Evaluation of Specific Causes of Chronic Liver Diseases in Egyptian Children with Overweight or Obesity

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Abstract: *Purpose*: Hepatic steatosis is a common hepatic comorbidity in children with overweight or obesity. Concurrent chronic liver diseases that may mimic or coexist with steatosis should be searched for properly to provide timely management. We aimed to screen a group of Egyptian children with obesity or overweight who were suspected of having Metabolically-dysfunction-associated steatotic liver disease (MASLD) for underlying causes of hepatic dysfunction using non-invasive tests.

Methods: This cross-sectional study was conducted on 77 children who were overweight or obese, presenting with elevated alanine aminotransferase (ALT) for more than 3 months or bright liver on imaging or both. All children underwent a comprehensive history and clinical examination, as well as liver function tests, lipid profile, HbA1c testing, screening tests for known chronic liver diseases, and an abdominal ultrasound.

Results: 66.3% of participants were obese, and 33.7% were overweight, with a mean age of 10.4±3.4 years, and an almost equal gender distribution. All participants had a bright hepatic echo pattern, and 40.3% had elevated ALT levels. Three patients (3.8%) had positive results: one with WD, one with chronic hepatitis C, and one with chronic hepatitis B. None of the participants met the diagnostic criteria for celiac disease, alpha-1 antitrypsin deficiency, autoimmune hepatitis, or thyroid dysfunction.

Conclusion: Among our studied children with obesity or overweight who were referred with persistently elevated ALT, bright liver or both, and suspected to have MASLD, 3.8% had positive screening for chronic liver disease using non-invasive tests.

Keywords: Children, Chronic liver disease, MASLD, Obese, Overweight, Metabolic syndrome.

INTRODUCTION

The world is facing an obesity pandemic among children and adolescents. In 2022, 37 million children under 5 years old were reported to be overweight [1]. Additionally, 160 million people aged 5-19 years were suffering from obesity [1]. In Egypt, the prevalence of obesity among children and adolescents aged 5 to 19 years increased from 9.8% in 1990 to 20.4% in 2022 [2].

Metabolically-dysfunction-associated steatotic liver disease (MASLD) [3], formerly known as non-alcoholic fatty liver disease, has emerged as a serious health problem with rising incidence parallel to the obesity pandemic among children worldwide. Its prevalence in obese children is 5 times that of normal children in general (34.2% vs. 7.6%) [4]. MASLD is the most prevalent liver disease in adolescents; it is now being increasingly recognized in preschool-aged children [5]. It refers to a broad spectrum of histological hepatic lesions rather than a singular hepatic abnormality. It progresses from simple steatosis to non-alcoholic steatohepatitis, cirrhosis, and even hepatocellular carcinoma [6].

Even though liver biopsy is the gold standard for diagnosing MASLD, the NASPGHAN guidelines recommend ALT level as a screening test in children with obesity. However, ALT interpretation should rely on gender-specific upper limit of normal (ULN) values in children (22 U/L for girls and 26 U/L for boys), not the laboratory ULN. Elevated ALT more than twice the ULN for more than 3 months should be evaluated for MASLD or other causes of chronic hepatitis [7]. The use of ultrasound as a valid screening tool for MASLD in children does not meet international consensus. In children with obesity, some guidelines advise ultrasound use to screen for MASLD [6], and others advise against its use due to variable sensitivity and specificity [7].

Although MASLD is the main primary concern as a cause of liver dysfunction among the overweight/obese population, overestimation of this health issue is problematic [8]. Previous pediatric studies had

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diagnosed liver disorders among children with obesity other than MASLD in 2% [5] and 18% [9]. When caring for patients with suspected MASLD, it remains critical to evaluate for concurrent other chronic diseases that may mimic or coexist with steatosis, because timely diagnosis is crucial to prevent its progression [10].

In our work, we aimed to screen for possible underlying causes of elevated ALT or bright liver among a group of Egyptian children and adolescents with obesity or overweight who were initially suspected to have MASLD, using non-invasive tests.

PATIENTS AND METHODS

This cross-sectional study included 77 children with obesity or overweight who were suspected of having MASLD. Participants were recruited from the Endocrinology Clinic of the Diabetes, Endocrine, and Metabolism Pediatric Unit. Participants underwent a thorough assessment at the Hepatology Clinic at Cairo University's Children's Hospital in Cairo, Egypt. The study was conducted from July 2022 to June 2023. Approval was obtained from the institutional review board of Kasr Al-Ainy Medical School (IRB: MD-278-2022) on March 30, 2022. Consent was obtained from one of the parents before enrollment, following an explanation of the study details.

