The NAFLD–MAFLD debate through the lens of the Arab world

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Abstract

The most common liver disease in the world is fatty liver disease related to metabolic dysfunction, yet neither patients nor medical professionals are fully aware of this. The disease, formerly known for decades as non-alcoholic fatty liver disease (NAFLD), has been renamed metabolic (dysfunction)-associated fatty liver disease (MAFLD), with many international consensus groups making recommendations on how the condition should be diagnosed and treated. This point of view explores the nomenclature change from the standpoint of Arab medical professionals and patients. The call for a name change brought up serious issues with the current nomenclature, which refers to the condition as NAFLD, and its diagnostic criteria, including the necessity for excluding alcohol consumption. The Arab world has its unique situation as regards both old and new nomenclatures. This is because of the low alcohol consumption rates in most Arab Muslim countries besides the reported high prevalence rates of obesity and its related comorbidities in the region. In our opinion, such unclarities acted as a significant roadblock to several crucial aspects of disease management in the Arab countries, including patient–doctor communication, patient awareness, partnership working, patient motivation to make lifestyle changes, and promotion of multiple health behavior changes. Many Arab world hepatologists thus wholeheartedly endorse this call to redefine the disease as they believe it will eventually positively impact the understanding and awareness of fatty liver disease, enhance patient treatment and quality of life, and reduce the load on the healthcare system.

Keywords: Arab, fatty liver, MAFLD, NAFLD, obesity

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Many diseases have had their names changed throughout time, and for a name change to be effective, it must make sense, be simple to say and type, get support from professional bodies, and maintain the same acronym. A change in a disease's name often denotes a better knowledge of the condition, whether in terms of its clinical manifestations, natural history, or pathophysiological features. The trials for changing the nomenclature of nonalcoholic fatty liver disease (NAFLD) to metabolic-associated fatty liver disease (MAFLD) have raised much debate and interest about the impact of this change on disease management, course, and prognosis. The definition of NAFLD was proposed and remained unchanged since 1986, defined

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by the presence of evident hepatic steatosis (by imaging or histology) and absence of other causes of hepatic fat accumulation, such as significant alcohol intake, long-term use of a steatogenic drug, or hereditary disorders.[1] According to this definition, the diagnosis of NAFLD is a diagnosis of exclusion.[2] Moreover, this requires an exhaustive workup to exclude many diseases and neglect the association between some diseases and steatosis, such as the hepatitis C virus.[3,4] The main differences between NAFDL and MAFLD definitions are listed in Table 1.

There is a global debate about this medical term. The "non-" prefix is usually used to describe a minor condition and distinguish it from a more critical condition. In the case of NAFLD, this is responsible for trivializing the disease.[5]Also, exclusion of alcohol intake is problematic[1] as there is no objective uniform standard for determining significant alcohol intake.[6,7] The role of alcohol as a cause of the liver disease is variable according to many factors, and it is clearly observed that Arab countries have a lower prevalence of alcohol use than western countries due to cultural and religious differences, as alcohol is prohibited in Islam, the predominant religion of the region.[8] Moreover, the term NAFLD confuses patients about the real cause of their disease.[9]

For the reasons mentioned above, Eslam *et al*.[10] proposed the change in the terminology of NAFLD to MAFLD in 2020. The diagnostic criteria for MAFLD include the presence of hepatic steatosis with one of the three following criteria: obesity or overweight, type 2 diabetes mellitus (DM), or evidence of metabolic dysregulation. These criteria are more practical, simple, and easy to apply. This helps deal with the whole patient rather than focusing on a specific organ. Therefore, MAFLD captures the entire disease spectrum.[11] This term has been significantly accepted among patients,[12] physicians,[13] nurses, and other liver societies.[14]

This new definition helps detect the effect of more than one chronic liver disease or a metabolic abnormality present simultaneously in a single patient,[15] such as alcohol, virus infection, or drugs.[16] Also, this allowed adding more subjects who fulfilled the definition of MAFLD but not the NAFLD criteria. Therefore, we can expect an increase in the prevalence of fatty liver disease by at least 25% after applying the new definition;[17] however, the situation may be different in the Arab countries. The multiplicity of the criteria required for diagnosing MAFLD makes it challenging to precisely predict the increase in the disease prevalence with the new definition. In addition, lean patients with fatty liver are expected to be under-recognized due to the absence of the classical risk factors that allow the detection of such cases. A recently published study found that NAFLD exists in 31.6% of young Egyptian adults[18] and 57.65% of obese Egyptian adolescents.[19] NAFLD was also found to affect one-quarter of the population in Saudi Arabia and the United Arab Emirates.[20] The expected increase in the prevalence of fatty liver disease, after the definition change, is a concern in Arab countries, where massive growth in population exceeds the capacity of healthcare systems, which are already fragile and under-resourced.[21]

