

Addressing the looming epidemic of metabolic dysfunction-associated steatotic liver disease in Pakistan: A call for action

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The term metabolic dysfunction-associated steatotic liver disease (MASLD), which evolved from its predecessor, nonalcoholic fatty liver disease (NAFLD),^[1] refers to a chronic condition characterized by hepatic steatosis. It more accurately reflects the pivotal role of cardiometabolic risk factors in its pathogenesis.^[2–4] When liver steatosis is present, the identification of at least one of the following five cardiometabolic risk factors – 1) a body mass index (BMI) over 25 kg/m² (23 kg/m² for Asian individuals), or a waist circumference greater than 94 cm for men and 80 cm for women, with ethnicity-specific adjustments, 2) blood pressure above 130/85 mm Hg or undergoing specific anti-hypertensive drug treatment, 3) plasma triglycerides levels exceeding 150 mg/dL, or currently under lipid-lowering treatment, 4) plasma HDL cholesterol levels under 40 mg/dL for men or less than 50 mg/dL for women, or currently under lipid-lowering treatment, 5) fasting serum glucose level exceeding 100 mg/dL, or 2-hour post-load glucose levels over 140 mg/dL, or glycated hemoglobin concentrations above 5.7%, or diagnosed with type 2 diabetes mellitus (DM), or currently undergoing treatment for type 2 DM – can lead to a diagnosis of MASLD.^[2–4] Therefore, contrary to NAFLD, MASLD's identification does not require the exclusion of other liver diseases. However, it does necessitate the presence of indicators pointing toward disrupted cardiometabolic function. In the context of steatotic liver disease (SLD), the term MetALD is utilized to denote the interplay of two pivotal factors: metabolic anomalies (which include any cardiometabolic criteria) and alcohol consumption (daily intake ranging between 20 and 50 g for women and 30 and 60 g for men).^[2–4] These two factors coalesce to contribute significantly to both the onset and progression of liver disease. When other causes of steatosis are identified, a diagnosis of mixed etiology is given. In scenarios where no overt cardiometabolic criteria are met, other potential causes should be ruled out. If no cause is found, the condition is termed cryptogenic SLD. However, depending on clinical judgment, it may also be considered potential MASLD, warranting periodic reassessment on an individual basis.^[2–4]

With the global surge in its prevalence, MASLD is increasingly becoming the primary underlying cause for advanced liver disease and the leading indication for liver transplantation.^[5,6] In Pakistan, there is mounting concern that MASLD could morph into the next epidemic due to the increasing prevalence of cardiometabolic risk factors.^[7] Further fueling this concern are lifestyle factors that are becoming more common in the country. A surge in urbanization, sedentary living, and high-calorie diet consumption has notably amplified the rates of MASLD risk factors. In a study by Ghani et al.^[8] the NAFLD definition was used to investigate metabolic risk factors associated with this condition in the Pakistani population. The study found that the overall prevalence of NAFLD was 14.8%, with a higher rate among individuals aged 40 years and above (19.9%).^[8] The sex distribution showed a prevalence of 13.4% in women and 16.1% in men.^[8] Additionally, based on the World Health Organization's Asia-Pacific BMI cutoffs, the overall weighted prevalence rates of central and generalized obesity were 73.1% and 57.9%, respectively.^[9] Alarmingly, 22.2% of individuals over 15 years of age can be classified as obese, indicating that approximately one in every four adult Pakistani individuals is battling obesity.^[10] In addition, Pakistan holds the third position globally for the prevalence of type 2 DM, with China and India leading the ranks, according to data from the International Diabetes Federation.^[11] It is alarming to note that 26.7% of Pakistan's adult population, approximately 33 million individuals, are living with type 2 DM.^[11] These statistics, which are expected to rise annually, are indeed disconcerting. A detailed sub-analysis of the second National Diabetes Survey of Pakistan, conducted by Basit et al.^[12] also revealed that 39.3% of the general population had elevated cholesterol levels, with a prevalence of 48.9% for hypertriglyceridemia. Additionally, 39.7% of the population had elevated LDL cholesterol levels, while low HDL levels were found in 90% of women and 83.9% of men. The age group most affected by high cholesterol and triglyceride levels was between 50–59 years, whereas decreased HDL and elevated LDL were most commonly observed among the 40–49 years age group.^[12] The survey also reported that the prevalence rates of hypertension in rural and urban areas were 46.8% and 44.3%, respectively.^[13]

Given the alarming data, it is essential to implement both public and individual preventive strategies against MASLD in the country. The repercussions of MASLD are extensive and significantly influence public health and the healthcare system.^[14] For example, a specific group of patients with MASLD can develop advanced forms of liver disease, leading to cirrhosis, hepatocellular carcinoma, and liver failure. Notably, hepatocellular carcinoma may develop in MASLD even without the presence of cirrhosis. Compared to the general populace, patients with MASLD face a heightened risk of liver-related, cardiovascular, and overall mortality.^[15] Notably, MASLD not only increases the risk but also exacerbates the pathophysiology of DM, cardiovascular diseases, and chronic kidney

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disease. Furthermore, MASLD can be associated with a host of other health issues, including obstructive sleep apnea, osteoporosis, stroke, polycystic ovarian syndrome, and various extrahepatic malignancies.^[15]

Tackling MASLD and its associated complications necessitates a comprehensive approach that integrates public health initiatives, education, and policy amendments. Several strategies can be employed to mitigate the disease's impact, including public awareness campaigns, school-based interventions, enhanced healthcare infrastructure, and the design and implementation of effective policies. Firstly, it is vital to increase public awareness about MASLD's risk factors, preventive strategies, signs, and repercussions. Educational campaigns aimed at the wider community and healthcare professionals can facilitate early detection and prevention. Moreover, endorsing healthy lifestyle habits, including a balanced diet and regular exercise, is paramount in alleviating the strain of cardiometabolic disorders and MASLD. Secondly, the establishment of educational programs in schools should be geared towards cultivating healthy habits, encouraging physical activity, and offering nutritious meals to children. This approach directly addresses the escalating issue of childhood obesity. Thirdly, an all-encompassing healthcare strategy is essential to holistically manage MASLD. This requires the fortification of primary healthcare services to ensure early detection, diagnosis, and treatment of cardiometabolic disorders. Healthcare professionals should undergo training in the identification and management of MASLD, and the creation of specialized clinics is necessary to provide comprehensive care. Lastly, policy changes are integral to effectively combating MASLD. The introduction of regulations to manage the availability and promotion of unhealthy food products and beverages, particularly those high in sugar and trans fats, can aid in reducing the prevalence of cardiometabolic disorders. Tax policies that deter the consumption of sugary beverages and processed foods can also contribute to curbing the obesity epidemic and its associated complications. Encouraging a collaborative environment among healthcare professionals, researchers, and policymakers is crucial. This synergy will aid in the development of evidence-based guidelines for the prevention, diagnosis, and treatment of MASLD.

In summary, it is of utmost importance that we take prompt action to curb the spread of MASLD and prevent it from turning into an epidemic in Pakistan. By effectively addressing the root causes of cardiometabolic disorders and implementing focused preventive measures with the collaboration of relevant stakeholders, we can lighten the strain on our healthcare systems. This, in turn, will substantially enhance the overall health and well-being of the Pakistani population.

Conflict of Interest: Yusuf Yilmaz has served as a consultant to Cymabay, Zydus, Novo Nordisk, and Echosens. The other authors have no conflict of interest.

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