REVIEW ARTICLE

CONTENTS

The relationship between metabolic dysfunction-associated fatty liver disease and hormonal disorders in children: A literature review

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ABSTRACT

This narrative review summarizes current evidence regarding hormonal disturbances associated with metabolic dysfunction-associated fatty liver disease in children. Focus was given to thyroid function, insulin sensitivity, gonadal hormones in boys, and vitamin D levels in relation to hepatic and metabolic abnormalities. A comprehensive search of PubMed, Scopus, and Web of Science was conducted for literature published between January 2015 and June 2025. Studies included children aged 0–18 years with confirmed metabolic dysfunction-associated fatty liver disease based on imaging, histological, or biochemical criteria. Eligible articles reported data on at least one hormonal axis and included original research, meta-analyses, or high-quality narrative reviews. Adult-only studies, case series with fewer than ten participants, and articles lacking full text or endocrine data were excluded. Subclinical hypothyroidism occurred in 18–42% of affected children, insulin resistance in over 65%, reduced testosterone and sex hormone-binding globulin in boys, and vitamin D deficiency in 55–70% of cases. These disturbances correlated with liver enzyme elevations and steatosis severity. Weight reduction of 7–10% improved insulin resistance, thyroid and sex hormone parameters, and vitamin D status. Preliminary findings support potential benefits of vitamin D supplementation and levothyroxine therapy, though large-scale trials remain limited. Metabolic dysfunction-associated fatty liver disease in children is a multisystem condition where hormonal dysfunction contributes to disease progression. Comprehensive endocrine evaluation should be part of standard care. Further research is needed, particularly in younger children, girls, and diverse populations.

KEY WORDS: insulin resistance, hypothyroidism, testosterone, vitamin D, gonadal axis.

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INTRODUCTION

Metabolic dysfunction–associated fatty liver disease (MAFLD) has emerged as one of the most prevalent chronic liver conditions in children [17]. While the previous term "nonalcoholic fatty liver disease" (NAFLD) focused on the absence of alcohol as an etiological factor, MAFLD more explicitly emphasizes the metabolic dysfunction that underlies hepatic fat accumulation [1, 17, 21]. Prevalence estimates suggest that MAFLD affects approximately 10–20% of the general pediatric population and over 30% of obese children [20].

Importantly, MAFLD in children manifests as a multisystem disorder: liver injury is only the most visible feature, while endocrine disturbances—affecting thyroid hormones, insulin signaling, sex steroids, and vitamin D metabolism—play critical roles in disease pathophysiology, progression, and long-term outcomes [4, 6, 7, 8, 9]. Pediatric patients with MAFLD often present with subclinical hypothyroidism, marked insulin resistance, lower testosterone and SHBG levels (in boys), and vitamin D deficiency. These alterations can impair somatic growth, delay or disrupt pubertal progression, and heighten lifelong cardiometabolic risk [5, 10, 24].

This narrative review collates peer-reviewed publications from 2015 to June 2025 that address each of these hormonal axes in pediatric MAFLD. Our goal is to synthesize prevalence data, clarify pathophysiological links, and highlight clinical implications—ultimately guiding more effective screening, monitoring, and early intervention strategies.

MATERIALS AND METHODS

To construct this narrative review, we performed a comprehensive search of PubMed, Scopus, and Web

of Science to identify relevant literature published between January 2015 and June 2025. Search terms included combinations of "MAFLD" or "NAFLD" with "children," "pediatric," "hormonal disorders," "thyroid," "insulin resistance," "testosterone," and "vitamin D." No language restrictions were applied, but only English-language articles were retained. We screened titles and abstracts for relevance, focusing on original research, clinical trials, meta-analyses, and high-quality narrative reviews that addressed hormonal parameters in pediatric MAFLD populations. Studies were included if they involved participants aged 0–18 years with confirmed MAFLD or NAFLD diagnosis—based on imaging, histology, or established biochemical criteria—and reported data on at least one endocrine axis (thyroid function, insulin sensitivity, gonadal hormones, or vitamin D status). Exclusion criteria comprised adult-only cohorts, case reports or series with fewer than ten participants, and articles lacking full text or endocrine measurements. After removing duplicates and evaluating full texts, we synthesized findings from the final selection of studies, emphasizing prevalence estimates, correlation analyses, interventional outcomes, and proposed pathophysiological mechanisms. Given the narrative nature of the review, formal quality scoring tools (e.g., NOS or AMSTAR) were not uniformly applied, but methodological rigor and sample size were noted when interpreting individual study results.

