Health Science Reports

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ORIGINAL RESEARCH OPEN ACCESS

Web of Science-Based Visualization of Metabolic Dysfunction-Associated Fatty Liver Disease in Pediatric and Adolescent Populations: A Bibliometric Study

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Received: 4 September 2024 | **Revised:** 31 December 2024 | **Accepted:** 14 January 2025

Funding: The authors received no specific funding for this work.

Keywords: adolescents | children | MAFLD | visual analysis

ABSTRACT

Background and Aims: The prevalence of metabolism-associated fatty liver disease (MAFLD) in children is on the rise. This study employs visualization and analysis to evaluate the research implications, current advancements, and emerging trends in pediatric MAFLD, with the aim of elucidating its pathogenesis and informing the development of clinical treatment strategies.

Methods: Using visualization software, we conducted a visual analysis and mapping of the journal distribution, leading institutions, prominent authors, annual publication trends, and keyword frequencies among the 1179 scholarly articles retrieved from the Web of Science Core Collection for this study.

Results: The overall publication volume demonstrated an upward trend, with a total of 200 journals, contributions from 63 countries, 882 research institutions, and 5605 authors involved, including 84 who were identified as core authors. The main research team is led by Nobili, Valerio. The main research institutions are concentrated in Italy, the United States, and China. A total of 473 keywords were included, and the keywords with high frequency and medium centricity are insulin resistance, metabolic syndrome, children, steatohepatitis, adolescents, hepatic steatosis, nash, obesity, diagnosis, and fibrosis, which resulted in six keyword clusters.

Conclusion: MAFLD represents a significant public health concern. Research on children and adolescents with MAFLD continues to attract high interest. Noninvasive diagnostic methods, pathogenesis (intestinal microbiota research), disease prediction (gene research) are current research hotspots.

1 | Introduction

Nonalcoholic fatty liver disease (NAFLD) is a metabolic stress liver injury that is closely linked to genetic susceptibility and insulin resistance (IR) [1]. The disease progresses from simple steatosis to nonalcoholic steatohepatitis (NASH) with hepatocellular injury, necroinflammation, and activation of hepatic fibrosis, and ultimately progresses to end-stage liver disease [2], which is thought to be the most prevalent cause of chronic liver disease globally [3]. The terminology for NAFLD has sparked controversy recently. In 2020, Dr. Eslam M.'s team proposed renaming it to metabolism-associated fatty liver disease (MAFLD), highlighting the role of metabolic risks like type 2 diabetes mellitus (T2DM) and obesity [4]. It is estimated that

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between 7.6% and 9.6% of children globally have MAFLD, and the prevalence of obese children and adolescents has risen significantly to 34% [5].

In recent years, the prevalence of obesity has continued to rise globally. The World Health Organization estimates that the prevalence of overweight or obesity in children and adolescents has risen sharply from 8% in 1990 to 20% in 2022. By 2022, approximately 340 million adolescents and 39 million children were obese worldwide [6]. Rising obesity rates increase the risk of dyslipidemia in children and adolescents, and liver fat content in MAFLD is also strongly associated with the severity of metabolic diseases such as obesity and T2DM [7]. Thus, MAFLD in children and adolescents has emerged as an important public health challenge and increases the risk of disease progression in adulthood. Identifying and intervening early in MAFLD can reduce long-term morbidity and mortality from the disease. Several diagnostic methods are available, such as ultrasonography, liver biopsy, abdominal computed tomography (CT), and magnetic resonance imaging (MRI). However, ultrasonography alone may have limited accuracy, liver biopsy is invasive, CT carries a risk of radiation exposure, and MRI is costly and time-consuming, making them unsuitable for disease screening in children and adolescents.

Bibliometrics, first coined by Alan Pritchard in 1969, has played an important role in understanding the research hotspots and trends in specific fields, the influence of academic journals, the academic status of different countries and regions, and the direction of researchers' work. The current global literature analysis on MAFLD in children and adolescents spans various disciplines such as pediatrics, hepatology, nutrition, and endocrinology. Bibliometric studies can help promote communication and collaboration between different disciplines and increase awareness of MAFLD. This paper provides a comprehensive and systematic account of the current status and future trends of MAFLD by mapping knowledge using CiteSpace and VOSviewer software.

2 | Information and Methodology

2.1 | Data Collection and Organization

The Web of Science Core Collection (WOSCC), which comprises the Science Citation Index Expanded (SCIE), Current Chemical Reactions, and Index Chemistry databases, provided the research literature for this work. The search was conducted from January 1, 1985, to January 12, 2024, using an advanced retrieval technique. And the search strategy was: (TS = ("nonalcoholic fatty liver disease") OR TS = ("NAFLD") OR TS = ("nonalcoholic steatohepatitis") OR TS = ("NASH") OR TS = ("MAFLD") OR TS = ("metabolic-dysfunction-associated fatty liver disease") OR TS = ("MASH") OR TS = ("Metabolic Steatohepatitis") OR TS = ("MASLD") OR TS = ("metabolic dysfunction-associated steatotic liver disease") OR TS = ("metabolic dysfunction associated steatotic liver disease")) AND (TS = ("children") OR TS = ("pediatrics") OR TS = ("pediatrics") OR TS = ("adolescen*") OR TS = ("teenager") OR TS = ("youth")), with the type of literature limited to Article and the language limited to English, yielding 1469 articles. A third party decided whether a decision could be made after two researchers manually sorted the literature according to the inclusion and exclusion criteria. The research methodology described above yielded a total of 1179 documents.

2.2 | Selection Standards for Literature

Inclusion criteria: (1) studies focus on MAFLD in children and adolescents; (2) research encompassed a range of study designs, including cross-sectional, prospective, retrospective, cohort, time series, case studies, and randomized controlled trials.

Exclusion criteria: (1) articles withdrawn from databases; (2) relevant reviews, conference papers, letters to the editor, abstracts, and other nonfull-text publications.