We enrolled children with body mass index (BMI) above the 85th percentile for age and gender, who aged 3 to 18 years, presenting with elevated serum ALT above gender specific ULN (22 U/L for girls and 26 U/L for boys) for more than 3 months, or hepatic steatosis on ultrasound or both [6, 7]. Children with serum ALT above 500 U/L [5], known chronic liver disease, using hepatotoxic medications, or those with elevated creatinine kinase were excluded.

All participants underwent a relevant history and clinical assessment.

A single experienced Endocrinologist performed anthropometric measurements. Weight was measured using a Seca scale. The height was measured using a Harpenden stadiometer. Measures were approximated to the nearest 0.1 unit. BMI was calculated as weight (kg) divided by the square of height (m). We defined overweight as a BMI between the 85th and 95th percentiles, and obesity as a BMI at or above the 95th percentile for age and gender [11], using the Egyptian Growth charts [12]. The waist circumference (WC) was taken while the patient was standing and breathing normally and measured at a level midway between the lower rib margin and iliac crest at the level of the umbilicus using a flexible non-stretchable plastic tape all around the body in a horizontal position, then was plotted on WC centiles [13].

The blood pressure assessment was performed using a mercury sphygmomanometer. The technique, frequency, and interpretation of blood pressure were performed according to the American Academy of Pediatrics Guidelines [14].

All participants underwent the following tests: liver function tests (ALT, aspartate aminotransferase (AST), γ-glutamyl transferase (GGT), alkaline phosphatase (ALP), total bilirubin, direct bilirubin, serum albumin, prothrombin time, and INR).

The following tests were performed to screen for possible underlying chronic liver disease: Hepatitis B surface antigen (HBsAg), hepatitis B core antibody (HBc Ab) total, and hepatitis C virus antibody (HCV Ab). Children were tested for serum ceruloplasmin, and those with low results underwent a 24-hour urinary copper excretion test. Alpha-1 antitrypsin protein level, serum thyroid-stimulating hormone (TSH), free tetraiodothyronine (T4), and free triiodothyronine (T3) levels were also measured. Additionally, total immunoglobulin (Ig) A, tissue transglutaminase IgA antibody, anti-nuclear antibody, anti-smooth muscle antibody, anti-liver-kidney microsomal antibody, and total IgG levels were assessed. In addition, the Lysosomal acid lipase (LAL) test was performed in cases with a bright liver, elevated transaminases, and a marked reduction in HDL to exclude cholesteryl ester storage disease.

Additionally, an 8-hour fasting sample was obtained to assess fasting plasma glucose (FPG), hemoglobin A1c (HbA1c), and lipid profiles (total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides). Interpretation of these tests and the assessment of metabolic status were performed according to international recommendations [15-18].

A single experienced radiologist performed an abdominal ultrasound using a Sony Aplio 400 device (Japan) to obtain B-mode ultrasound images with a convex probe (3.5 MHz) and a linear probe (7 MHz). The liver dimensions were calculated using the convex probe. The parenchymal echogenicity was assessed to evaluate the grades of hepatic steatosis as follows: grade 1: diffusely increased hepatic echogenicity with

appreciable periportal and diaphragmatic echogenicity; grade 2: diffusely increased hepatic echogenicity, obscuring periportal echogenicity but with appreciable diaphragmatic echogenicity; and grade 3: diffusely increased hepatic echogenicity, obscuring both periportal and diaphragmatic echogenicity [19]. Grades 1 and 2 were considered mild brightness, and grade 3 was considered severe brightness.

Statistical Analysis of the Data

Statistical analysis was conducted using IBM SPSS (Statistical Package for the Social Sciences; IBM Corp, Armonk, NY, USA), version 22, for Microsoft Windows. Data were statistically described using means ± standard deviations, medians and interquartile range, or frequencies and percentages, as appropriate. Numerical data were tested for normality using the Kolmogorov-Smirnov test. Comparison of numerical variables between the study groups was performed using the Student t-test for independent samples for normally distributed data or large sample sizes, and the Mann-Whitney U test for independent samples for non-normal data. Comparison of numerical variables between more than two groups was performed using the Kruskal-Wallis test if the data were not normally distributed or the sample size was small. Two-sided p-values less than 0.05 were considered statistically significant.