REVIEW

Although diagnostic modalities vary (ultrasound, MRI, sometimes biopsy), most reports agree that the metabolic profile of children with MAFLD commonly includes obesity, dyslipidemia, and insulin resistance [4, 8, 16, 20]. The shift from the term "NAFLD" to "MAFLD" in 2019 helped sharpen focus on associated metabolic derangements, not just hepatic fat content [1, 17, 24]. Importantly, MAFLD criteria require evidence of hepatic steatosis plus one of the following: overweight/obesity, type 2 diabetes, or evidence of metabolic dysregulation (e.g., elevated waist circumference, hypertension, hypertriglyceridemia, low HDL, prediabetes, or insulin resistance) [1, 17].

In children, MAFLD prevalence is closely tied to the rising rates of pediatric obesity. Lifestyle factors—high-calorie diets and sedentary behavior—compound genetic predispositions (e.g., PNPLA3, TM6SF2, MBOAT7 polymorphisms) to foster early fat accumulation in the liver [5, 6]. Overall, the burden of MAFLD in childhood sets a trajectory toward adult cardiometabolic disease if left unaddressed.

THYROID AXIS IN PEDIATRIC MAFLD

PREVALENCE AND CORRELATIONS

Multiple observational studies report subclinical hypothyroidism (elevated TSH with normal free T4) in approximately 18–42% of children with MAFLD, compared to 5–10% in age-matched controls [1–6, 12, 13, 15, 29]. Elevated TSH—often within the upper end of the normal range—correlates positively with serum ALT and AST ($r = 0.32–0.47$, $p < 0.05$ in several cohorts), suggesting that even mild thyroid dysfunction exacerbates hepatic inflammation and steatosis [3, 4, 12].

PATHOPHYSIOLOGICAL LINKS

Thyroid hormones are key regulators of lipid and carbohydrate metabolism. In hepatocytes, T3 stimulates lipid mobilization and oxidation; relative T3 deficiency or resistance may impair these pathways, promoting de novo lipogenesis [1, 2, 13]. Animal models show that low thyroid action in the liver upregulates sterol regulatory element-binding protein-1c (SREBP-1c), increasing triglyceride synthesis [1, 15]. In human pediatric cohorts, high TSH is associated with greater severity of steatosis on imaging or histology, even after adjusting for BMI and insulin resistance [3, 4, 12].

CLINICAL IMPLICATIONS

Routine screening of thyroid function (TSH, free T4) in children diagnosed with MAFLD is therefore advised. While overt hypothyroidism is uncommon, early subclinical dysfunction may worsen metabolic control. Some centers advocate for levothyroxine (L-T4) therapy in those with TSH persistently above 4.5 mIU/L, especially if ALT/AST remain elevated despite lifestyle interventions [13, 29]. However, large-scale pediatric trials of L-T4 in MAFLD are lacking, and most evidence comes from small interventional or observational series [6, 12].

INSULIN RESISTANCE AND THE INSULIN AXIS

PREVALENCE AND SEVERITY

Insulin resistance is one of the most consistent findings in pediatric MAFLD. Cross-sectional data indicate that at least 65% of children with MAFLD demonstrate HOMA-IR values > 3, compared to about 15% in non-MAFLD obese or normal-weight peers ($p < 0.001$) [1, 4, 8–11, 14, 16, 20]. HOMA-IR correlates strongly with hepatic fat fraction on MRI and with ALT levels.

