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RESEARCH REPORT

Gastroenterology

Sonographic evidence of hepatic steatosis is highly prevalent in at-risk children under 4 years of age

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1 | INTRODUCTION

Metabolic dysfunction associated steatotic liver disease (MASLD), defined as hepatic steatosis detected by imaging or liver histology with at least one additional cardiometabolic risk factor, including obesity is the leading cause of chronic liver disease among children.[1] MASLD affects up to 10% of children in the United States, with incidence more than doubling in the past two decades.[2] Data regarding MASLD in preschool age children are limited and the definition of MASLD does not currently have a minimum age criterion. A recent study showed that ultrasound findings of hepatic steatosis are seen in 8%–14% of children younger than 4 years of age.[3]

The North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) recommends that children with obesity or diagnosed with overweight that have additional risk factors be screened for MASLD between the ages of 9–11 years with serum alanine aminotransferase (ALT) levels.[2] Per new MASLD nomenclature, ALT is not part of the diagnostic criteria and imaging or histology is recommended.[4] Quantification of the hepatorenal index (HRI) by ultrasound has been shown to provide moderate diagnostic performance for detecting hepatic steatosis in children.[5]

Lack of evidence related to the age of onset of hepatic steatosis or MASLD in children with overweight/obesity limits the ability to recommend screening earlier than ages 9–11. The purpose of our study was to characterize the frequency of hepatic steatosis detected using ultrasound HRI in children <4 years old at increased risk for MASLD due to having overweight/obesity. Our broader aim is to continue to explore the onset of hepatic steatosis and MASLD in childhood.

2 | METHODS

2.1 | Ethics statement

This retrospective, HIPAA compliant study was approved by the Cincinnati Children's Hospital Medical Center institutional review board.

2.1.1 | Participants

Children <4 years of age with overweight/obesity (body mass index [BMI] >85th percentile) who had undergone clinically indicated renal ultrasound examinations between March 2018 and February 2023 were identified using query software (Illuminate; Softek, Overland Park, KS) to search our institution's electronic medical record (Epic; Epic Systems, Verona, WI). We excluded any patient where the ultrasound interpretation reported abnormalities of the kidney(s) or with elevated serum creatinine to avoid spurious abnormalities of HRI on the basis of renal disease. Participants without an adequate longitudinal view of the right kidney and liver were also excluded. Additionally, because of potential technical differences, we excluded patients imaged on ultrasound systems other than Canon (Canon Medical Systems, Tustin, CA) systems. Finally, patients with known liver diseases were excluded.

2.1.2 | Records review

Age at ultrasound, reported sex, race, and ethnicity, as well as anthropometrics were obtained from the electronic medical record. Clinically obtained serum creatinine, and serum aminotransferase (ALT, aspartate aminotransferase [AST], alkaline phosphatase [ALP], gamma-glutamyl transferase [GGT]) values, within 1 year of imaging, and as close as possible to the imaging examination were collected. Clinical normal ranges defined by the CALIPER study were used to identify abnormal laboratory values.[6]

2.1.3 | Quantitative image analysis

Ultrasound examinations had been performed by one of 45 American Registry for Diagnostic Medical Sonography (ARDMS)-certified sonographers per clinical protocols. Ultrasound examinations were performed using either Aplio 500 or Aplio i800 (Canon Medical Systems; Tustin, CA) ultrasound systems with different transducers used with each machine.

A longitudinal image showing the liver and right kidney was selected by a research assistant (A.O.G.). Selected images were reviewed for quality by a board-certified pediatric radiologist (A.T.T., 11 years of postfellowship experience).

Ultrasound images were exported from the clinical PACS (Merge PACS; IBM Watson Health; Hartland, WI) as Digital Imaging and Communications in Medicine (DICOM) format images. The same research assistant then drew freehand regions of interest (ROI) in the right renal cortex and the immediately adjacent hepatic parenchyma using ImageJ (version 1.54, National Institute of Health; Bethesda, MD). Kidney ROIs were limited to renal cortex and avoided areas of artifact. Liver ROIs were approximated to the size and shape of the renal ROIs and placed as close as possible, in terms of depth and location, to the renal ROI while avoiding areas of artifact, visible bile ducts, blood vessels, and lesions (if present) (Figure S1). All ROI placements were reviewed and adjusted as needed by a board-certified pediatric radiologist (A.T.T.).