RESULTS

During our study period, 480 children with obesity or overweight were referred to the Obesity Clinic; 77 (16%) met the study selection criteria. The mean age of participants was 10.4 ± 3.4 years, with almost equal gender distribution. Fifty-one patients (66.3%) were obese, and 26 (33.7%) were overweight. Family history was positive for liver diseases in 13 (16.9%), gall bladder stones in 22 (28.6%), and obesity in 26 (33.8%) participants.

During clinical assessment, we observed a WC percentile above the 90th percentile in 67 (87.1%) patients, acanthosis nigricans at the neck in 48 (62.3%) patients, pre-hypertensive status in 23 patients (29.9%), and hypertension in 33 patients. The liver was palpable in 37 patients (48.1%), with no palpable splenomegaly or manifestations suggestive of chronic liver disease.

Comparisons between children with obesity and those with overweight showed that they were comparable regarding age, gender, and acanthosis nigricans rates. Hepatomegaly was observed more frequently among the obese group than the overweight group, with a near-significant value. Hypertension, stage 1 and 2, was significantly common among children with obesity (Supp Table **1**). No significant differences were observed between children with overweight and those with obesity for ALT, AST, HbA1c, glucose metabolic status, lipid profile, metabolic syndrome, hepatomegaly, or liver brightness grading by ultrasound (Data not shown).

Among the study group, impaired fasting glucose was reported in 2 patients (2.6%), and one patient (1.3%) had diabetes. The mean HbA1c level was 5.5 ± 0.4 (4.3%-8%), indicating that 7 patients (9.1%) are in the prediabetes stage and 1 patient (1.3%) has diabetes. The child diagnosed with type 2 diabetes had a fasting plasma glucose of 135 mg/dl, HbA1c of 8%, fasting insulin levels of 14.3 (normal: 2-25 µIU/mL), fasting C-peptide of 1.38 (normal: 0.78-1.89 ng/mL), and HOMA-Insulin Resistance index of 4.4.

Regarding lipid profile abnormalities, 24 patients (31.2%) had elevated cholesterol levels, 38 (49.4%) had elevated triglyceride levels, 18 (23.4%) had elevated LDL levels, and 13 (16.9%) had low HDL levels. Seventy out of 77 (90.9%) children had at least one abnormal lipid profile.

Serum ALT level was elevated in 31 patients (40.3%); it was less than 2 times ULN in 21 (27.3%) and more than 2 times ULN in 10 (13%). Cases with ALT above 2-fold ULN also had elevated AST levels. All recruited patients had normal levels of ALP, GGT, total and direct bilirubin, prothrombin time, and serum albumin. Table **1** presents comparisons of ALT status groups on demographic and clinical data. Children with ALT above the ULN had significantly higher mean systolic and diastolic blood pressure, as well as a higher frequency of high blood pressure, than those in other groups.

Ultrasound examination revealed a bright liver echo pattern in all cases, and hepatomegaly in 37 (48.1%) patients. Most patients (71, 92.2%) exhibited mild hepatic brightness (grades 1 and 2), while 6 (7.8%) showed severe hepatic brightness (grade 3). No significant differences were detected between cases with mild and those with severe brightness regarding BMI Z-score, weight Z-score, WC, HbA1c, glucose metabolic status, cholesterol, triglycerides, and LDL. However, mean serum ALT and AST levels, as well as

Table 1: Comparisons Between Demographic and Clinical Data Among Different Patients' Groups According to ALT Statuses (N=77)

Variables	ALT status			P value
	Normal (N = 46)	≤ 2-fold ULN (N = 21)	> 2-fold ULN (N = 10)	
Age (years); Mean ± SD	10.52 ± 3.8	9.86 ± 3.57	11.07 ± 2.40	0.6
Sex; N (%) *Male* *Female*	 27 (58.7) 19 (41.3)	 7 (33.3) 14 (66.7)	 4 (40%) 6 (60%)	 0.1
Family history of obesity; N (%)	17 (37)	5 (23.8)	4 (40)	0.5
Family history of liver diseases; N (%)	8 (17.4)	2 (9.5)	3 (30)	0.4
Diastolic blood pressure (mmHg); Mean ± SD	74.76 ± 11.42	72.86 ± 13.09	84.6 ± 11.22	0.03*
Systolic blood pressure (mmHg); Mean ± SD	114.4 ±11.047	111.67 ±15.11	124.2 ±12.77	0.04*
Blood pressure status; N (%) *Normal* *Prehypertension* *HTN grade 1* *HTN grade 2*	 11 (23.9) 15 (32.6) 18 (39.1) 2 (4.3)	 9 (42.9) 7 (33.3) 1 (4.8) 4 (19)	 1 (10) 1 (10) 4 (40) 4 (40)	 0.003*
Hepatomegaly in abdominal examination; N (%)	23 (50)	8(38.1)	6 (60)	0.5

*P value is considered significant at < 0.05.

the presence of hepatomegaly on ultrasound, were significantly higher among children with severe brightness than in those with mild brightness. Additionally, HDL levels were significantly lower in children with severe echogenicity (Table **2**).