MECHANISTIC CONSIDERATIONS

Hepatic steatosis itself contributes to insulin resistance by increasing intrahepatic diacylglycerol content, which activates protein kinase Cε, impairing insulin receptor signaling [4, 8, 10]. Conversely, systemic insulin resistance promotes adipose lipolysis, raising free fatty acids delivered to the liver, perpetuating steatosis—a classic "vicious circle" [1, 4, 8, 20]. Chronic insulin resistance also activates pro-inflammatory cascades via JNK and NF-κB pathways, exacerbating hepatocellular injury [8, 10, 14].

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MPACTS OF WEIGHT REDUCTION

Lifestyle-based studies - emphasizing 7–10% weight reduction over 3–6 months - report a mean decrease in HOMA-IR by 1.5 units ($p < 0.01$) and ALT by approximately 25 U/L [1, 4]. Improvements in insulin sensitivity parallel reductions in hepatic fat on ultrasound or MRI. Some small trials of metformin in adolescents with MAFLD show favorable effects on HOMA-IR and liver enzymes, though findings are mixed and long-term safety data remain limited [10, 11, 16].

GONADAL AXIS: TESTOSTERONE AND SHBG IN BOYS

OBSERVED ALTERATIONS

In MAFLD-affected boys (typically in late preadolescence and adolescence), mean total testosterone declines from approximately 12.5 ng/dL (in age-matched controls) to about 8.7 ng/dL ($p < 0.01$) [7, 24, 25]. Furthermore, sex hormone-binding globulin (SHBG) levels are 20–35% lower in boys with MAFLD, correlating inversely with HOMA-IR ($r = –0.45$, $p < 0.01$) [7].

PATHOPHYSIOLOGICAL LINKS

Lower SHBG - largely produced by hepatocytes - reflects insulin-mediated suppression; hyperinsulinemia inhibits hepatic SHBG production, reducing circulating bound testosterone and raising free estradiol relative to testosterone [7, 24]. This hormonal milieu promotes central fat deposition and may delay the onset or progression of puberty [24]. Experimental data suggest that testosterone modulates hepatic lipid metabolism via PPAR α/γ receptors; low testosterone favors lipogenesis and visceral adiposity [24, 25].

CLINICAL CONSIDERATIONS

Endocrine evaluation in boys with MAFLD should include morning total testosterone and SHBG measurement. Although replacement therapy for hypogonadism is generally reserved for confirmed Leydig cell dysfunction (rather than functional suppression), some endocrinologists consider low-dose testosterone or interventions aimed at improving insulin sensitivity (e.g., metformin) to normalize SHBG and free testosterone levels [7, 25]. Longitudinal studies are needed to determine whether early normalization of testosterone/SHBG mitigates hepatic and metabolic progression.

VITAMIN D AXIS

PREVALENCE OF DEFICIENCY

In multiple cohorts, 55–70% of children with MAFLD have serum 25-hydroxyvitamin D [25(OH)D] levels below 20 ng/mL, compared to 30–40% of age-matched controls ($p < 0.01$) [9, 10, 19, 22]. Low vitamin D is more pronounced among obese MAFLD cases than lean controls, suggesting a synergistic effect of adiposity and hepatic fat on vitamin D sequestration.

MECHANISTIC LINKS

Vitamin D receptors in hepatocytes and adipocytes regulate genes involved in lipid metabolism, inflammation, and fibrogenesis. Deficiency may exacerbate insulin resistance by impairing insulin receptor expression and downstream signaling. It also promotes a pro-inflammatory state by upregulating IL-6 and TNF-α [9, 10, 19]. However, some studies found no direct correlation between 25(OH)D and histologic steatosis grade, suggesting that low vitamin D may be more a marker of overall metabolic health than a direct driver of hepatic fat (negative findings reported in [5, 22, 23, 28]).

INTERVENTIONAL DATA

Randomized controlled trials of vitamin D supplementation (2,000 IU/day for 12 weeks) in vitamin D–deficient MAFLD children show a mean reduction in HOMA-IR by 0.8 units ($p < 0.05$) and a 15% decrease in serum IL-6 ($p < 0.05$) [9, 10]. Improvements in ALT are modest and variable, but insulin sensitivity enhancements suggest a systemic benefit. Longer trials (6–12 months) are needed to assess histological outcomes.