2.3 | Data Specification

After screening, the manual data are standardized as follows: the country and region "Wales," "Scotlandm," "North Ireland," and "England" are unified into "UK," and "Taiwan" is unified into "Peoples R China"; institutions "Bambino Gesu Childrens Hosp IRCCS" and "IRCCS" are unified as "IRCCS Bambino GESU"; keywords "insulin resistance" and "insulin-resistance" are unified as "insulin-resistance."

2.4 | Research Methodology

The research data were exported to plain text files, and the related literature was analyzed and visualized in detail using CiteSpace 6.2.R7 (64-bit) Advanced and VOSviewer 1.6.18 software. In CiteSpace, the time span of the analysis was set from 2000 to 2024, with each year as a time slice. In "Selection Criteria" selection, the threshold value of "g-index" is set to 20. In the "node types" selection, focus on "keyword". "Pathfinder," "Pruning sliced network," and "Pruning the merged network" are used to optimize the visualization results. In VOSviewer, the VOS clustering algorithm is applied to analyze the co-occurrence of country, institution, and author collaborations to generate the corresponding relationship graphs.

3 | Results and Analysis

3.1 | Research Process

Annual publication analysis indicates increasing global interest in pediatric MAFLD research (Figure 1): (1) In 2000, the first pediatric NASH paper was published, noting that chronic liver diseases like NASH can impact all ages, including nondrinkers, despite NAFLD being a contentious term then [8]. (2) Since 2005, there's been an uptick in publications on childhood fatty liver disease, indicating increased awareness of inadequate screening, particularly in detecting hepatomegaly in obese children [9]. (3) From 2013 to 2022, pediatric MAFLD publications surged, peaking in 2021, emphasizing noninvasive

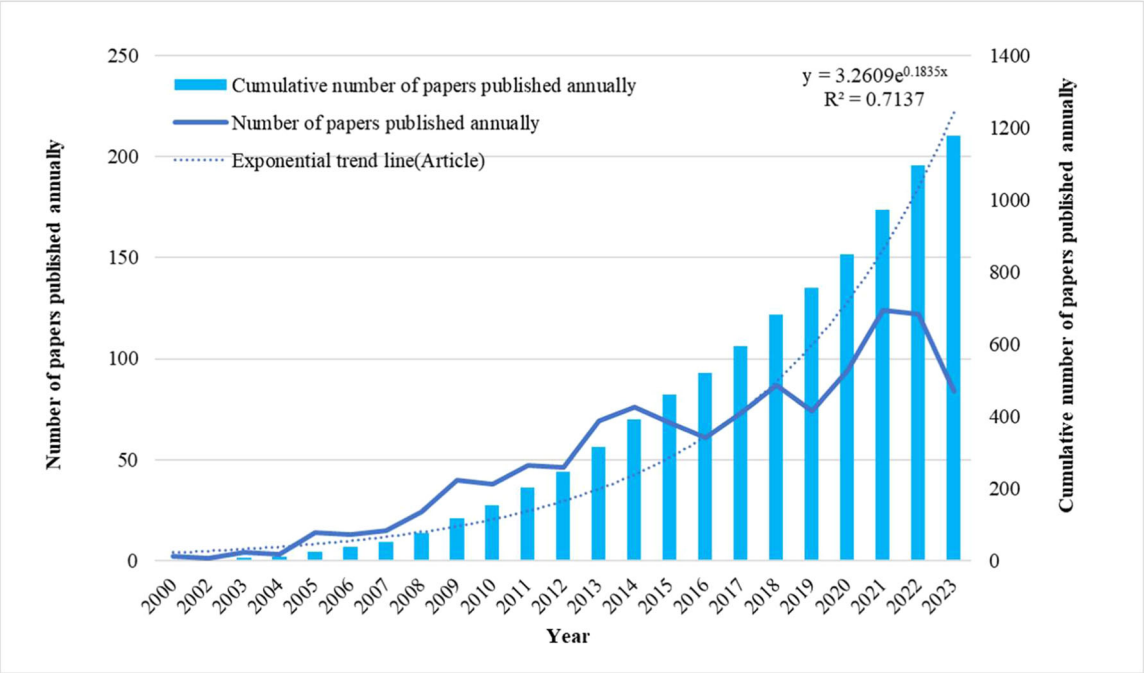

FIGURE 1 | Annual publication volume.

prediction and diagnostic methods, ultrasound techniques, and MAFLD's association with multi-system disorders such as IR, metabolic syndrome (MetS), hypopituitarism, and obstructive sleep apnea. (4) In 2023, MAFLD publications dropped from 2022s peak, suggesting ongoing challenges in predictive diagnosis and medication use for children, with no significant progress in these areas.

3.2 | Journal References Research

The 200 journals that comprise this study cover molecular and cellular biology, gastroenterology, hepatology, endocrinology, nutrition, and many other fields. The top 10 journals in terms of publications are: *Journal of Pediatric Gastroenterology and Nutrition*, *Pediatric Obesity*, *Hepatology*, *Journal of Pediatrics*, *Journal of Pediatric Endocrinology and Metabolism*, *PLoS One*, *World Journal of Gastroenterology*, *Frontiers in Endocrinology*, *Journal of Clinical Endocrinology and Metabolism*, *Nutrients*.

The journal with the highest number of articles was the American *Journal of Pediatric Gastroenterology and Nutrition* ($N = 69$). *Pediatric Obesity* in the UK ($N = 44$) and *Hepatology* in the USA ($N = 22$) followed closely behind. (2) American *Hepatology* (IF = 14.000), a leading international journal in the field of liver disease and a member of the prestigious international database SCIE, had the highest impact factor among the top ten journals. In second place was the journal *Nutrients* (IF = 5.900) from Switzerland.

3.3 | Key Countries and Institutions

The study involves 63 countries and 882 institutions (Table 1). The USA leads in publications ($N = 416$), followed by Italy ($N = 233$) and China ($N = 141$). Research is concentrated in Western countries, with less attention in developing nations, linked to economic development and lifestyles. Most leading institutions are American, except for Italy's Sapienza University Rome and IRCCS Bambino Gesu.

