

Metabolic Associated Fatty Liver Disease as the New Nomenclature for Nonalcoholic Fatty Liver Disease

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Abstract

Over the course of last few decades, the name “nonalcoholic fatty liver disease (NAFLD)” has faced severe criticism from numerous experts. This is because the term “non-alcoholic” in NAFLD plays a prominent role in the definition of NAFLD while underscoring the role of metabolic disease as the underlying pathophysiologic mechanism. It is well known to be associated with various components of metabolic syndrome such as, obesity and type 2 diabetes mellitus (T2DM). In fact, many experts consider NAFLD to be the hepatic manifestation of metabolic syndrome. The negative nomenclature has led to trivialization of NAFLD as a health condition in the past which might have resulted in it becoming a global pandemic. Hence a change in nomenclature from NAFLD to metabolic associated fatty liver disease or 'MAFLD' is welcoming. This change in nomenclature would bring this disease close to its pathophysiology and would also promote research, enhance clinician's understanding, and improve clinical care of the patients.

Introduction

In 1980, Ludwig et. al. identified a series of 20 patients with chronic liver disease in absence alcohol misuse and coined a new term “Nonalcoholic fatty liver disease (NAFLD)” based on histopathological findings similar to patients alcoholic liver disease (ALD)¹. But even since early days, the two diseases i.e., NAFLD and ALD, only share certain histological features such as steatosis, steatohepatitis, fibrosis, and Furthermore, even in the index study, majority of the patients had obesity and type 2 diabetes mellitus (T2DM), implicating underlying role of metabolic syndrome leading to chronic liver disease 1. This early correlation between NAFLD and metabolic syndrome with T2DM and obesity, got overlooked and the term ‘nonalcoholic’ became established since then. Numerous publications have recently proposed a new terminology for NAFLD i.e., metabolic associated fatty liver disease (MAFLD)²⁻⁴. This commentary discusses this change in the nomenclature and how it will enhance

future research and clinical practice in the field of liver disease.

Why change in terminology from NAFLD to MAFLD?

NAFLD is a global pandemic with a pooled prevalence of 25%⁵. In fact, it is the most common form of chronic liver disease in the United States with an estimated annual prevalence ranging from 10-46 %^{6,7}.

NAFLD is used as an umbrella term for a variety of liver diseases characterized by excess fat accumulation in the hepatocyte⁸. Diagnosis of NAFLD currently needs an exclusion of a history of more than moderate alcohol intake and absence of drug exposure as well as defined genetic disorders that can culminate in a similar phenotype of fatty liver⁹. While excess fat accumulation in the hepatocyte followed by inflammation and fibrosis is the common denominator in both NAFLD and ALD—the pathogenesis of fatty liver and subsequent progression to advance liver disease is significantly different in both ALD and NAFLD^{10,11}. In the study by Day et al in 1998, authors proposed role of two-hits model independent of origin, leading to oxidative stress and inflammation¹². The following year, Marchesini et al. suggested role of insulin resistance in the development of NAFLD¹³. Subsequently, hepatic insulin resistance was found to be the contributing factor in the development of NAFLD¹⁴.

Beside different pathophysiologic mechanism in the development and progression of liver disease in both these condition, there are significant differences in the clinical characteristics and outcomes. ALD falls under a broad spectrum of alcohol use disorders, is frequently associated with psychiatric comorbidities and is the most common cause of morbidity, and health care utilization in patients with alcohol use disorders^{10,11}. NAFLD occurs as an essential component of metabolic disorders and presents with various clinical and biochemically manifestations seen in patients with metabolic syndrome including T2DM, obesity and dyslipidemia⁹. Among patients with ALD, complications from liver disease are the leading cause of NAFLD, while cardiovascular disease is the most common cause of death in patients with NAFLD^{15,16}. Moreover, NAFLD is a progressive condition and its prevalence parallels global trends in obesity and diabetes suggesting underlying role of metabolic disease and NAFLD to be the hepatic manifestation of a systemic metabolic disorder. Despite

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these advances in our understanding of NAFLD and multiple studies showing role of metabolic syndrome in the pathogenesis of NAFLD, the term “NAFLD” have remained in use. Using the term ‘non-alcoholic’ to describe all fatty liver disease which are not associated with alcohol consumption has led to clumping of distinct and heterogeneous conditions together and have hampered more precise research in the past.

Based on the insights gained in the past, many experts have proposed use of new nomenclature for NAFLD — that is, “Metabolic associated fatty liver disease (MAFLD)”. The new nomenclature to MAFLD is a welcome and promising change as it is clearer and more comprehensive. The new nomenclature clearly establishes this disease as a metabolic disorder and opens the door to develop and implement a set of ‘positive’ criteria to define the condition rather than relying on a ‘non’ or ‘negative’ definition. This is supported by the fact that current and updated guidelines to diagnose MAFLD requires presence of obesity or overweight, T2DM, or evidence of metabolic dysregulation¹⁷.

Abbreviations: MAFLD= Metabolic Associated Fatty Liver Disease, NAFLD = Nonalcoholic Fatty Liver Disease, ALD= alcoholic liver disease, T2DM = Type 2 diabetes mellitus.

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