48. **doi**: 10.3390/children4060048. **PMID**: 28598410; **PMCID**: PMC5483623.

3. Rehm JL, Connor EL, Wolfgram PM, Eickhoff JC, Reeder SB, Allen DB. Predicting hepatic steatosis in a racially and ethnically diverse cohort of adolescent girls. J Pediatr. 2014 Aug;165(2):319-325.e1. **doi**: 10.1016/j.jpeds.2014.04.019. Epub 2014 May 22. **PMID**: 24857521; **PMCID**: PMC4131842.

4. Welsh JA, Karpen S, Vos MB. Increasing prevalence of nonalcoholic fatty liver disease among United States adolescents, 1988-1994 to 2007-2010. J Pediatr. 2013 Mar;162(3):496-500.e1. **doi**: 10.1016/j.jpeds.2012.08.043. Epub 2012 Oct 17. **PMID**: 23084707; **PMCID**: PMC3649872.

5. Hegarty R, Deheragoda M, Fitzpatrick E, Dhawan A. Paediatric fatty liver disease (PeFLD): All is not NAFLD - Pathophysiological insights and approach to management. J Hepatol. 2018 Jun;68(6):1286-1299. **doi**: 10.1016/j.jhep.2018.02.006. Epub 2018 Feb 20. **PMID**: 29471012.

6. Ruhl CE, Everhart JE. Determinants of the association of overweight with elevated serum alanine aminotransferase activity in the United States. Gastroenterology. 2003 Jan;124(1):71-9. **doi**: 10.1053/gast.2003.50004. **PMID**: 12512031.

7. World Health Organization. Obesity and overweight. Ginebra, Suiza 2018. **SU**: Sheets/obesity

8. Anderson EL, Howe LD, Jones HE, Higgins JP, Lawlor DA, Fraser A. The Prevalence of Non-Alcoholic Fatty Liver Disease in Children and Adolescents: A Systematic Review and Meta-Analysis. PLoS One. 2015 Oct 29;10(10):e0140908. **doi**: 10.1371/journal.pone.0140908. **PMID**: 26512983; **PMCID**: PMC4626023.

DOI: Digital Object Identifier. **PMID**: PubMeD Identifier. **SU**: Short URL

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