Figure 2a,b depict research country and institution collaborations (≥ 1 frequency for countries, ≥ 9 for institutions) using VOSviewer software:

(1) From the timeline: Pediatric MAFLD research started earlier in developed countries, initially in Europe and the United States (including the USA, UK, and Italy), then expanded to Asia (including the China, Korea, Malaysia, and Jordan) and Africa (including the South Africa, Morocco, and Nigeria).

(2) Multinational research collaborations are emerging, led by the United States and Italy. Studies indicate that low-sugar diets can help prevent MAFLD in Hispanic children [10], and research has also reviewed the effects of nutraceuticals on MAFLD parameters [11] and identified genes/pathways associated with the disease in multiethnic pediatric cohorts [12]. Second, Italy and the UK collaborate closely on studies comparing lipidomic profiles in pediatric and adult fatty liver diseases, which show similar pathways but different lipid profiles in children [13]. They also explore life-span/healthspan-related genetic polymorphisms in MAFLD, finding IL-6 rs1800795 and ANRIL rs1556516 genes significant, but requiring larger studies for confirmation [14].

(3) Institutional collaboration is notable between IRCCS Bambino Gesu and Sapienza University Rome, with key studies including the predictive value of high blood uric acid in fatty liver disease risk [15] and the genetic and environmental influences of MAFLD and β-Klotho proteins' protective role in hepatocytes [16].

TABLE 1 | The top 10 countries/institutions.

Rank	Institution	Number	Rank	Country	Number
1	IRCCS Bambino Gesu	144	1	USA	416
2	University of California System	92	2	Italy	233
3	University of California San Diego	78	3	Peoples R China	141
4	Sapienza University Rome	61	4	UK	77
5	Cincinnati Children's Hospital Medical Center	55	5	Turkiye	62
6	Rady Childrens Hospital San Diego	49	6	Germany	55
7	Emory University	45	7	Canada	49
8	Johns Hopkins University	43	8	South Korea	42
9	University System of Ohio	41	9	Poland	41
10	Columbia University	40	10	Australia	35

3.4 | Lead Authors and Teams

The study involved 5605 authors, with Italy and the UK taking the lead in top publications (refer to Table 2). Nobili, Valerio, and Irccs Bambino Gesu in Italy were most prolific. Price's Law identified 84 core authors with ≥ 9 publications, forming teams with strong internal but limited external collaboration due to different disciplines.

Figure 3, using VOSviewer, maps author collaborations (≥ 9 frequency) to visualize core authors' collaboration levels and academic impact. It depicts six teams (color-coded), each with primarily internal focus and limited inter-team collaboration:

(1) Nobili, Valerio, as a core author, facilitates communication and collaboration across teams, engaging in extensive research including histological, immunohistochemical, and immunofluorescence studies on liver visceral adipose tissue and liver specimens from obese MAFLD adolescents post-gastrectomy, which uncovered a distinctive adipose tissue-fatty liver interaction in pediatric patients [17]. His comparison of North American and European MAFLD screening strategies suggests the former may overlook at-risk children [18], and he found a higher prevalence of abnormal glucose tolerance in biopsied MAFLD children versus non-MAFLD peers [19].

(2) The Mouzaki, Marialena team is emerging with research on α1 antitrypsin risk variants in pediatric MAFLD [20] and developing a clinical prediction model for fibrosis in MAFLD, known as “Fibrosis in Pediatric NAFLD” or “Fibro-PeN” for short [21]. The Di Sessa, Anna team, a newly emerged group, highlights that COVID-19 adversely affects cardiac metabolic health in children with chronic kidney disease who have MAFLD [22], necessitating careful management, and notes the TM6SF2 E167K mutation's protective effect against subclinical hypothyroidism in obese MAFLD patients [23].

3.5 | Research Basis

Table 3 lists the top 10 co-cited MAFLD research articles in children. Some of the second and seventh most cited articles were published in *Hepatology*, and the fifth and eighth most cited articles were published in *Journal of Pediatric Gastroenterology and Nutrition*. *Prevalence of fatty liver in children and adolescents*, by far the most cited article ($N = 317$), focused on 742 children aged 2–19 years who were autopsied between 1993 and 2003, with significant differences in the prevalence of fatty liver by race and ethnicity, and the obese children had the highest rates of fatty liver [24].

3.6 | Primary Research Directions

3.6.1 | Keyword Co-Occurrence Analysis

Key words serve as the article's central theme and essence, providing a concise summary of the primary focus and direction of the study. Examining keyword distribution and frequency helps researchers understand the focus and latest developments in the field. The top 10 keywords in this study: MAFLD, insulin-resistance, fatty liver disease, metabolic syndrome, children, prevalence, steatohepatitis, adolescents, hepatic steatosis, and NASH. Figure 4 presents a keyword co-occurrence graph with 473 nodes and a network density of 0.0085. The purple nodes indicate nine keywords with mediator centrality ≥ 0.1, including: blood-pressure, adipose-tissue, cardiovascular risk, adiponectin, body-composition, hepatic-fibrosis, disease, follow up, and expression.

Figure 4 is characterized by the following features: (1) Co-occurrence relations are mainly focused on insulin-resistance, metabolic syndrome, steatohepatitis, hepatic steatosis, NASH, obesity, diagnosis, fibrosis, and other high-frequency word nodes. (2) Mediated centrality is a key indicator of the importance of nodes in a knowledge graph. blood-pressure has the highest mediated centrality and more connecting lines than other nodes and is the most important node in the network. “Blood-pressure” has the highest mediational centrality and more lines in the graph, and is an important “link” between “BMI,” “uric acid,” “cardiovascular risk-factors” and “insulin sensitivity”. It is also associated with MAFLD risk factors such as obesity, IR, cardiovascular risk factors, carotid atherosclerosis and carotid intima-media thickness.