Table 1: Summary of the main differences between NAFLD and MAFLD definitions

	NAFLD	MAFLD
Hepatic steatosis	Yes	Yes
Excluding other etiologies of chronic liver disease	Yes	Not essential
Alcohol intake	Moderate/heavy drinkers are excluded	Independent from alcohol intake
Type 2 diabetes mellitus	Not essential	Yes
Overweight or obesity	Not essential	Yes
Metabolic risk factors	Not essential	Yes
Liver biopsy	Required for diagnosing NASH	Not required

This high prevalence of fatty liver disease in Arab countries could be attributed to many factors, such as excess carbohydrate and fast-food intake, high-calorie energy intake, decrease in fresh fruits and vegetable intake, decreased physical activity, the habit of sedentary behavior, and so on,[22,23] with a rapid increase in the rate of obesity among the Arab population. Egypt, as an example, shows higher rates of obesity among women compared with men due to cultural aspects.[24,25] Also, there is a spike in the prevalence of diabetes in the Middle East. The Gulf region has experienced a sudden increase in the rates of diabetes, with Kuwait, Saudi Arabia, and Bahrain ranking among the top 10 countries with the highest prevalence of type 2 diabetes worldwide.[26] For example, the prevalence of DM increased dramatically in Saudi Arabia to reach 25.4% of the population.[27] Egypt was ranked ninth in the number of diabetes cases, with a prevalence of 15.56% among adults.[28]

Although there are scant data on the magnitude of MAFLD in the Arab world, available data suggest that Egypt has one of the highest prevalence of MAFLD, affecting more than one-third of the population, compared to a global prevalence of about 25%.[29,30] However, this is likely to be underestimated because of under-diagnosis and under-reporting. In response to the alarming increase in NAFLD prevalence and the proposed change in the landscape of liver diseases in Egypt over the last decade, a clinical practice guideline for MAFLD screening,

diagnosis, and management was recently issued by a group of Egyptian opinion leaders.[31] This guidance aimed to consider the local situation and the burden of clinical management of NAFLD for the healthcare sector.

The change in nomenclature from NAFLD to MAFLD could be of value in clinical practice at multiple levels, including patient diagnosis, care, and research. Also, it has great value in clinical communication.[14] However, the term still leaves significant ambiguity due to many debatable points. First, the new term is associated with a lack of awareness by many physicians. This may result in mismanagement of the disease, which will affect its prognosis.[2] Also, other "metabolic" diseases such as Wilson's disease may result in fatty liver but are not covered under the term MAFLD.[32] Moreover, NAFLD patients with non-metabolic risk are missed as they do not fulfill the MAFLD criteria. Unfortunately, their potential risk can be the cause of future diseases.[33] Therefore, some experts believe that now is not the time to endorse the new term that needs to be corrected as the disease's understanding continues to improve.[34,35]

Regardless of the proper name describing this real disease, we know well that it is going to be the most significant liver disease with related morbidity and mortality worldwide. In reality though, we are challenged to identify and manage it. Therefore, a name change should follow a clearer understanding of disease nature, pathogenesis, and management. It is not the name but the disease's nature that decides the patient outcome.

In conclusion, the outdated term "NAFLD" exaggerates the role of alcohol consumption, which is not a primary cause of liver disease in many regions, including the Muslim Arab world, while downplaying the significance of metabolic dysfunction in this disease. The definition of MAFLD is straightforward, practical, and performs better than the previous NAFLD definition in identifying patients likely to have adverse hepatic and extrahepatic outcomes in the future. It also raises awareness of fatty liver disease related to obesity, representing a significant health challenge in the Arab region. Professional societies and multi-stakeholder groups released further position statements on redefining fatty liver over the past few years. Although the prevalence of MAFLD has been roughly matched to that of NAFLD, it is somewhat greater because its definition considers the presence of other liver disorders. The new term for MAFLD is only a name change; patients with fatty liver will eventually need to be categorized and appropriately managed.

The term MAFLD is closely related to other highly prevalent metabolic diseases overlapping in public health. This requires the interaction of many specialties in a multi-disciplinary team (including collaboration between endocrinologists, cardiologists, nutritionists, and liver specialists) to prevent, manage, and follow up on these diseases.

Further studies are required to confirm the acceptability and applicability of this novel terminology in specific geographical regions and its potential role in moving the field forward. This change requires extensive collaboration between local scientific societies, governments, organizations, and other stakeholders through a careful exchange of ideas to guide decision-making from a clinical perspective, taking into considering changes and preparing for them. Finally, future discussions and expert opinions should focus on updating the guidance statements to direct international agencies for drug development.

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