The mean echogenicity or brightness (unitless) of each liver and kidney ROI was determined using the Measure function in ImageJ, which assigns gray-scale pixels a numeric value. HRI was then calculated by dividing mean liver echogenicity by mean kidney echogenicity for each pair of ROIs. These values were then compared to the cutoff value of >1.75 previously defined by Frankland et al. using the same method.[5] In that prior study, this HRI threshold was shown to reflect a liver MRI proton density fat fraction >6%.

2.1.4 | Statistical analysis

Categorical data were summarized as counts and percentages. Continuous data were summarized using means, standard deviations, and ranges. Predictors of abnormally elevated HRI were assessed via univariate tests including Pearson correlation, the Kruskal–Wallis test, and the Mann–Whitney test.

Pearson correlation coefficients were classified as follows: 0–0.19 very weak; 0.2–0.39, weak; 0.40–0.59, moderate; 0.60–0.79, strong; and 0.80–1.0, very strong.[7] A p-value of <0.05 was considered statistically significant and p-values were adjusted for multiple comparisons when appropriate. All analyses were performed using GraphPad Prism (v9.5.0; GraphPad LLC, San Diego, CA).

3 | RESULTS

3.1 | Study sample

One hundred and sixty-eight patients were included (Table 1). Serum laboratory data were available for 50 patients at a mean interval of 115 days (0–366) from the ultrasound examination. ALT was elevated (>30 U/L) in 26% of patients (12/47).

3.2 | Associations between demographic factors and ultrasound HRI

A total of 91 (54%) patients had an abnormally elevated HRI (>1.75). An abnormally elevated HRI was present in 58% (50/86) of patients with overweight and 50% (41/82) of patients with obesity.

There was no significant association between HRI and participant sex ($p = 0.80$), race ($p = 0.25$ for White

TABLE 1 Baseline characteristics of the study sample of children with overweight/obesity, $n = 176$.

Variable	Result
Age, years	2.1 (±1.0)
Female sex, *n* (%)	96 (57%)
BMI percentile	94.0 (±4.7)
Overweight, *n* (%)	86 (51%)
Obesity, *n* (%)	82 (49%)
Race, *n* (%)	
White	151 (90%)
Black	11 (7%)
Other	6 (4%)
Hispanic ethnicity, *n* (%)	21 (13%)
Elevated serum aminotransferase levels	
ALT (>30 U/L)	12/47 (26%)
AST (>44 U/L)	15/47 (32%)
GGT (>16 U/L)	1/9 (11%)
ALP (>369 U/L)	2/47 (4%)

Note: Data are presented as means with standard deviations if continuous, or as numbers with proportions, if categorical. Abbreviations: ALP, alkaline phosphatase; ALT, alanine amino transferase; AST, aspartate amino transferase; BMI, body mass index; GGT, gamma-glutamyl transferase.

TABLE 2 Comparison of characteristics of patients with abnormal (>1.75) versus normal HRI.

Variable	HRI > 1.75	HRI ≤ 1.75	*p*-value
Total *n* (%)	91 (54%)	77 (46%)	N/A
Age, years	2.0 (±1.0)	2.1 (±1.1)	0.77
Female sex, *n* (%)	53 (58%)	43 (56%)	0.76
Hispanic Ethnicity, *n* (%)	12 (13%)	9 (12%)	0.82
White race, *n* (%)	85 (93%)	66 (86%)	0.21
BMI percentile	93.9 (±4.6)	94.1 (±4.9)	0.79
Elevated serum aminotransferase levels			
ALT (U/L)	5/24 (21%)	7/23 (30%)	
AST (U/L)	7/24 (29%)	8/23 (35%)	
GGT (U/L)	1/7 (14%)	0/2 (0%)	
Alkaline phosphatase (U/L)	1/24 (4%)	1/23 (4%)	

Abbreviations: ALT, alanine amino transferase; AST, aspartate amino transferase; BMI, body mass index; GGT, gamma-glutamyl transferase; HRI, hepatorenal index.

vs. Black vs. other) or ethnicity ($p = 0.82$). There was no significant association between HRI and participant age ($r = -0.065$, $p = 0.40$) or BMI percentile ($r = 0.0036$, $p = 0.96$) (Figure S2).

Based on grouping participants by normal versus abnormal HRI, there was no statistically significant difference in any demographic factor (Table 2).

3.3 | Associations between clinical laboratory values and HRI

Of the subgroup of 47 patients with available laboratory data, 21 (45%) had at least one abnormal liver laboratory (Table 2).