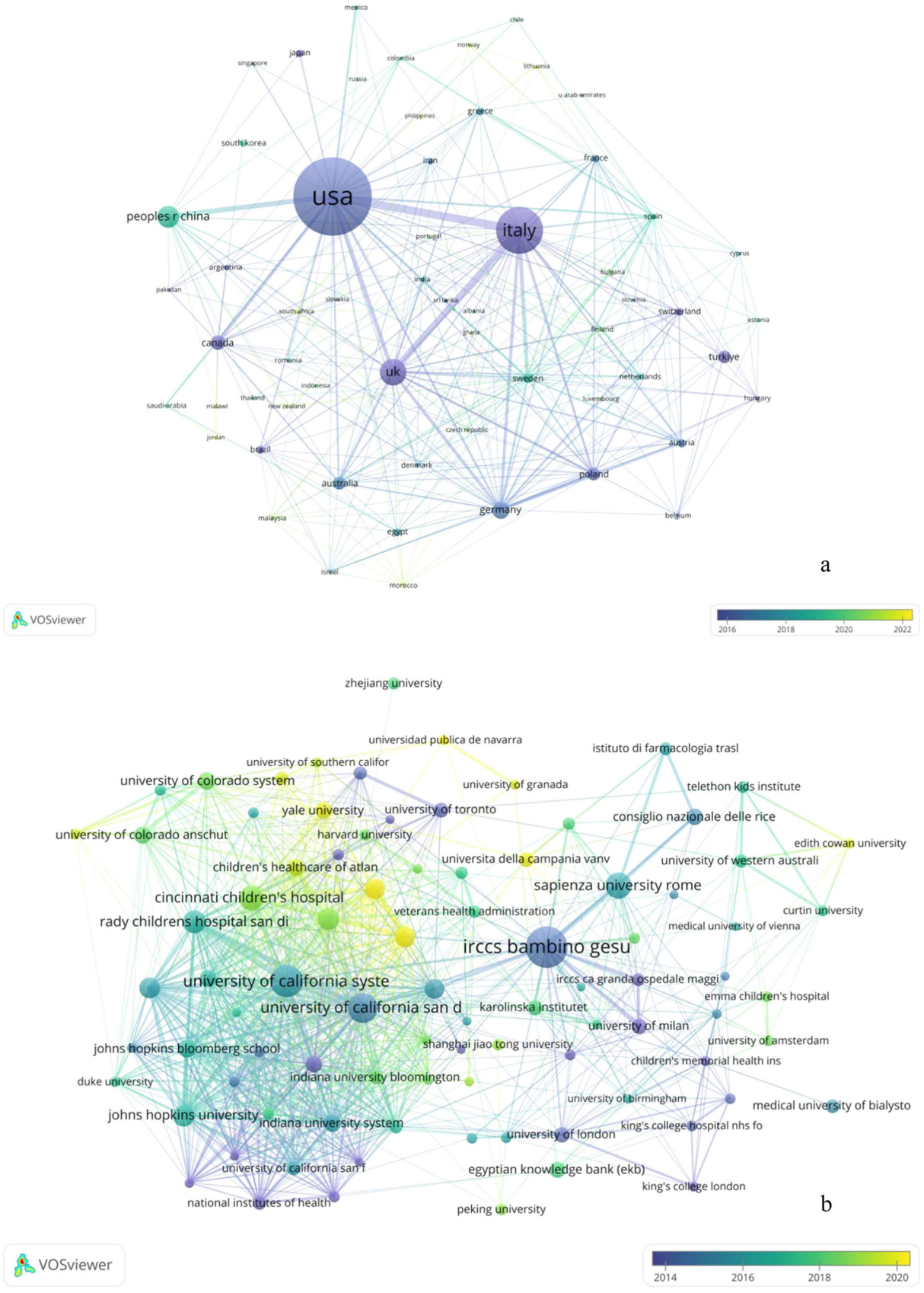

FIGURE 2 | (a) Collaborative mapping of major issuing countries. (b) Collaborative mapping of major issuing organizations.

TABLE 2 | The top 10 authors.

Rank	Author	Number	Institution
1	Nobili, Valerio	124	Irccs Bambino Gesu
2	Alisi, Anna	87	Irccs Bambino Gesu
3	Schwimmer, Jeffrey B.	58	University of California San Diego, Rady Childrens Hospital San Diego
4	Lavine, Joel E.	43	Columbia University
5	De Vito, Rita	37	Irccs Bambino Gesu
6	Vos, Miriam B.	37	Emory University
7	Mosca, Antonella	36	Irccs Bambino Gesu
8	Xanthakos, Stavra A.	33	Cincinnati Children's Hospital Medical Center
9	Mouzaki, Marialena	29	Cincinnati Children's Hospital Medical Center
10	Alkhouri, Naim	28	Cleveland Clinic Foundation, University of Texas Health Science Center at San Antonio