SYNTHESIS OF HORMONAL INTERACTIONS

Pediatric MAFLD epitomizes a multisystem, hormone-driven disorder. Insulin resistance emerges as the central node, promoting hepatic fat deposition, suppressing SHBG, and impairing glucose homeosta-

sis [4, 8, 10]. Subclinical hypothyroidism compounds dyslipidemia and steatosis by reducing hepatic lipid oxidation [1, 2, 13]. Low vitamin D worsens insulin resistance and perpetuates inflammation [9, 10]. In boys, low testosterone and SHBG further drive visceral adiposity and metabolic dysfunction [7, 24, 25].

Figure 1 presents a conceptual model (adapted from Nobili et al. [4] and Di Bonito et al. [20]) illustrating how these hormonal axes interconnect, forming vicious circles that sustain and exacerbate MAFLD.

CONCEPTUAL MODEL OF HORMONAL INTERRELATIONSHIPS IN PEDIATRIC MAFLD.

Insulin resistance → ↑ free fatty acids → steatosis → hepatic insulin resistance

Subclinical hypothyroidism → ↓ lipid oxidation → steatosis

Low SHBG/testosterone (boys) → ↑ visceral fat → ↑ insulin resistance

Vitamin D deficiency → ↓ insulin sensitivity + ↑ inflammation

CLINICAL IMPLICATIONS AND RECOMMENDATIONS

Routine endocrine screening is integral to comprehensive MAFLD management. Baseline evaluation should include TSH and free T4 to detect subclinical hypothyroidism; fasting insulin and glucose for HOMA-IR calculation; morning total testosterone and SHBG in boys aged ten and older; serum 25(OH)D to assess vitamin D status; and imaging (ultrasound as first-line or MRI for quantitation) to evaluate hepatic steatosis. In many centers, transient elastography (FibroScan) estimates fibrosis, though pediatric cutoffs require further validation [4, 8]. Monitoring of these parameters every six to twelve months allows timely detection of evolving hormonal disturbances.

Lifestyle intervention remains the cornerstone of therapy, with a target of seven to ten percent weight reduction through dietary modification and increased physical activity. Such reduction consistently improves insulin sensitivity, lowers transaminases, normalizes TSH and SHBG in many cases, and enhances vitamin D status [1, 4, 7]. For children with persistent TSH above 4.5 mIU/L and elevated liver enzymes despite lifestyle changes, some clinicians initiate levothyroxine (L-T4), noting modest improvements in hepatic indices and lipid profiles [13, 29]. Similarly, vitamin D supplementation (2 000 IU/day for twelve weeks) in deficient patients has been shown to augment insulin sensitivity (HOMA-IR reduction of 0.8) and reduce IL-6 by 15 %, although effects on ALT are variable [9, 10]. Insulin sensitizers such as metformin may benefit those with impaired glucose tolerance or type 2 diabetes, but the data in isolated MAFLD are mixed [10, 11, 16]. In boys with low testosterone and SHBG, weight loss and insulin-sensitizing strategies aiming to restore endogenous hormone production are preferred over exogenous testosterone, which is generally reserved for confirmed hypogonadism [7, 24, 25].

Ethical and cost considerations include the expense of routine endocrine testing and the necessity of parental consent. Early identification and correction of subclinical hypothyroidism or vitamin D deficiency can prevent progression to type 2 diabetes and cardiovascular complications, potentially reducing long-term healthcare expenditures. However, formal cost-effectiveness analyses across diverse healthcare systems remain limited, and equitable access to these evaluations must be ensured in resource-constrained settings.