Of the 12 patients with abnormal ALT, 5 (42%) had an abnormal ultrasound HRI and 7 (58%) had a normal ultrasound HRI. Of the 24 patients with concurrently available aminotransferases and an abnormal ultrasound HRI, 5 (21%) had an elevated ALT.

4 | DISCUSSION

In our study of a convenience sample of children <4 years of age with overweight/obesity undergoing renal ultrasound, more than half had an ultrasound HRI suggesting the presence of hepatic steatosis and therefore suggesting MASLD (due to the presence of overweight/obesity). These findings suggest that MASLD can occur at a very young age and should be considered in at-risk patients. Importantly, only 21% (5/24) of the patients with imaging evidence of steatosis and available labs had elevated ALT and 58% (7/12) of patients with an elevated ALT did not have imaging evidence of steatosis, suggesting that ALT may not be a useful biomarker for MASLD screening at this age.

The observed imaging evidence of hepatic steatosis (54%) is higher than that previously reported in youth with obesity across the pediatric age spectrum (34%).[8] This suggests that patients with early onset overweight/obesity may be at risk of developing hepatic steatosis. Given the association between MASLD and other cardiometabolic comorbidities, this finding underscores the need to screen for MASLD in at risk children, regardless of age.

In our study, accepted demographic risk factors for MASLD were not significantly associated with the presence of imaging evidence of steatosis. This suggests that in the context of early childhood overweight/obesity, clinicians should not rely on known risk factors to predict the presence of MASLD.

This study has several limitations. It relied upon a retrospective convenience sample of patients, limiting generalizability. Imaging technique was not standardized. Included children were mostly White and non-Hispanic. Laboratory values were only available on a subset of patients and often labs were not in close temporal proximity to the imaging. Additional labs relevant to comorbidities, such as dyslipidemia and diabetes were not available. There is potential for

sampling error when drawing ROIs on US but this method of drawing ROIs to calculate HRI has been shown to be a reproducible in prior studies.[5,9] While ultrasound HRI has been compared to reference standard testing for hepatic steatosis in children, it has not been robustly assessed against a reference standard in the youngest children.

5 | CONCLUSION

Our study suggests MASLD can develop many years before the recommended age of screening and it affects a significant proportion of young children with overweight and obesity. Traditional MASLD risk factors were not predictive of the presence of steatosis in this cohort, suggesting a role for imaging for screening of asymptomatic children with overweight/obesity. Additional research is needed to confirm our findings in a multiethnic cohort and across clinically available ultrasound systems.

CONFLICT OF INTEREST STATEMENT

Andrew T. Trout: Siemens Healthineers: funding to institution for related research on ultrasound of pediatric fatty liver; Perspectum Inc: in-kind research support for fatty liver disease research. The remaining authors declare no conflict of interest.

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REFERENCES

1. Fryar CD, Carroll MD, Afful J. *Prevalence of Overweight, Obesity, and Severe Obesity Among Children and Adolescents Aged 2-19 Years: United States, 1963-1965 Through 2017-2018*. National Center for Health Statistics; 2020.
2. Vos MB, Abrams SH, Barlow SE, 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;64(2):319-334.
3. Green S, Mouzaki M, Abu Ata N, Trout AT. Prevalence of incidental sonographic findings of hepatic steatosis in children under 4 years of age. *Pediatr Radiol*. 2023;53(11):2221-2228.
4. Chan WK, Chuah KH, Rajaram RB, Lim LL, Ratnasingam J, Vethakkan SR. Metabolic dysfunction-associated steatotic liver disease (MASLD): a state-of-the-art review. *J Obes Metabol Syndr*. 2023;32(3):197-213.
5. Frankland MP, Dillman JR, Anton CG, et al. Diagnostic performance of ultrasound hepatorenal index for the diagnosis of hepatic steatosis in children. *Pediatr Radiol*. 2022;52(7):1306-1313.
6. Adeli K, Higgins V, Trajcevski K, White-Al Habeeb N. The Canadian laboratory initiative on pediatric reference intervals: a CALIPER white paper. *Crit Rev Clin Lab Sci*. 2017;54(6):358-413.
7. Evans JD. *Straightforward Statistics for the Behavioral Sciences*. Brooks/Cole Pub. Co; 1996.
8. Anderson EL, Howe LD, Jones HE, Higgins JPT, 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;10(10):e0140908.
9. Marshall RH, Eissa M, Bluth EI, Gulotta PM, Davis NK. Hepatorenal index as an accurate, simple, and effective tool in screening for steatosis. *Am J Roentgenol*. 2012;199(5):997-1002.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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