

Nonalcoholic Fatty Liver Disease vs Metabolic-associated Fatty Liver Disease vs Metabolic Dysfunction-associated Steatotic Liver Disease: What's in the Name?

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People ... arrive at their beliefs not on the basis of proof, but on the basis of what they find attractive."

– Blaise Pascal

Nonalcoholic fatty liver disease (NAFLD) is one of the biggest public health problems today and it would be no exaggeration to say that NAFLD has assumed the form of a global pandemic. The global prevalence of NAFLD has been estimated to be 32%—one in three individuals—while the overall incidence has been estimated to be 46.9 cases per 1000 person-years.¹ These are indeed alarming figures and what makes things even more concerning is the lack of effective management strategies for the treatment of NAFLD. This problem therefore requires serious attention at a global level, not just regarding the management aspects but also the preventive strategies required to curb the spiraling menace of NAFLD. Furthermore, NAFLD and its associated comorbidities have been shown to cause profound socioeconomic, financial, and clinical burdens worldwide. The economic burden of NAFLD and its associated comorbidities and complications has been calculated to be \$908 billion over a period of 10 years.² In addition, it has also been observed that worldwide, among all liver diseases, NAFLD accounts for the highest increase in disability-adjusted life years (DALYs).³

It is also important to note that while the burden of NAFLD has been increasing, the approach of physicians to the disease entity has also changed over the years. The general approach by physicians toward NAFLD had largely been to consider it as an "artifact." Indeed, it has been reported that NAFLD is seldom looked for in the US Veterans Health Care system.⁴ Elevated liver enzymes without an apparent cause were usually glossed over; even when fatty liver was diagnosed, no lifestyle interventions were offered. The situation has changed significantly over the years. There are studies which have documented the rising incidence and prevalence of the diagnosis of NAFLD.⁵ This change in attitude toward NAFLD has taken almost five decades of rigorous work—spreading awareness about the disease, educating primary care physicians about the disease and its associated complications and focusing on prevention and management of NAFLD. The role of research on the pathogenesis of the entity, natural history and outcomes and therapeutic aspects have fostered interest among clinicians worldwide. Preventive programs have played crucial roles in educating the lay public about the disease. India has played a notable role in this regard, by becoming the first country in the world to incorporate NAFLD in the National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke which aims at tackling

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the problem of noncommunicable diseases.⁶ Needless to say, in the efforts to tackle this major public health problem, a lot of resources, funds and energy have been invested. This has paid dividends as evident from the data that awareness of having liver disease among NAFLD patients has increased over time.⁷

However, the entire process of creating awareness, educating the lay public and physicians alike, focusing on drug development and preventive strategies seems to have got derailed in the last couple of years primarily due to the nomenclature imbroglio. The current upheaval on the issue of what should be the appropriate terminology for this disease—the occurrence of fatty liver in people who do not drink alcohol—has assumed a war-like situation. Unfortunately, this has not augured well for NAFLD research and the hoopla has been more about the name of the entity, with leading researchers, hepatologists, and medical scientists having taken biased, entrenched positions.

Ever since the coming into being of this entity in medical literature, a number of myths have been propagated about NAFLD. The first of these was that NAFLD was primarily a disease of the Western world and a direct effect of industrialization and the

Table 1: Comparison of the three terminologies

Guiding principle	NAFLD	MAFLD	MASLD
Affirmative (nonstigmatizing and respectful of other branches of medicine)	Yes (affirms that these patients “do not drink alcohol” and “frees” them “from the stigma associated with alcohol”)	No (includes Patients who drink alcohol; patients will be subject to repeat questioning by physician regarding alcohol intake, quantity, frequency, advise for deaddiction)	No (includes patients who drink alcohol; also includes a subclassification called MetALD which contains the term “alcohol”)
Accurate (in its description of the condition)	Yes—acknowledges that NAFLD is a heterogenous entity	No (includes patient with multiple etiologies—alcohol, viral and other etiologies, excludes lean NAFLD patients; likely to make the entity more heterogeneous)	No (includes patient with multiple etiologies—alcohol, viral and other etiologies, excludes lean NAFLD patients; likely to make the entity more heterogeneous)
Adoptable (providing a platform that allows for inclusion of past, present, and future knowledge)	Yes	Difficult to comment—confusion prevails at the moment	Difficult to comment
Adaptable (simple, clear, and understandable as well as translatable)	Yes	Definitely “No” (has already created confusion among physicians and primary care providers)	Definitely “No” (has already created confusion among physicians and primary care providers)
Applicable (across all patients and full age spectrum [pediatric through adult])	Yes	No (confusion between pediatric metabolic liver diseases and MAFLD)	No (confusion between pediatric metabolic liver diseases and MASLD)
Able to define contribution of alcohol when greater than previously permitted	Can be defined as dual etiology	Yes	Yes