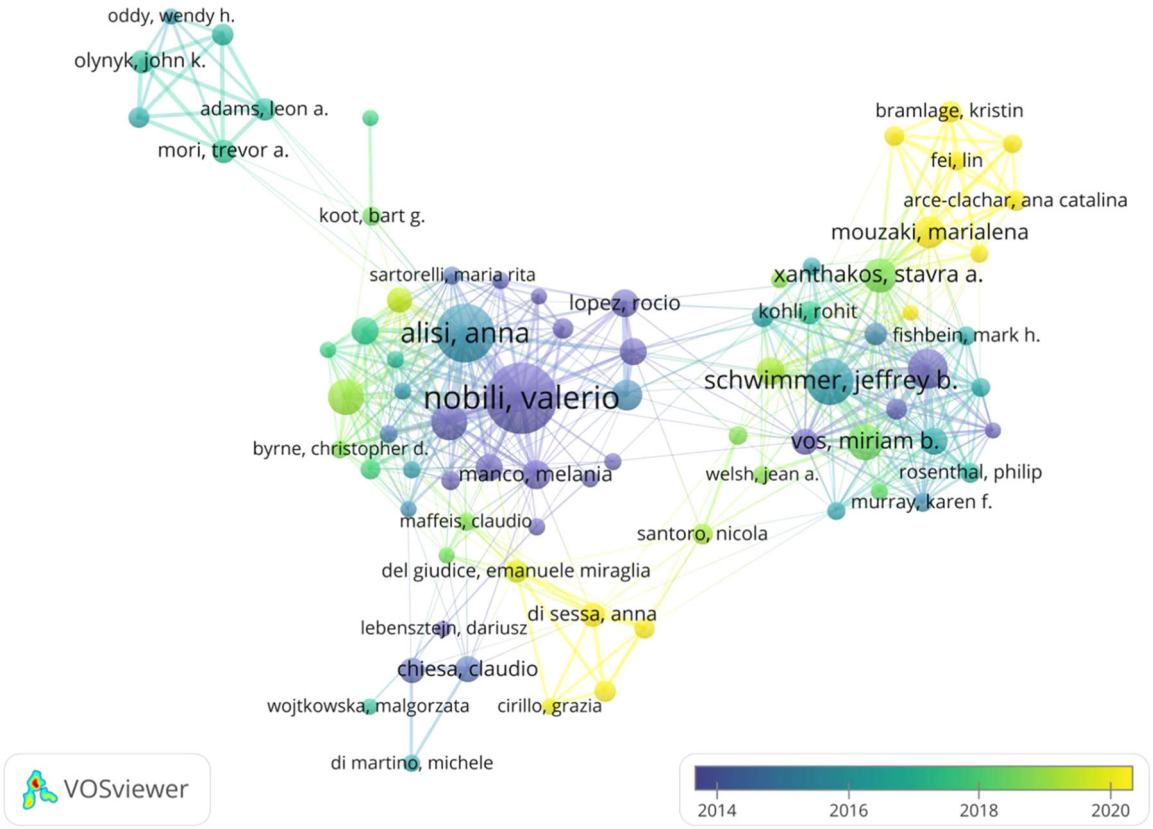

FIGURE 3 | Core author collaboration mapping.

3.6.2 | Keyword Clustering Analysis

Figure 5a, through keyword co-occurrence analysis, highlights six research clusters in MAFLD: (1) cluster 1, focuses on MAFLD diagnosis, encompassing noninvasive methods and expert-recommended guidelines; (2) cluster 2, is epidemiological, examining MAFLD trends, particularly its association with obesity; (3) cluster 3, concentrates on obese children with MAFLD, examining BMI and hyperinsulinemia; (4) cluster 4, emphasizes genetic research into the genetic aspects of MAFLD; (5) cluster 5, provides a scientific basis for clinical practice, covering MAFLD's pathophysiology and therapeutic approaches; (6) cluster 6, investigates MAFLD risk factors like insulin resistance and metabolic abnormalities.

Noninvasive diagnostic techniques are a key focus of MAFLD research (Figure 5b), with studies on gut microbiota and genetics offering insights for treatment and guiding future research directions.

TABLE 3 | Top 10 co-cited articles.

Rank	Article title	First author	Vintages	Citations
1	Prevalence of fatty liver in children and adolescents	Schwimmer, JB	2006	317
2	Design and validation of a histological scoring system for nonalcoholic fatty liver disease	Kleiner, DE	2005	282
3	Homeostasis model assessment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man	Matthews, DR	1985	216
4	The natural history of non-alcoholic fatty liver disease in children: a follow-up study for up to 20 years	Feldstein, AE	2009	184
5	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)	Vos, MB	2017	184
6	The Prevalence of Non-Alcoholic Fatty Liver Disease in Children and Adolescents: A Systematic Review and Meta-Analysis	Anderson, EL	2015	167
7	Histopathology of pediatric nonalcoholic fatty liver disease	Schwinnner, JB	2005	151
8	Diagnosis of Nonalcoholic Fatty Liver Disease in Children and Adolescents: Position Paper of the ESPGHAN Hepatology Committee	Vajro, P	2012	148
9	Establishing a standard definition for child overweight and obesity worldwide: international survey	Cole, TJ	2000	120
10	Obesity, insulin resistance, and other clinicopathological correlates of pediatric nonalcoholic fatty liver disease	Schwimmer, JB	2003	116

4 | Discussion

This study shows an increasing trend in the number of publications, with the majority of authors and published journals coming from Italy, the USA, and the countries most involved in international partnerships. Nobili, Valerio is the most prolific author, while Irccs Bambino Gesu is the most prolific institution. Keyword analysis revealed six clusters, focusing on pathogenesis (gut microbiota), disease prediction (genetics), and noninvasive diagnostics as research priorities.

4.1 | Epidemiology

The rise in MAFLD among children and adolescents correlates with increased obesity and metabolic factors, though data are limited. The risk of death in this group is unclear, but mortality rates are higher in children with MAFLD compared to adults.

IR is associated with MAFLD in children and adolescents, but studies on T2DM patients are limited. A cross-sectional study conducted in South Korea revealed that high blood sugar levels and the presence of MAFLD in adolescents serve as long-term risk factors for cardiovascular disease, with their increased prevalence being associated with higher total energy and fat intake [25]. A US study links hypertension, dyslipidemia to increased MAFLD risk, with most affected being males, obese, or having high blood glucose, insulin, HbA1c, liver enzymes, lipids, and uric acid [26].

MAFLD prevalence in children and adolescents varied significantly by gender and research stage, with exercise, healthy eating, and parenting being important factors. A study done in Shenyang, Liaoning Province, found that obese children had the highest prevalence of MAFLD [27]. This finding may relate to glucolipid metabolism issues and pubertal stage. A European study in overweight kids showed MAFLD at 18% in males, 11% in females, peaking in early adolescence for females and increasing with age and puberty in males [28], suggesting higher male prevalence during puberty. Therefore, early care under parental supervision and changing lifestyle habits are particularly important.