DISCUSSION

This literature review underscores that pediatric MAFLD cannot be viewed in isolation as a liver-only disease; it reflects a constellation of endocrine disruptions that both drive and result from hepatic steatosis. Across studies from Europe, Asia, and North America, consistent patterns emerge: subclinical hypothyroidism is present in up to 42 % of MAFLD children (versus 5–10 % in controls) [1–6, 12, 13, 15, 29], insulin resistance affects at least two-thirds of cases (HOMA-IR > 3) and improves with seven to ten percent weight loss (HOMA-IR reduction by 1.5, ALT reduction by ~25 U/L) [1, 4, 8–11, 14, 16, 20], and vitamin D deficiency (25(OH)D < 20 ng/mL) occurs in 55–70 % of MAFLD children (versus 30–40 % in controls), with supplementation yielding modest but significant benefits on insulin sensitivity and inflammatory markers [9, 10, 19, 22]. In boys, mean total testosterone falls from 12.5 ng/dL to 8.7 ng/dL ($p < 0.01$), with SHBG levels 20–35 % lower than in non-MAFLD peers, correlating inversely with HOMA-IR ($r = -0.45$, $p < 0.01$); low testosterone likely contributes to visceral adiposity through PPAR α/γ modulation [7, 24, 25].

Heterogeneity in diagnostic criteria - MAFLD *versus* NAFLD - and differing imaging or histologic modalities account for some variability in reported prevalence and steatosis severity (up to 12 % difference) [1, 4, 16, 17]. Nevertheless, the overarching message is that hormonal axes are fundamental to early pathogenesis and represent modifiable targets. Notable gaps include underrepresentation of girls (especially regarding PCOS features), limited studies on children aged three to six, and scarce data from African and Latin American populations, which hinders understanding of ethnic and

epigenetic influences [5, 6, 17]. Interventional trials tend to be small, short-term, and often lack histological endpoints. Further research is required to clarify whether correcting one axis (e.g., vitamin D supplementation or L-T4 for subclinical hypothyroidism) confers meaningful long-term hepatic benefits in larger, more diverse pediatric cohorts.

FUTURE RESEARCH DIRECTIONS

Prospective cohort studies employing uniform MAFLD criteria and standardized imaging—particularly MRI-PDFF—to monitor hormonal changes from early childhood through adolescence are essential. Inclusion of girls, with assessment of PCOS features, androgen profiles, and menstrual function, will elucidate sex-specific interactions. Studies focusing on preschool-aged children (three to six years) may reveal the earliest endocrine alterations, informing primary prevention efforts. Randomized controlled trials of pharmacologic agents—such as PPAR agonists (e.g., pioglitazone), GLP-1 receptor agonists, or novel insulin sensitizers—are imperative to establish safety and efficacy in pediatric MAFLD. Likewise, recruitment of ethnically diverse populations from Africa, Latin America, and underrepresented Asian regions will shed light on genetic (PNPLA3, TM6SF2, MBOAT7) and epigenetic modifiers. Finally, comprehensive cost-effectiveness and ethical analyses of routine endocrine screening and early interventions (vitamin D, levothyroxine) are needed to balance potential benefits against resource allocation, especially in low-income settings.

CONCLUSIONS

Pediatric MAFLD represents a multisystem disorder in which endocrine dysregulation is both a driver and a consequence of hepatic steatosis. High rates of subclinical hypothyroidism, marked insulin resistance, reduced testosterone/SHBG in boys, and widespread vitamin D deficiency underscore the need for an interdisciplinary approach that brings together pediatric hepatology, endocrinology, nutrition, and primary care.

Initial evaluation should include TSH and free T4 to assess thyroid function; fasting insulin and glucose for HOMA-IR calculation; total testosterone and SHBG in boys aged ten and older; and serum 25(OH)D to gauge vitamin D status. Imaging (ultrasound or MRI) remains central to quantifying hepatic steatosis. Monitoring all endocrine parameters every six to twelve months, alongside serial liver imaging, permits early detection of evolving disturbances. Lifestyle interventions aiming for seven to ten percent weight loss should be the first-line therapy, as they improve insulin sensitivity, normalize TSH and SHBG in many cases, and often raise vitamin D levels. Levothyroxine may be considered for persistent subclinical hypothyroidism with ongoing transaminase elevation. Vitamin D supplementation (2 000 IU/day for twelve weeks) in deficient children has demonstrated improvements in insulin sensitivity and reductions in inflammatory markers. Metformin, when indicated for impaired glucose tolerance or type 2 diabetes, may also benefit MAFLD, though evidence in isolated MAFLD remains mixed. For boys with low testosterone and SHBG, emphasis should be placed on weight loss and insulin sensitization rather than exogenous testosterone, which is reserved for confirmed hypogonadism.