ensuing social affluence.⁸ Although this sounded politically correct, this “theory” was soon debunked when data began to emerge that showed NAFLD to be as common, if not more prevalent, in rural and agrarian societies.^{9,10} In the study published from the Eastern part of India two decades ago, in a predominantly rural population, it was found that one fourth of the subjects, people who were untouched by industrialization and affluence, had NAFLD.⁹

The whole nomenclature bandwagon seems to be driven by myths only. One of these myths is the claim that NAFLD is driven by insulin resistance and NAFLD is the hepatic manifestation of the metabolic syndrome (MS).¹¹ This is a Western concept and is not substantiated by evidence from South Asia. There is enough data to suggest that this is not true.^{12–14} The other major myth which has led people to think of alternatives to the existing terminology is that the word “fatty” is stigmatizing. While there cannot be any doubt regarding the fact that in matters of medicine and science, any change should be based on evidence, it is surprising to note that the wise men in hepatology strove to do the opposite! NAFLD was changed to metabolic-associated fatty liver disease (MAFLD) first and then, efforts were made to justify such a change. And it was palpable that these efforts at justifying the name change were based more on perceptions and notions rather than on hard evidence. Hitherto, there is no evidence in medical literature, apart from the contentious claim raised in the paper published in *Gastroenterology*, that the word “fatty” is stigmatizing.¹⁵ It has been the duty of doctors and health care professionals to advise people not to get fatty, educating them regarding the perils associated with increased body fat. For the record, here is what Hippocrates had to say 2500 years ago: “It is very injurious to health to take in more food than the constitution will bear, when, at the same time, one uses no exercise to carry off this excess.”¹⁶ He noted that premature death was more common in fatty people compared to those who were lean.¹⁶ Galen went a step ahead and commented

the following: “A polysarkos (morbidly obese person) ‘cannot walk without sweating, cannot reach when sitting at the table because of the mass of his stomach, cannot breathe easily, cannot give birth, cannot clean himself.’”¹⁷ Certainly, we would not put these ancient masters to the sword for doing such great (dis)service by educating humankind regarding health and disease! The attitude of certain patient advocacy groups in this context has been suspicious in the sense that they have indulged in *argumentum ad passiones* and have succeeded, to an extent, in swaying the medical fraternity toward a logical fallacy.

The proponents of NAFLD, MAFLD, and MASLD have taken such entrenched positions that it has become very difficult for them to see things from a different perspective. In a recent article which described the consensus process for the name change in NAFLD, guiding principles in the selection of new nomenclature were enunciated.¹⁸ It has been proposed that the principles underpinning the change of nomenclature should be—affirmative, accurate, adoptable, adaptable, applicable across all patient formats and able to define contribution of alcohol. However, a comparison of the three terminologies keeping in mind these guiding principles, in fact, makes things very clear that it is the term “NAFLD” which actually fulfils majority of these guiding principles (Table 1).

The genesis of the entire name change issue can be traced to the publication of the article “MAFLD: A Consensus-driven Proposed Nomenclature for Metabolic Associated Fatty Liver Disease” in *Gastroenterology*.¹⁵ The definition of “dysmetabolism” was defined by a set of seven arbitrary criteria, the presence of two of which would render a person dysmetabolic. However, soon after, a number of articles were published across the globe which emphasized upon the point that such a change in terminology would be premature, confusing and lacking in objective evidence.^{19–21}

Hepatologists in South Asia certainly needed no convincing that the change in nomenclature of NAFLD would certainly create

confusion and that the term NAFLD was well accepted amongst the patient community keeping in view the cultural ecosystem of South Asia where people are very sensitive to the connotation of the term “alcoholic.” Singh et al. surveyed patients across five South Asian countries and found that patients were happy with the term “NAFLD” and it destigmatized them from the taboo of alcohol.²² It is apparent that the term “nonalcoholic” in NAFLD makes a loud and bold statement that the patient “does not consume alcohol” and therefore absolves the patient of the stigma of alcohol use. This is contrary to what the proponents of the name change would forcibly make us to believe! Since the issue of name change is a contentious one, experts from the Indian National Association for Study of the Liver (INASL) and the South Asian Association for Study of the Liver (SAASL) met in March 2022 to deliberate the merits of a name change.²³ The crux of the consensus was that NAFLD should not be renamed MAFLD simply because there were no cogent reasons to justify a name change and a forced change was replete with demerits.

