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Review Article

The Silent Burden: A Comprehensive Review of Pediatric Non-Alcoholic Fatty Liver Disease and Its Metabolic Drivers

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Introduction

Childhood obesity affects 340 million children and adolescents between 5 and 19 years worldwide according to the WHO. At the same time, fatty liver disease is increasingly recognized as the most common chronic liver disease at all ages, though prevalence varies depending on the definition used [1-5]. NAFLD affects 5.5-10.3% of children globally, with figures ranging from 3% to 10% according to different epidemiological studies [5,6]. These data increase significantly in children and adolescents with obesity, reaching values of 22.4-44.0% [7] and up to 34% in some studies, suggesting a relationship between NAFLD, obesity, and metabolic syndrome. The geographical distribution shows marked heterogeneity, reflecting the influence of environmental, socio-cultural, and metabolic factors [4,8]. Currently, the classical "two-strike theory" has evolved into a "multiple-strike" model [9]. Fat accumulates in the liver of patients with NAFLD mainly in the form of triglycerides; steatosis begins when there is an imbalance between synthesis, flow, oxidation, and lipid export [10]. Insulin Resistance (IR) refers to a defective metabolic response to the hormone in target cells. IR in adipose tissue causes insulin to be unable to suppress lipolysis, sending a massive flow of free fatty acids into the liver [10]. This excess exceeds mitochondrial oxidation capacity, generating free radicals that damage mitochondrial DNA and cell membranes, causing inflammation and lipoapoptosis [11,12].

Diet is a crucial factor, especially the consumption of sugars such as fructose from sugary drinks. High fructose intake correlates with the epidemic increase in obesity and NAFLD. Furthermore, children with this disease often exhibit gut dysbiosis—an imbalance in intestinal microbiota—which increases intestinal permeability and triggers inflammation [10,7]. Genetic factors such as PNPLA3 (associated with fat accumulation and fibrosis), GCKR (modulating lipogenesis), and TM6SF2 also play significant roles [9].

Clinical Manifestations and Diagnosis

NAFLD usually remains asymptomatic until significant damage occurs; diagnosis is often incidental during physical examinations or routine blood tests [13]. Clinical markers include acanthosis nigricans, increased waist circumference, and hepatomegaly. Some patients may experience right upper quadrant pain, fatigue, irritability, or difficulty concentrating [11-13].

Pediatric NAFLD is frequently characterized by analytical alterations:

a) Alanine Amino Transferase (ALT): Elevated ALT levels are a common indicator, with sex-specific cut-offs determined at 22 U/L for girls and 26 U/L for boys [14,15]. However, ALT is not always a sensitive marker for disease severity.

b) Aspartate Aminotransferase (AST): An increase in the AST/ALT ratio may reflect progressive conditions like fibrotic steatohepatitis (EHNA).

c) Gamma-Glutamyl Transferase (GGT): Elevated levels represent a risk factor for advanced fibrosis [11].

d) Lipid Profile: While it reflects abnormal metabolism, its clinical utility in pediatric liver disease remains under investigation [11].

Diagnosis is established after excluding other pathologies [16]. Initial assessment focuses on history and indicators of visceral adiposity [3,13]. While ultrasound is widely used for its non-invasive nature, it has limited sensitivity for mild steatosis [3,15]. Liver biopsy remains the "gold standard" for assessing inflammation and fibrosis, though its use is limited in children due to its invasive nature [15].

Treatment

There are no drugs specifically approved for NAFLD treatment. According to NASPGHAN and AASLD guidelines, lifestyle modification is the primary method of treatment [12].

a. Diet: Limiting carbohydrates and reducing sugars, especially fructose, is essential [5,10,13].

b. Exercise: At least 60 minutes of daily exercise and limiting screen time to under 2 hours are recommended [11-12].

c. Experimental Options: If lifestyle changes are insufficient, options like Vitamin E (antioxidant) or metformin (insulin sensitizer) may be considered, although evidence for their specific use in NAFLD remains limited [3,5,11,13]. Omega-3 fatty acids and probiotics are also promising areas of research for treating pediatric NAFLD [3,5,7,10,13].

Methodology

A literature review was conducted using PubMed and Google Scholar for articles published between 2015 and 2025. The search occurred between October 2025 and January 2026 using keywords such as "Non-alcoholic Fatty Liver Disease" and "Prevalence". From 408 identified articles, 20 were selected based on relevance and quality (reviews, meta-analyses, and clinical guides).

Results

Pediatric NAFLD prevalence shows an increasing trend, estimated at 7.6% in the general population and rising to 34.2% in children with obesity. In cases of severe obesity, steatosis can reach 70-80%. A clear male predominance is observed, with some studies showing rates of 50.2% in boys versus 35.3% in girls. Ethnic variations indicate that Hispanics lead the prevalence with 40-45%. Insulin Resistance (IR) is the most critical endocrine factor in pathogenesis. Approximately 23.4% of children with NAFLD have prediabetes and 6.5% have type 2 diabetes. Adipokine imbalance, specifically high leptin and low adiponectin, serves as a biomarker for disease severity [10-12]. At puberty, growth hormone production can exacerbate liver damage, though estrogens may play a protective role in females until that stage [3,17]. The gut-liver axis and intestinal dysbiosis also play central roles, weakening the intestinal barrier and promoting hepatic lipogenesis. Additionally, perinatal factors such as maternal obesity and gestational diabetes increase early vulnerability to the disease [17-21].

Discussion

The prevalence of NAFLD has increased dramatically, particularly among obese and Hispanic populations. The shift to a "multiple-strike" model highlights the complexity of the disease, involving IR, adipokine dysfunction, and gut dysbiosis. However, the invasive nature of biopsies and the low sensitivity of ultrasound remain significant diagnostic limitations. Future research should focus on validating non-invasive biomarkers and investigating the impact of lifestyle factors such as sleep and screen time.

Conclusions

a. NAFLD is the most frequent cause of chronic liver disease in children and adolescents globally.

b. Prevalence increases significantly with obesity and shows a clear male predominance.

c. Insulin resistance is the central pathogenic factor of the disease.

d. Gut dysbiosis and increased intestinal permeability are central to pediatric pathogenesis.

Acknowledgement

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Conflict of Interest

None.

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