4.2 | Pathophysiology

MAFLD's complex pathophysiology in youth presents different histologic features than adults, with studies indicating more severe steatosis in children [29]. The multifactorial origin and progression of MAFLD, linked to cardiometabolic risks like obesity, dyslipidemia, insulin resistance, and hypertension, are not fully understood.

Gut microbiota significantly influences MAFLD pathophysiology via the gut-liver axis. Recent studies hypothesize links between gut microbiota changes and MAFLD pathophysiology, including the role of butyrate-producing bacteria in MAFLD development in children [30] and the contribution of small intestinal bacterial overgrowth to MAFLD [31].

IR is a pathophysiologic hallmark of MAFLD and one of the key components of MetS. Factors like genetics, T2DM, obesity

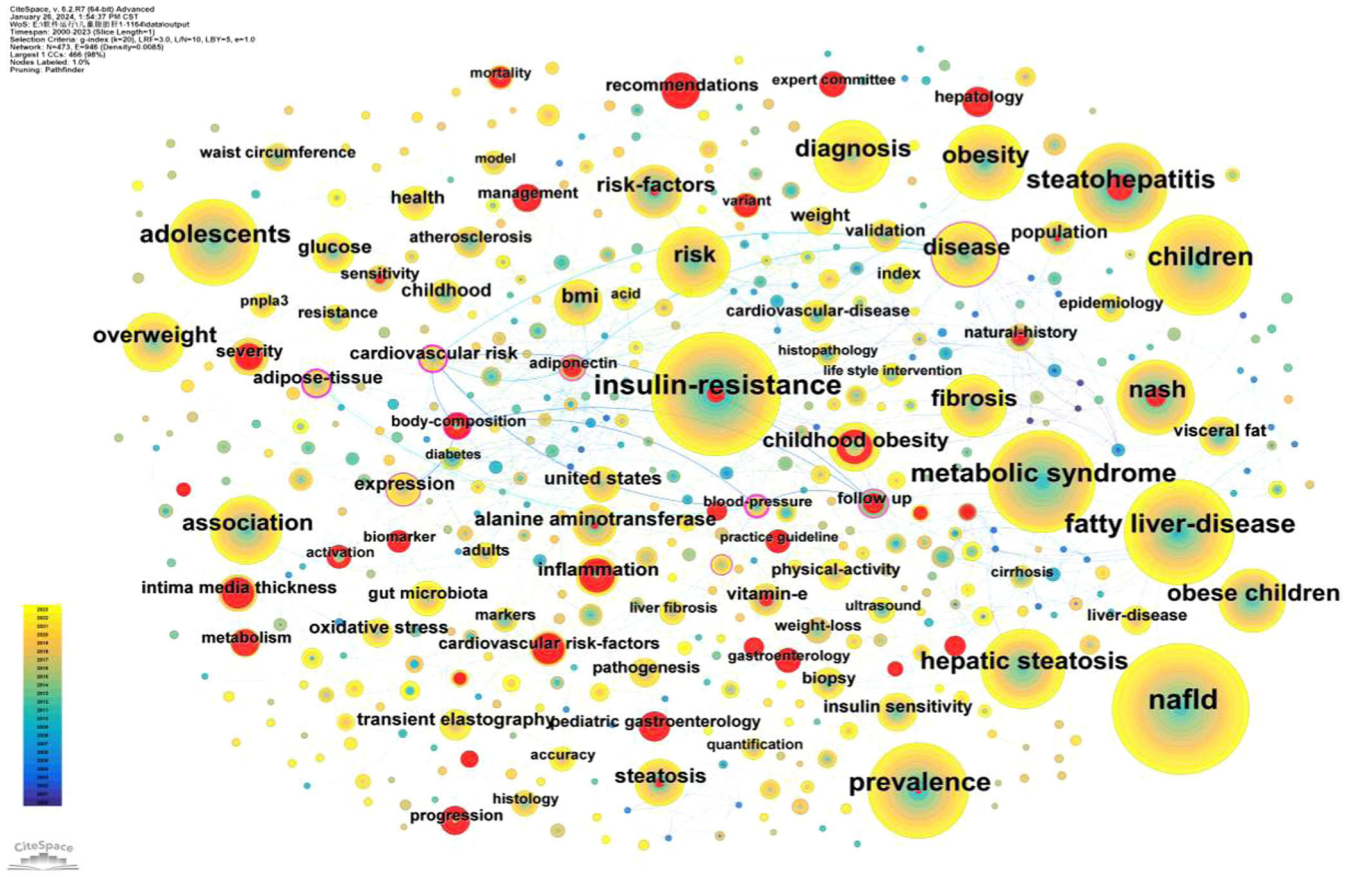

FIGURE 4 | CiteSpace keyword co-occurrence map.

contribute to insulin resistance. Fructose intake in youth is linked to MAFLD, with high-fat diets in pregnancy raising offspring's risk and adolescent fructose consumption speeding MAFLD onset in adulthood. This highlights the impact of maternal diets on the liver's response to metabolic insults [32]. T2DM significantly contributes to youth MAFLD susceptibility, with liver histology at diagnosis and T2DM onset showing correlation in studies [33]. Targeted strategies are essential to prevent T2DM in youth with MAFLD.

4.3 | Screen-Diagnosis

Liver biopsy, the gold standard for diagnosing hepatic steatosis, is not advised for routine screening in youth due to high cost, invasiveness, and risks. Accurate noninvasive diagnosis and staging are crucial in high-risk populations like pediatric patients with diabetes or obesity, given the increased risk of MAFLD progression to end-stage liver disease [34].