A word regarding the way journals and editors have taken up positions concerning the whole debate. Scientific debates are not boxing arena bouts, and headlines in leading journals such as “Let the contest begin” reminds the reader of an intense Ali-Frazier bout where physical strength and dexterity mattered the most.²⁴ Unfortunately, science is not a show of muscle power and such an attitude belies the very purpose of a scientific journal. Journal editors also need to tone down their approach while dealing with papers that use any of the terms—“NAFLD,” “MAFLD,” or “MASLD.” It is not proper to reject or discourage papers simply on the basis of usage of any one of the terms by the unsuspecting authors.

Ever since this “contest” began, there has been an avalanche of articles on the proposed change of nomenclature. It is another thing however, that the plethora of such publications have done little to advance the field of NAFLD! What do these studies really say? The results of one of these studies indicate that the prevalence of MAFLD is similar to the prevalence of NAFLD and that the clinical characteristics of patients with both entities, in general, are similar, particularly when adjusting the metabolic parameters that define MAFLD; the percentage of overlap between both entities was around 80%.²⁵ Hagström et al. too observed that 99% of patients with NAFLD met MASLD criteria, and the natural history was therefore identical.²⁶ Another study from Brazil also reported that the prevalence and factors associated with steatotic liver disease (SLD) using the NAFLD, MAFLD, and MASLD criteria were not significantly different. This study also showed that although MAFLD was found to increase the overall risk for total mortality compared to NAFLD, the difference was nonsignificant when metabolic parameters were adjusted.²⁷ Besides, the risks for cardiovascular, malignancy and diabetes-related mortality were also similar between MAFLD and NAFLD. To make matters worse, Younossi et al. dropped the bombshell when they observed that insulin resistance, a hallmark of metabolic abnormality, was not a predictor of liver mortality among MAFLD patients!¹⁴ If this is indeed true, then the very basis of a need for change in nomenclature becomes redundant! This brings us to the moot problem: “So much hullabaloo for nothing?”

The time, effort and resources spent by the consensus group to rename “NAFLD” as “MASLD” is really commendable. This was a well-orchestrated and rigorous academic exercise which the various liver societies and the individuals representing these societies took part in and managed to pull through. However, does the end justify the means? All that the consensus achieved was to change “fatty” in MAFLD to “steatotic” in MASLD. A lot has been done to popularize the term “MASLD” among the lay public. One is led to

wonder whether such dedicated efforts in making patients aware of the dangers of NAFLD a decade earlier would have reduced to some extent the spiraling rise of the NAFLD pandemic. There have been some concerns about the very consensus process itself. It has been claimed that the method itself is associated with various biases which include incentive bias, possible confirmation bias, Ben Franklin effect, courtesy bias, and acquiescence bias.²⁸ In the midst of this deadlock, there also has been an appeal to take a cue from Alexander the Great and slice through the Gordian knot. Perhaps, the authors say, this could be achieved by rebranding NAFLD as “Ludwig disease.”²⁹

Whether one slices through the Gordian knot or tries to undo the knot by loosening it, the point is that we need to move the field of NAFLD forward. The changes in nomenclature that have been proposed, unfortunately, have failed to do that and have only created a maze of confusion. In a reply to a correspondence article, Newsome et al emphasized upon the point that researchers and patients may choose to use NAFLD or MAFLD, but a unified approach is the way forward.³⁰ There have been calls for unity toward a more precise nomenclature, but this can only be achieved when the problems are acknowledged from a scientific viewpoint free from all sorts of bias. However, as someone aptly remarked, “We all see only that which we are trained to see.”

It is prevention alone which can curb the pandemic of NAFLD and lead us into a healthier future. No major changes in disease management can be expected from this “change of nomenclature” conundrum. Not that we expect tectonic shifts, but a slow and steady progress toward curbing this menace of fatty liver disease can be made only with real efforts at spreading awareness, advising people regarding lifestyle modification and healthy habits. Confusion creates problems, and we need to take collective responsibility for the bedlam we have created. The buck stops here.

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