

# Insidious danger for young adults: Metabolic (dysfunction)-associated fatty liver disease

Eda Kaya<sup>1,2</sup>, Yusuf Yilmaz<sup>3,4</sup>

<sup>1</sup>Section of Hepatology and Gastroenterology; and <sup>2</sup>Department of Medicine, Universitätsklinikum Knappschafts Krankenhaus Bochum, Ruhr University Bochum, Bochum, Germany; <sup>3</sup>Department of Gastroenterology, Marmara University School of Medicine, Istanbul, Turkey; <sup>4</sup>Institute of Gastroenterology, Marmara University, Istanbul, Turkey

Nonalcoholic fatty liver disease (NAFLD) is conceptualized as a clinical spectrum from simple steatosis to liver cirrhosis, and its burden is increasing parallel to the growing obesity pandemics.<sup>[1]</sup> Indeed, NAFLD is considered the main driver of the increased liver-related morbidity and mortality in both the adult and the pediatric population.<sup>[2,3]</sup> Currently, there is an ongoing international effort in renaming and redefining NAFLD as metabolic (dysfunction)-associated fatty liver disease (MAFLD). According to the new definition, MAFLD is defined in light of a positive set of criteria, which consists of having diabetes mellitus type 2, being overweight, and/or showing metabolic dysfunction in addition to hepatic steatosis.<sup>[3]</sup> The new definition “MAFLD” reflects the disease etiology better and conveys a more practical approach in daily clinical practice than NAFLD, considering its close association with metabolic syndrome.<sup>[4]</sup>

Recently, Nastasa et al.<sup>[5]</sup> described the prevalence of hepatic steatosis and fibrosis among apparently young adults in Romania. They identified a total of 426 medical students with a mean age of 22±2 years. All of the participants underwent vibration-controlled transient elastography examinations. According to the controlled attenuation parameter cutoff value of 248 dB/m, 74 (17.4%) individuals had any grade of hepatic steatosis and 149 (35.0%) patients had any stage of fibrosis. Previously, we reported similar results for apparently healthy young medical students using transient elastography for defining NAFLD (23.2%).<sup>[6]</sup> The data obtained from National Health and Nutrition Examination Survey from 2007 to 2016 revealed that the prevalence of NAFLD defined by the fatty liver index was 18.7% for individuals between 18 and 24 years of age. For older individuals (25-29 years), the survey found a higher prevalence (24%). Moreover, the authors observed a dramatically significant increase in the prevalence of NAFLD in individuals between 18 and 24 years of age, from 10.7% (2007-2008) to 24.8% (2015-2016) (p=0.018).<sup>[7]</sup> Similarly, Aziz et al.<sup>[8]</sup> conducted a study with

153 apparently healthy, lean (body mass index [BMI] <25 kg/m<sup>2</sup>), and young medical professionals (median age 23 years, interquartile range 5 years). Despite excluding the metabolically unhealthy population, their study showed an ultrasonographically diagnosed NAFLD prevalence of 20.3%. In 2016, Okur and Karacaer<sup>[9]</sup> detected a NAFLD prevalence of 10.6% among 254 young male individuals [median age 27 years (21-41)] in a military hospital. This low prevalence was probably due to the nonsedentary lifestyle and normal BMI values of the study population.<sup>[9]</sup>

In another study conducted with 120 apparently healthy college students in Egypt, NAFLD prevalence was detected to be 31.8% by transient elastography.<sup>[10]</sup> However, this high prevalence was expected for this region owing to the previous meta-analysis considering ethnic and geographic factors. In the same meta-analysis, the overall prevalence of NAFLD in the world was 25%.<sup>[11]</sup> In line with these data, the NAFLD prevalence of 17.4% for such a young population could not be considered as low. Indeed, NAFLD prevalence increases with age. Probably, due to the longer duration of the disease, the likelihood of progressing to liver fibrosis and cirrhosis is greater in older individuals.<sup>[12]</sup> Unfortunately, both prevalence and incidence of NAFLD have increased in the last three decades independently of age, sex, and region. There is a global increase in NAFLD incidence even in children, adolescents, and young adults, which is associated with the shift of obesity to younger ages.<sup>[13]</sup> Moreover, the presence of hepatic steatosis in younger ages (≤25 years) is predicted to be particularly aggressive. A biopsy-proven Swedish study conducted with 718 children and young adults revealed that the presence of hepatic steatosis increased the overall mortality risk 5.26-fold and nonalcoholic steatohepatitis 11.51-fold over a median follow up of 15 years.<sup>[14]</sup> On the other hand, the data from the Third National Health and Nutrition Examination Survey revealed that for patients between 60 and 74 years of age, presence of NAFLD was associated with 1.6-fold and 1.22-fold increased risk for 5-year and 10-year all-cause mortality, respectively. For patients older than 74 years, NAFLD did not show any significant impact on mortality.<sup>[15]</sup>

One important question about redefining the disease as MAFLD was, “What kind of an impact does the redefinition of the disease have on the defined population?” The recent meta-analysis by Lim et al.<sup>[16]</sup> showed that defining a patient as having MAFLD was significantly higher than NAFLD. Moreover, MAFLD presented a significantly severe disease compared with NAFLD. Similarly, in our population-based study, we found that patients with MAFLD had a significantly severer metabolic profile. As previously shown, in MAFLD, increasing age was associated with increased NAFLD prevalence. The prevalence of MAFLD was lower for both older age (>80 years) and younger age (<30 years).<sup>[17]</sup> Li et al.<sup>[18]</sup> showed similar results in their Chinese cohort.

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**Corresponding author:** Yusuf Yilmaz; Marmara Universitesi Tip Fakultesi, Gastroenteroloji Bilim Dalı, Istanbul, Turkey

**Phone:** +90 216 399 97 50; **e-mail:** dryusufyilmaz@gmail.com



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In light of this evidence, the presence of NAFLD presents a significant public health burden for particularly young individuals. However, considering the severer disease profile and higher frequency of MAFLD, MAFLD would be associated with a severer burden if the patients in those studies were defined as having MAFLD. Therefore, the high prevalence of MAFLD in the young population should alert the policymakers to develop national health programs for the management of MAFLD.

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