Thirty patients (38.9%) fulfilled the criteria of metabolic syndrome. Demographic data, the presence of hepatomegaly, ALT and AST levels, or a bright liver on ultrasound were comparable between cases with metabolic syndrome and those with healthy status (Supp Table **2**).

In our screening for chronic diseases, 3 patients (3.8%) tested positive: 1 with WD, 1 with chronic hepatitis C, and 1 with chronic hepatitis B (Table **3**). None of the participants met the diagnostic criteria for celiac disease, alpha-1 antitrypsin deficiency, autoimmune hepatitis, or thyroid dysfunction. Only 4 participants were candidates for LAL testing with negative results.

DISCUSSION

In the current study, 16% of children with obesity or overweight attending the Obesity Clinic had either ALT elevation or hepatic hyperechoic pattern by ultrasound or both. The observed prevalence of liver dysfunction among children with high BMI is considerable and necessitates further medical attention. In line with our observations, pediatric guidelines recommend screening children with overweight or obesity for hepatic involvement, namely MASLD [6, 7, 20].

Regarding blood pressure status among our cohort, hypertension was significantly observed more frequently among obese than overweight individuals, and among those with ALT levels more than double the ULN, compared to the rest of the group. In agreement with ours, Abolfotouh *et al.* [21] reported a prevalence of 5.7% for prehypertension and 4% for hypertension among their studied 1500 Egyptian adolescents with obesity, with or without suspected MASLD. In addition, children with MASLD had significantly higher systolic and diastolic blood pressure than children without MASLD, in a biopsy-based study for 150 overweight children [22].

From our observations, acanthosis nigricans was present in 48 (62.3%) of the studied children. Acanthosis nigricans has been found in 36-49% of children with biopsy-proven MASLD [23].

We observed frequent lipid profile abnormalities among our study group, with 90.9% of children having at least one abnormal lipid profile. Similar to ours, elevated total cholesterol was reported in 14.3%, LDL in 16.8%, and low HDL levels in 61.3% of 357 Egyptian

Table 2: Comparison of Patient Characteristics According to Grades of Liver Brightness (N=77)

Parameters	Mild brightness (N = 71)	Severe brightness (N = 6)	P value
Age(years); Mean ±SD	10.4 ± 3.49	10.4 ± 2.62	0.9
Sex; N (%) *Female* *Male*	 38 (53.5) 33 (46.5)	 1 (16.7) 5 (83.3)	 0.1
BMI; Mean ± SD	29.1 ± 6.2	29.9 ± 4.1	0.7
Waist circumference percentiles ≥ 90th; N (%)	62(87.4)	5 (83.3%)	0.07
ALT (U/L); Median (IQR) Status; N (%) *Elevated* *Double upper limit*	 22 (12-373) 18 (25.4) 8 (11.3)	 22 (19-88) 3 (50) 2(33.3)	 0.03* 0.07
AST (U/L); Median (IQR) *Elevated AST; N (%)*	37 (12-158) 8 (13.7)	38 (20-55) 2 (33.3)	0.03* 0.17
HbA1c (%); Mean ± SD	5.28 ± 0.47	5.45 ± 0.38	0.138
Glucose metabolic state; N (%) *Normal* *Pre-diabetic* *Diabetic*	 64 (90.1) 6 (8.4) 1 (1.4)	 5 (83.3) 1 (16.7) 0 (0)	 0.725
Cholesterol (mg/dl); Mean ± SD - ElevatedCholesterol; N (%)	175.9 ± 37.04 20 (28.2)	191 ± 38.9 4 (66.7)	0.3 0.1
Triglycerides (mg/dl); Mean ± SD - ElevatedTriglycerides; N (%)	125.49 ± 50.44 38 (53.5)	94 ± 25.6 0 (0)	0.2 0.009*
LDL (mg/dl); Mean ± SD - ElevatedLDL; N (%)	105.27 ± 32.55 15 (21.1)	128.83 ± 30.28 3 (50)	0.07 0.3
HDL (mg/dl); Mean ± SD - LowHDL; N (%)	49.01 ± 12.60 10 (14.1)	38.67 ± 5.502 3 (50)	0.01* 0.04*
Hepatomegaly in ultrasound; N (%)	31 (43.7)	6 (100)	0.010*

