



## Opinions

## Simultaneous Metabolic and Alcohol-associated Fatty Liver Disease (SMAFLD) and Simultaneous Metabolic and Alcohol-associated Steatohepatitis (SMASH)



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Seventy percent of adults in the United States are either overweight or obese [1]. Obesity is associated with a metabolic syndrome of co-related risk factors, including insulin resistance, atherogenic dyslipidemia, and hypertension [2]. Patients with metabolic syndrome are at increased risk of developing the nonalcoholic fatty liver disease (NAFLD) or nonalcoholic steatohepatitis (NASH) [3]. NAFLD is one of the leading worldwide causes of liver disease, affecting up to 25% of the global population [4]. In Western countries, the prevalence in the general population is estimated to be up to 30 percent [5]. NASH, a progressive subtype with hepatic neuroinflammatory manifestations in the setting of steatosis, is estimated to be prevalent in 3–6 percent of the population and carries an increased risk of developing advanced fibrosis, cirrhosis, cardiovascular complications and hepatocellular carcinoma [6]. Direct medical costs attributed to NAFLD and its sequelae are estimated to be \$1.3 billion annually and are projected to continue rising [7].

Alcohol is an equally important and common cause of chronic liver disease. Among adults in the United States, alcohol use disorder has an estimated lifetime prevalence of 18% and is strongly associated with alcoholic liver disease (ALD). This latter comprises a spectrum of diseases ranging from alcoholic fatty liver disease (AFLD) to more advanced forms, including alcohol associated hepatitis (AH), alcohol associated steatohepatitis (ASH), alcohol associated cirrhosis (as well as its inherent complications). The prevalence of AFLD among adults in the United States is ~ 4.7 percent [8].

Fatty liver disease and steatohepatitis are similarly to occur in individuals who also have both metabolic syndrome and an excessive

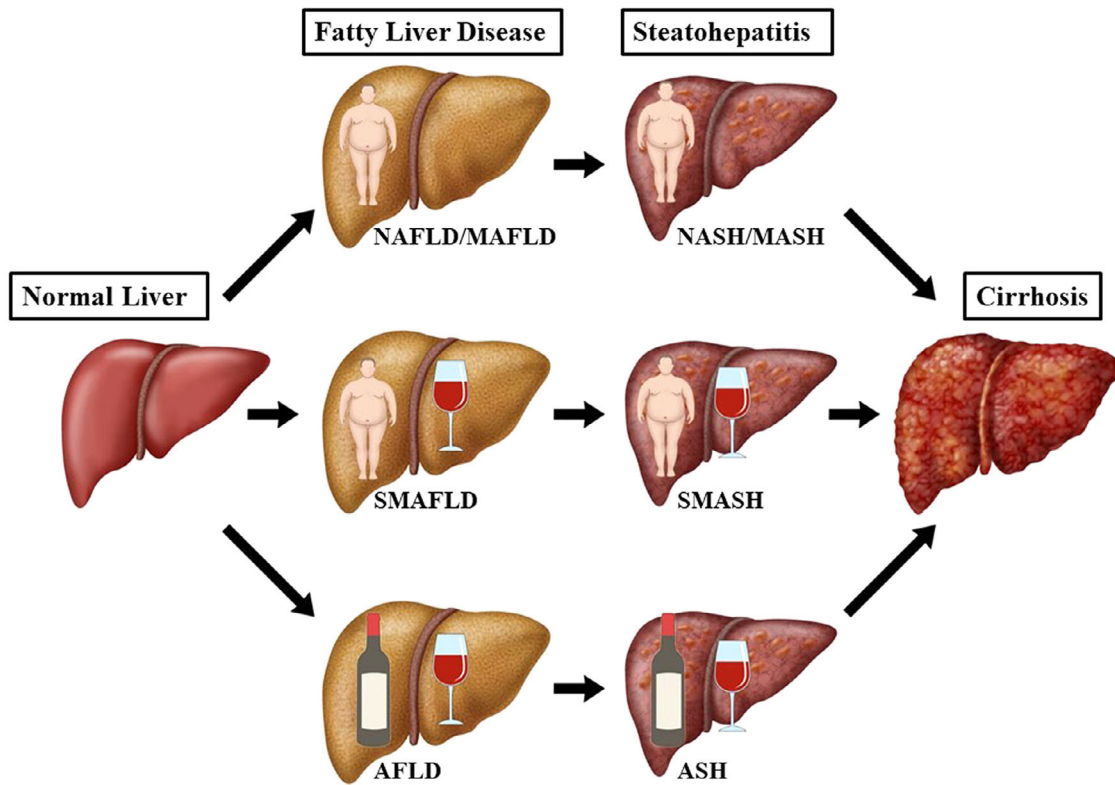
alcohol intake, suggesting concurrent causes of the liver condition and a distinct phenotype of disease with a prevalence of 0.84 percent, corresponding to an estimated 1.24 million Americans being affected [9]. When compared to those with NAFLD alone, patients who had concurrent alcohol use had higher aminotransferases, lower platelet counts and more advanced fibrosis [9]. The nomenclature initially suggested describing this subset of the population was an acronym of both alcoholic and NAFLD (BAFLD) [9]. We agree with recent papers suggesting that the current terminology using the acronym NAFLD does not accurately reflect the pathogenesis or current knowledge associated with the disease state and that metabolic (dysfunction) associated fatty liver disease (MAFLD) should be used [10,11].