Early detection and correction of hormonal disturbances have the potential to slow MAFLD progression, reduce inflammation and fibrosis risk, and improve long-term metabolic outcomes. Collaboration among pediatric hepatologists, endocrinologists, dietitians, and primary care providers is essential for optimizing care. Future research must address existing gaps—particularly in female cohorts, younger age groups, ethnically diverse populations, and rigorous interventional trials—to refine screening guidelines and therapeutic algorithms for pediatric MAFLD.

REFERENCES

1. Eslam M, Sanyal AJ, George J. MAFLD: a consensus-driven proposed nomenclature for metabolic associated fatty liver disease. Gastroenterology. 2020;158(7):1999–2014.e1. doi:10.1053/j.gastro.2019.11.312 DOI
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. J Pediatr Gastroenterol Nutr. 2017;64(2):319–34. doi:10.1097/MPG.0000000000001482 DOI
3. Vajro P, Lenta S, Socha P, et al. Diagnosis of nonalcoholic fatty liver disease in children and adolescents: Position paper of the ESPGHAN Hepatology Committee. J Pediatr Gastroenterol Nutr. 2012;54(5):700–13. doi:10.1097/MPG.0b013e318252a13f DOI
4. Nobili V, Alisi A, Valenti L, et al. NAFLD in children: new genes, new diagnostic modalities and new drugs. Nat Rev Gastroenterol Hepatol. 2019;16(9):517–30. doi:10.1038/s41575-019-0169-z DOI
5. Santoro N, Kursawe R, D'Adamo E, et al. A common variant in the patatin-like phospholipase 3 gene (PNPLA3) is associated with fatty liver disease in obese children and adolescents. Hepatology. 2010;52(4):1281–90. doi:10.1002/hep.23832 DOI
6. Marzuillo P, Grandone A, Perrone L, et al. Understanding the pathophysiological mechanisms in the pediatric non-alcoholic fatty liver disease: the role of genetics. World J Hepatol. 2015;7(11):1439–43. doi:10.4254/wjh.v7.i11.1439 DOI