ALT: alanine aminotransferase; AST: aspartate aminotransferase; HbA1c: hemoglobin A1c; HDL: high-density lipoprotein; LDL: low-density lipid. *P value is considered significant at < 0.05.

children with obesity. Obesity was associated with the prevalence of at least one abnormal lipid level [24]. Interestingly, in children with obesity and biopsy-proven MASLD, 46% had cholesterol elevation [25], and 46% had triglyceride elevation, showing a significant frequency compared to the matched cohort without MASLD [22].

Among our study group, cases with severe brightness had significantly higher ALT, AST, and triglyceride levels, lower HDL levels, and more frequent hepatomegaly than cases with mild brightness. We did not observe statistically significant differences in blood pressure and metabolic syndrome statuses among groups with different brightness levels. A study of 861 school-aged children with obesity showed that, the presence of moderate and severe bright liver by ultrasound carried a high risk of dyslipidemia (OR: 7.99, 95% CI: 4.34-14.73), impaired fasting glucose (OR: 3.65, 95% CI: 1.04-12.85), hypertension [odds ratio (OR): 2.18, 95% CI: 1.27-3.75], and metabolic syndrome (OR: 3.77; 95% CI: 1.90 7.47, p < 0.01) [26].

Our screening tests revealed that three patients (3.8%) out of 77 children referred with suspected MASLD were positive for alternative chronic liver diseases; one had chronic hepatitis C, another one had chronic hepatitis B infection, and the third had WD. In accordance with our findings, Yodoshi *et al.* [5] reported that 2% of children with obesity or overweight who presented with elevated serum ALT and/or hepatic steatosis on imaging had chronic liver disease. They retrospectively studied 900 children and reported different diagnoses other than MASLD, such as celiac

Table 3: Characteristics and Laboratory Data of Cases with Positive Screening for Chronic Liver Disease

Parameters	Wilson Disease	Chronic HCV Infection	Chronic HBV Infection
Age in (years)	10.2	3.1	8.2
Gender	Female	Female	Male
Family history of obesity	Yes	No	Yes
Family history of liver disease	No	No	Yes
Weight percentile	90th	> 97th	> 97th
Height percentile	50th	75th	95th
BMI percentile	> 90th	>95th	> 95th
Waist circumference percentile	> 95th	> 99th	> 99th
Blood pressure status	Prehypertension	Normal	Stage 1 hypertension
Acanthosis nigricans	No	No	Yes
Hepatomegaly by examination	Yes	No	Yes
ALT (U/L)	373 (> 10 ULN)	34 (< 2 ULN)	85 (> 2 ULN)
HbA1c (%)	5.1 (normal)	5.2 (normal)	5.4 (normal)
Fasting blood glucose (mg/dl)	72 (normal)	74 (normal)	75 (normal)
Lipid profile (mg/dl) *Cholesterol* *Triglycerides* *LDL* *HDL*	 186 (borderline) 84 120 (borderline) 49	 149 96 (borderline) 88 42 (borderline)	 245 (high) 143 (high) 169 (high) 48
Metabolic syndrome	No	No	Yes
Positive diagnostic tests	Low ceruloplasmin 1 mg/dl, 24-hour urinary copper 1107 µg/Day	Positive HCV Ab, HCV RNA 54300 IU/ml	Positive HBs Ag, HBc Ab total, HBV DNA 34900 IU/ml
Enlarged liver in U/S	Yes	No	No
Liver echogenicity brightness	Grade (1)	Grade (1)	Grade (1)

ALT: alanine aminotransferase; AST: aspartate aminotransferase; BMI: body mass index; HbA1c: hemoglobin A1c; HBcAb: hepatitis B core antibody; HBsAg: hepatitis B surface antigen; HCV Ab: hepatitis C virus antibody; HDL: high-density lipoprotein; LDL: low-density lipid.

disease, alpha-1 antitrypsin deficiency, thyroid dysfunction, Hodgkin's lymphoma, and hemophagocytic lymphohistiocytosis. Strikingly, Schimmer *et al.* [9] reported underlying chronic liver disease in 18% of their children with obesity or overweight, who were referred with suspicion of MASLD. They studied 225 children aged 10 years or older. Autoimmune hepatitis was diagnosed in 11 (4.9%) children.