Ultrasound is a simple, safe, and efficient noninvasive technique for early diagnosis and monitoring of hepatic steatosis. Despite NASPGHAN's recommendation against its use for MAFLD diagnosis in children, noninvasive methods like transient elastography (TE), ultrasound attenuation imaging (ATI), and quantitative ultrasound are attracting research interest. Vibration-controlled transient elastography (VCTE) with controlled attenuation parameter (CAP) is employed to evaluate liver fibrosis and steatosis, with liver stiffness measurement and CAP aiding in detecting fibrosis and fat buildup in obese children with MAFLD [35]. Specifically, the CAP holds greater diagnostic significance for identifying moderate-to-severe hepatic steatosis in children [36] and is particularly valuable for screening high-risk pediatric and adolescent populations. Adolescent MAFLD correlates with early adulthood mortality, prioritizing metabolically abnormal obese and overweight youth for VCTE screening [37], with early screening considering gender, age, BMI, and pubertal status. ATI uses the attenuation of ultrasound waves to image and analyze substances, with studies suggesting it's an objective alternative for detecting hepatic steatosis in pediatric obese patients [38]. Quantitative ultrasound, assessing liver nature via wave propagation and attenuation, offers moderate diagnostic value for pediatric hepatic steatosis, correlating with MRI proton density fat fraction [39]. These measurements correspond with MRI results and reliably evaluate steatosis in children [40].

Noninvasive biomarkers are valuable in the rising MAFLD prevalence, but studies in children and adolescents are limited. BMI is the most significant risk factor, alanine aminotransferase (ALT) has a high predictive value for MAFLD, and age is also a risk factor, especially in prepubertal obese children with late puberty [41]; increased serum levels of leukocyte-derived chemokine 2, linked to IR in muscle and liver disease, are a potential diagnostic biomarker for MAFLD in children aged 2-17 [42]; imbalance of the growth hormone/IGF-1 axis is associated with increased incidence of MAFLD and rapid progression of advanced liver disease, and decreased growth

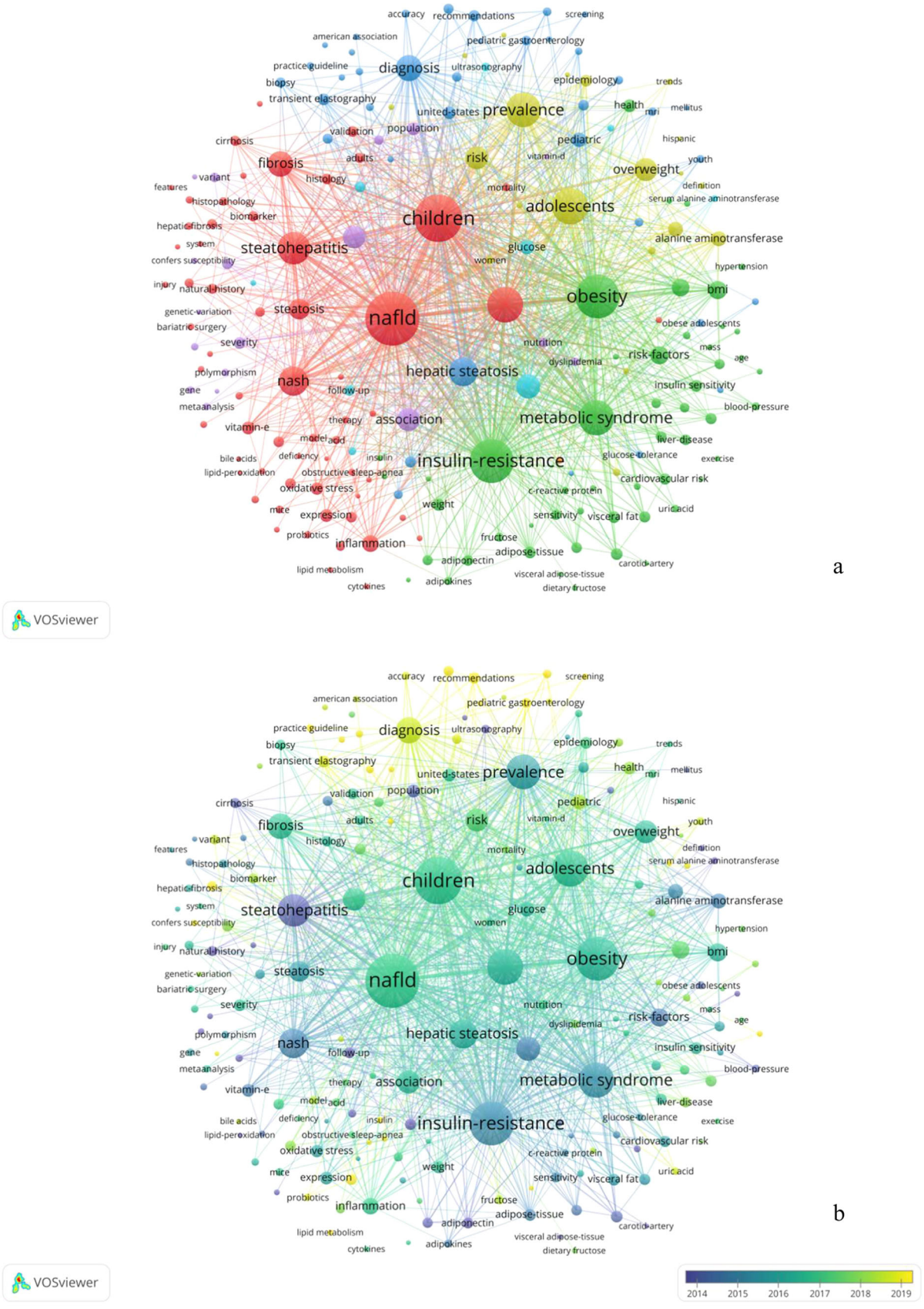

FIGURE 5 | (a) Vosviewer keyword clustering map. Legend: Clusters - Cluster 1: dark blue, Cluster 2: yellow, Cluster 3: light blue, Cluster 4: purple, Cluster 5: red, Cluster 6: green. (b) Vosviewer Keyword Timeline Chart.

hormone in the liver leads to hepatic steatogenesis, steatosis, and fibrosis [43]; the urinary C-peptide creatinine ratio is a highly sensitive and specific predictor of MAFLD in obese children, surpassing indicators like age, triglycerides (TG), ALT, and fasting C-peptide [44]; Fatty liver index, an algorithm combining waist circumference, BMI, TG, and glutamyltransferase, is a reliable tool for screening overweight and obese children for MAFLD in community and epidemiological settings [45]; the abbreviated fat tolerance test's 4-h postprandial triglyceride response is useful for differentiating MAFLD cases from noncases, highlighting its potential as a screening tool for pediatric MAFLD [46]; among others. These biomarkers could help identify MAFLD patients for early treatment, but further studies in pediatric and adult populations are required.