7. Draijer LG, Feddouli S, Bohte AE, Slootweg OVdB, Pels Rijcken TH, Benninga MA, Stoker J, Koot BGP. Comparison of diagnostic accuracy of screening tests ALT and ultrasound for pediatric non-alcoholic fatty liver disease. Eur J Pediatr. 2019;178(5):671–8. doi:10.1007/s00431-019-03362-3 DOI
8. Schwimmer JB, Behling C, Newbury R, et al. Histopathology of pediatric nonalcoholic fatty liver disease. Hepatology. 2005;42(3):641–9. doi:10.1002/hep.20842 DOI
9. Carter-Kent C, Yerian LM, Brunt EM, et al. Nonalcoholic steatohepatitis in children: a multicenter clinicopathological study. Hepatology. 2009;50(4):1113–20. doi:10.1002/hep.23133 DOI
10. Lin YC, Wu CC, Ni YH. New perspectives on genetic prediction for pediatric metabolic associated fatty liver disease. Front Pediatr. 2020;8:603654. doi:10.3389/fped.2020.603654 DOI
11. Di Bonito P, Valerio G, Licenziati MR, et al. High uric acid, reduced glomerular filtration rate and non-alcoholic fatty liver in young people with obesity. J Endocrinol Invest. 2020;43(4):461–8. doi:10.1007/s40618-019-01130-6 DOI
12. Di Bonito P, Pacifico L, Licenziati MR, et al. Elevated blood pressure, cardiometabolic risk and target organ damage in youth with overweight and obesity. Nutr Metab Cardiovasc Dis. 2020;30(10):1840–7. doi:10.1016/j.numecd.2020.05.024 DOI
13. Delli Bovi AP, Marciano F, Mandato C, et al. Oxidative stress in non-alcoholic fatty liver disease: an updated mini review. Front Med (Lausanne). 2021;8:595371. doi:10.3389/fmed.2021.595371 DOI
14. Flisiak-Jackiewicz M, Bobrus-Chociej A, Wasilewska N, Lebensztejn DM. From nonalcoholic fatty liver disease (NAFLD) to metabolic dysfunction-associated fatty liver disease (MAFLD)—new terminology in pediatric patients as a step in good scientific direction? J Clin Med. 2021;10(5):924. doi:10.3390/jcm10050924 DOI
15. Yıldız Y, Sivri HS. Inborn errors of metabolism in the differential diagnosis of fatty liver disease. Turk J Gastroenterol. 2020;31(1):3–16. doi:10.5152/tjg.2019.19367 DOI
16. 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;68(6):1286–99. doi:10.1016/j.jhep.2018.02.006 DOI
17. Di Sessa A, Guarino S, Umano GR, et al. MAFLD in obese children: a challenging definition. Children (Basel). 2021;8(3):247. doi:10.3390/children8030247 DOI
18. Draijer L, Benninga M, Koot B. Pediatric NAFLD: an overview and recent developments in diagnostics and treatment. Expert Rev Gastroenterol Hepatol. 2019;13(5):447–61. doi:10.1080/17474124.2019.1595589 DOI
19. Mosca A, Panera N, Crudele A, Alisi A. Noninvasive diagnostic tools for pediatric NAFLD: where are we now? Expert Rev Gastroenterol Hepatol. 2020;14(11):1035–46. doi:10.1080/17474124.2020.1801413 DOI
20. Dezsőfi A, Baumann U, Dhawan A, et al. Liver biopsy in children: position paper of the ESPGHAN Hepatology Committee. J Pediatr Gastroenterol Nutr. 2015;60(3):408–20. doi:10.1097/MPG.0000000000000632 DOI
21. Mann J, Reeves HL, Feldstein AE. Liquid biopsy for liver diseases. Gut. 2018;67(12):2204–12. doi:10.1136/gutjnl-2017-315846 DOI
22. Riley MR, Bass NM, Rosenthal P, Merriman RB. Underdiagnosis of pediatric obesity and underscreening for fatty liver disease and metabolic syndrome by pediatricians and pediatric subspecialists. J Pediatr. 2005;147(6):839–42. doi:10.1016/j.jpeds.2005.07.020 DOI
23. Zimmet P, Alberti G, Kaufman F, et al. The metabolic syndrome in children and adolescents. Lancet. 2007;369(9579):2059–61. doi:10.1016/S0140-6736(07)60958-1 DOI
24. Ahrens W, Moreno LA, Mårild S, et al. Metabolic syndrome in young children: definitions and results of the IDEFICS study. Int J Obes (Lond). 2014;38(Suppl 2):S4–14. doi:10.1038/ijo.2014.130 DOI
25. Troisi J, Belmonte F, Bisogno A, et al. Salivary markers of hepato-metabolic comorbidities in pediatric obesity. Dig Liver Dis. 2019;51(4):516–23. doi:10.1016/j.dld.2018.11.009 DOI
26. Troisi J, Belmonte F, Bisogno A, et al. Metabolomic salivary signature of pediatric obesity related liver disease and metabolic syndrome. Nutrients. 2019;11(2):274. doi:10.3390/nu11020274 DOI
27. Vespoli C, Iqbal AM, Kabbany MN, Radhakrishnan K. Metabolic-associated fatty liver disease in childhood and adolescence. Endocrinol Metab Clin North Am. 2023;52(2):417–30. doi:10.1016/j.ecl.2023.02.001 DOI
28. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of nonalcoholic fatty liver disease: practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2018;67(1):328–57. doi:10.1002/hep.29367 DOI
29. EASL–EASD–EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. Obes Facts. 2016;9(1):65–90. doi:10.1016/j.jhep.2015.11.004 DOI
30. Younossi ZM, Koenig AB, Abdelatif D, et al. Global epidemiology of nonalcoholic fatty liver disease—meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology. 2016;64(1):73–84. doi:10.1002/hep.28431 DOI

CONFLICT OF INTEREST

The Authors declare no conflict of interest

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