Using serum ceruloplasmin and 24-hour urinary copper excretion, we diagnosed WD in one child, representing 1.3% of the studied children. Fifty percent of WD cases present with moderate to severe hepatic steatosis, which is the earliest change seen in the liver pathology, and can be misdiagnosed as MASLD. The exact mechanism of hepatic steatosis in WD is largely unknown; it is generally considered to be a consequence of copper toxicity [27]. In addition, WD is characterized by modest elevations in ALT (100-500 U/L) and GGT levels, which are similar to the expected values in cases with MASLD [28].

Among our cohort, a child was diagnosed as having HCV infection. He had HCV antibody-positive results and was confirmed with an HCV RNA assessment. In children with chronic viral hepatitis, micro- and macro-vesicular steatosis is a common finding. The relationship between chronic hepatitis C and liver steatosis has been well documented. Steatosis occurs in about a quarter of children with chronic hepatitis C. Studies show a strong association between fatty liver and HCV genotype 3, while in cases with non-3 genotypes, the risk of steatosis is connected to a

higher BMI [29]. In Egypt, HCV genotype 4 is the most prevalent variant, accounting for more than 90% of isolates [30].

The diagnosis of chronic hepatitis B was reached in one of our cases using the hepatitis HBs Ag and HBc Ab total and confirmed with a HBV DNA quantification. Additionally, this case met the criteria for metabolic syndrome. The presence of steatosis here is likely associated with the abnormal metabolic status rather than with hepatitis B infection. The prevalence of liver steatosis in HBV-infected children was estimated to range from 4% to 13% [31].

From our results, no cases showed positive results for celiac disease screening. Similarly, Hill *et al.* [31] reported absent positive results for celiac disease among their studied 120 children with obesity undergoing evaluation for MASLD. In addition to the risk of developing celiac hepatopathy, patients with celiac disease may be at increased risk of MASLD, which may in part reflect excess weight gain that occurs with consuming a highly processed gluten-free diet [32].

Alpha-1 antitrypsin deficiency was not found among our study population. In contrast, 0.3% of 900 patients under 18 years referred for suspected MASLD were found to have A1AT deficiency [5]. This difference may be related to ethnic variation.

In our study, neither biochemical nor clinical thyroid dysfunction was reported among the screened children. Unlike ours, subclinical hypothyroidism (elevated TSH levels with standard free T4 and T3) was reported in up to 23% [33], and true hypothyroidism in 14% of children with obesity [34]. Clinical hypothyroidism is significant in the context of MASLD because it impairs fatty acid oxidation and triglyceride export from hepatocytes, thereby favoring hepatic steatosis [35].

Limitations of our study included its single-center design, small sample size, and cross-sectional nature, which may limit its external validity. Also, the lack of liver biopsy to establish a definitive diagnosis for MASLD and to entirely exclude overlapping or subclinical liver pathologies. Besides, tests for rare conditions, such as hemochromatosis, ornithine transcarbamylase deficiency, or citrin deficiency, were not available.

CONCLUSION

Among the studied children with obesity or overweight who were referred with persistently elevated ALT or bright liver and suspected to have MASLD, 3.8% had positive screening for other chronic liver disease using non-invasive tests.

A selective, stepwise, risk-based diagnostic approach guided by clinical features, biochemical severity, and imaging findings, in line with ESPGHAN/NASPGHAN recommendations, is initially suggested for children with obesity or overweight presenting with hepatic dysfunction. Based on the screening results, further specific diagnostic modalities should be performed to guide proper management, in line with the recent pediatric guidelines.

Future multicenter studies incorporating histological assessment and investigations for rare conditions are recommended to define the true prevalence of alternative liver diseases and to optimize diagnostic algorithms in this population.

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CONFLICT OF INTEREST DISCLOSURES

No conflict to declare.

SUPPLEMENTARY TABLES

The supplementary tables can be downloaded from the journal website along with the article.

ETHICAL APPROVAL

Approval was obtained from the Institutional Review Board of Kasr Al-Ainy Medical School (IRB: MD-278-2022) on March 30, 2022.

CONSENT FOR PARTICIPATION AND PUBLICATION

It was obtained from participants before enrollment.

CONDUCTION SITE

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