Here we propose a more descriptive and more accurate nomenclature that better describes the overlapping spectrum of NAFLD and AFLD, namely simultaneous metabolic and alcohol associated fatty liver disease (SMAFLD) (Fig. 1). Similarly, we recommend a name that recognizes the concurrent presence of both NASH (or MASH) and ASH as simultaneous metabolic, and alcohol associated steatohepatitis (SMASH) (Fig. 1).

We submit that these acronyms could stimulate clinicians to consider that in many cases, several distinct important processes concur to cause a fatty liver and addressing only one of them is unlikely to arrest or cure the patient's disease. Awareness of the complex nature of the various factors involved, with appropriate classification, should bring more clarity and precision to both clinical diagnosis and research classification and enhance the nation's health.

*Abbreviations:* NAFLD, nonalcoholic liver disease; NASH, nonalcoholic steatohepatitis; ALD, alcohol associated liver disease; AH, alcohol-associated hepatitis; AFLD, alcohol-associated fatty liver disease; ASH, alcohol-associated steatohepatitis; MAFLD, metabolic (dysfunction) associated fatty liver disease; SMAFLD, simultaneous metabolic and alcohol-associated fatty liver disease; SMASH, simultaneous metabolic- and alcohol-associated steatohepatitis

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**Figure.** Interaction of various factors in the etiology of fatty liver diseases and steatohepatitis. Abbreviations: NAFLD, nonalcoholic liver disease; NASH, nonalcoholic steatohepatitis; AFLD, alcohol associated fatty liver disease; ASH, alcohol associated steatohepatitis; MAFLD, metabolic (dysfunction) associated fatty liver disease; MASH, metabolic (dysfunction) associated fatty liver disease; SMAFLD, simultaneous metabolic and alcohol associated fatty liver disease; SMASH, simultaneous metabolic and alcohol associated steatohepatitis.

**References**

- [1] Flegal KM, Kruszon-Moran D, MD Carroll, Fryar CD, Ogden CL. Trends in Obesity Among Adults in the United States, 2005 to 2014. *JAMA* 2016;315(21):2284–91. <https://doi.org/10.1001/jama.2016.6458>.
- [2] Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA* 2002;287(3):356–9. <https://doi.org/10.1001/jama.287.3.356>.
- [3] Neuschwander-Tetri BA. Nonalcoholic steatohepatitis and the metabolic syndrome. *Am J Med Sci* 2005;330(6):326–35. <https://doi.org/10.1097/00000441-200512000-00011>.
- [4] Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease—Meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology* 2016;64(1):73–84. <https://doi.org/10.1002/hep.28431>.
- [5] Bellentani S, Scaglioni F, Marino M, Bedogni G. Epidemiology of non-alcoholic fatty liver disease. *Dig Dis Basel Switz* 2010;28(1):155–61. <https://doi.org/10.1159/000282080>.
- [6] Sheka AC, Adeyi O, Thompson J, Hameed B, Crawford PA, Ikramuddin S. Nonalcoholic Steatohepatitis: A Review. *JAMA* 2020;323(12):1175–83. <https://doi.org/10.1001/jama.2020.2298>.
- [7] Younossi ZM, Blissett D, Blissett R, Henry L, Stepanova M, Younossi Y, et al. The economic and clinical burden of nonalcoholic fatty liver disease in the United States and Europe. *Hepatology* 2016;64(5):1577–86. <https://doi.org/10.1002/hep.28785>.
- [8] Wong T, Dang K, Ladhani S, Singal AK, Wong RJ. Prevalence of Alcoholic Fatty Liver Disease Among Adults in the United States, 2001–2016. *JAMA* 2019;321(17):1723–5. <https://doi.org/10.1001/jama.2019.2276>.
- [9] Khoudari G, Singh A, Noureddin M, Fritze D, Lopez R, Asaad I, Lawitz E, Poordad F, Kowdley K, ALKhoury N. Characterization of patients with both alcoholic and non-alcoholic fatty liver disease in a large United States cohort. *World J Hepatol* 2019;11(10):710–8. <https://doi.org/10.4254/wjh.v11.i10.710>.
- [10] Eslam M, Newsome PN, Sarin SK, Anstee QM, Targher G, Romero-Gomez M, et al. A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement. *J Hepatol* Published online April 2020: S016827820302014. <https://doi.org/10.1016/j.jhep.2020.03.039>.
- [11] 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. <https://doi.org/10.1053/j.gastro.2019.11.312>.