4.4 | Treatment

MAFLD, linked to glucose metabolism, oxidative stress, overnutrition, and IR, is increasingly a leading cause of liver transplantation. Therapeutic approaches, pharmacologic and nonpharmacologic, aim to improve symptoms, but the best strategy to improve liver status and reduce oxidative stress and inflammation in children and adolescents is still uncertain.

Weight loss is crucial for improving the histological characteristics of MAFLD, and the goal of nonpharmacological treatment is to reduce weight by changing lifestyle and dietary habits. Lifestyle management is the main treatment method, and overweight or obese children are more likely to develop MAFLD and elevated ALT in adulthood. Implementing a multidisciplinary lifestyle management plan for weight reduction can improve liver steatosis, lower transaminase levels, and reverse liver fibrosis [47]. Dietary habits can control fat and sugar intake by reducing calorie intake, improving dietary structure, and adjusting eating times. Research indicates that different dietary interventions such as low carbohydrate, low free sugar, low fructose, and low-fat diets, may be effective for MAFLD in children and adolescents [48]. For example, the Mediterranean, with its emphasis on low sugar, moderate saturated fat, high monounsaturated fat, fish, and antioxidants, exemplifies these strategies. It has been shown to decrease body mass index, fat mass, liver steatosis, and insulin resistance, and to positively affect inflammation and oxidative stress [49]. Research shows that increasing blood sugar levels and the incidence of MAFLD are directly associated with higher total energy and fat consumption. Therefore, promoting healthy dietary habits is vital for blood sugar regulation and MAFLD prevention, and constitutes a pivotal strategy to improve metabolic health [50]. An international expert consensus advocates for a balanced diet, controlled energy intake, and tailored nutrition. It suggests boosting consumption of whole grains, plant proteins, fish, seafood, low-fat dairy, vegetable oils, and dark fruits and veggies, while cutting down on red meat, processed foods, saturated fats, trans fats, added sugars, and alcohol [51]. In addition, the necessity of daily nutritional supplements for lifestyle improvement is not supported by sufficient evidence, warranting further research into their effectiveness and safety [48].

Children with MAFLD can benefit from medication that focuses on lowering cholesterol, reducing IR, antioxidants, and anti-inflammation. Zinc supplementation, affecting ALT, high-sensitivity C-reactive protein, and high-density lipoprotein cholesterol (HDL-C), could be a novel approach to improving NASH in overweight or obese children [52]; antioxidant hydroxytyrosol and vitamin E in children with MAFLD reduce inflammation, enhance interleukin-10 levels, and improve steatosis and hypertriglyceridemia [53]; omega-3 fatty acids, low-dose fat-soluble vitamins, and vitamin C therapy reduce inflammatory markers and lipid parameters [54]; probiotic supplementation, particularly Lactobacillus acidophilus with Bifidobacterium or Lactobacillus strains, improves lipid levels and liver enzymes, but the specific beneficial strains for liver histology improvement are yet to be identified [55]; recombinant human growth hormone therapy benefits liver enzymes and may alleviate cardiovascular and metabolic complications linked to obesity [56]; guava leaf extract might prevent IR in children with MAFLD [57]. These treatments could enhance MAFLD markers and mitigate complications.

4.5 | Prognosis

The degree of MAFLD liver fibrosis present is considered an important determinant of prognosis. Severely obese pediatric and adolescent patients are more susceptible to fibrosis compared to adults, and a combination of noninvasive methods [58], particularly high-performance noninvasive models, is recommended to assess its progression.

Combining noninvasive methods shows promise in MAFLD diagnosis and prediction, but existing fibrosis models need further research for pediatric application. Cytokeratin-18 is a promising noninvasive biomarker for liver fibrosis in children, and its combination with the waist circumference percentile forms a predictive model [59]; high TG/HDL-C ratios indicate a higher risk of liver fibrosis and advanced disease, making these ratios useful for patient stratification [60].

5 | Conclusion

MAFLD is a serious public health problem with a rising incidence in children and adolescents. While no standardized treatment can halt disease progression or improve prognosis, early nursing care and timely diagnosis and treatment can mitigate disease progression and reduce complications. However, there is still a lack of monitoring indicators and unified diagnostic and treatment consensus applicable to children and adolescents; the diagnostic accuracy of conventional biochemical indicators and noninvasive tests, such as ultrasound, remains low; and existing diagnostic and predictive models still require further validation and clinical application data. The research has revealed that examining gut microbiota and genes has emerged as a significant avenue for understanding the etiology and prognosis of MAFLD in kids and teenagers; IR is a key factor in the study of disease development; liver fibrosis is a focus of disease prognosis; and noninvasive diagnostic methods are hotspots in disease research. The present study provides systematic information to guide future research and helps to further study the mechanism and more efficient diagnosis and treatment of MAFLD in children and adolescents.

Author Contributions

Liangyu Hu: conceptualization, formal analysis, visualization, writing–original draft, writing–review and editing. **Huarong Du:** investigation, methodology, validation, writing–original draft. **QianQian Zhou:** data curation, visualization. **Chunlei Liu:** data curation, formal analysis. **Tiansong Zhang:** supervision, writing–review & editing. **Min Yuan:** project administration, resources, supervision, writing–review and editing.

Acknowledgments

The authors have no acknowledgments to declare for this manuscript.

Ethics Statement

The authors have nothing to report.

Consent

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

All relevant data are within the manuscript.

Transparency Statement

The lead author Tiansong Zhang, Min Yuan affirms that this manuscript is an honest, accurate, and transparent account of the study being reported, that no important aspects of the study have been omitted, and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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