EDITORIAL

DOI: http://dx.doi.org/10.15403/jgld-6041

Refining Nomenclature in Fatty Liver Disease: The Need for „MetVir" in Metabolic and Viral Overlap

Abdulrahman Ismaiel, Stefan-Lucian Popa, Dan L. Dumitrascu

2nd Department of Internal Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania.

Address for correspondence:
Stefan-Lucian Popa
2nd Department of Internal Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania
popa.stefan@umfcluj.ro

Received: 25.11.2024
Accepted: 30.11.2024

The field of hepatology is undergoing a significant evolution as researchers and clinicians strive to improve diagnostic clarity and develop tailored therapeutic strategies. In 2023, a milestone was reached with the introduction of new nomenclature, metabolic dysfunction-associated steatotic liver disease (MASLD) and metabolic and alcohol-associated liver disease (MetALD) [1]. This shift represented a departure from the traditional, somewhat rigid binary classifications of non-alcoholic fatty liver disease (NAFLD) and alcoholic liver disease (ALD). By emphasizing the influence of metabolic and alcohol-related factors on liver fat accumulation, these categories bring a new level of specificity to the understanding of steatotic liver disease (SLD) [2]. Despite this advancement, as nothing is perfect, a gap persists in capturing certain mixed etiologies, particularly cases of hepatic steatosis in individuals with coexisting metabolic and viral hepatitis.

Currently, viral causes of hepatic steatosis, primarily hepatitis B virus (HBV) and hepatitis C virus (HCV), are classified within the MASLD framework under „miscellaneous" SLD etiologies [1]. While this categorization acknowledges that viral infections can contribute to steatosis, it overlooks the complex interplay that often exists between viral and metabolic factors. Chronic HCV infection, for instance, is associated with extrahepatic manifestations such as type 2 diabetes (T2DM), cardiovascular disease, and chronic kidney disease, all of which frequently coexist with hepatic steatosis [3, 4]. Even after HCV eradication with high-efficacy antiviral therapy [5], metabolic dysfunction continues to influence SLD progression in many patients, underscoring the need to consider these metabolic drivers in clinical practice [6, 7].

Similarly, HBV infection is not yet explicitly addressed in the revised nomenclature. Emerging evidence suggests that fatty liver and obesity may improve HBV surface antigen clearance and reduce cirrhosis risk during antiviral therapy [3, 8, 9]. However, the coincidence of fatty liver and metabolic dysfunction has been linked to an increased risk of hepatocellular carcinoma (HCC), highlighting the complex interplay between HBV and SLD/MASLD [3, 10]. By excluding these mixed etiologies from explicit categorization, the current nomenclature misses an opportunity to guide more nuanced patient management. This omission may lead to an underappreciation of how metabolic factors exacerbate viral hepatitis or vice versa, resulting in suboptimal therapeutic strategies and less effective monitoring.

The cases of association between viral hepatitis and steatosis are relegated at the bottom of the classification, after lysosomal diseases.

As the prevalence of this association is high, we propose the introduction of „MetVir"- metabolic and viral-associated steatotic liver disease as outlined in Fig. 1. This term integrates both metabolic and viral factors. It encapsulates the idea that metabolic and viral drivers of hepatic steatosis are often synergistic, requiring distinct consideration within clinical and research settings. The introduction of „MetVir" would offer a more comprehensive classification, guiding hepatologists in the management of complex cases where metabolic and viral etiologies coexist. Moreover, as the term is similar to „MetALD", it could ease its acceptance and integration into the existing nomenclature framework.

For instance, patients with chronic HCV often present with hepatic steatosis due to both viral-induced metabolic dysregulation and traditional metabolic factors, such as insulin resistance and obesity [11]. Similarly, HBV-associated steatosis may occur in the context of metabolic dysfunction, which can influence disease outcomes [12]. By creating a unified classification like „MetVir", clinicians can ensure that both the

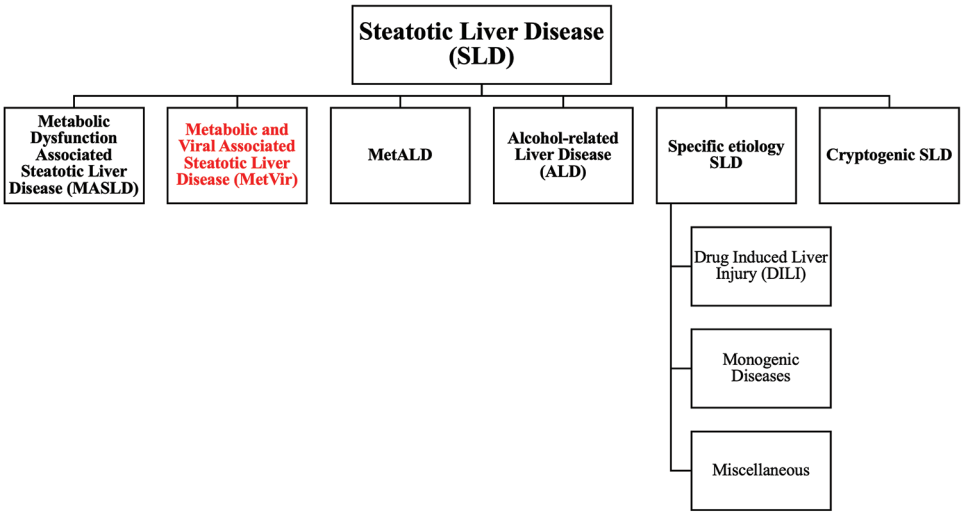

Fig. 1. Proposed modification to steatotic liver disease (SLD) classifications: inclusion of „MetVir" for metabolic and viral associated steatotic liver disease.

viral and metabolic components of steatosis are appropriately addressed in diagnosis, treatment, and follow-up care.

The implications of incorporating „MetVir" into the nomenclature are profound. First, it acknowledges the contribution of viral hepatitis in metabolic contexts, ensuring that the viral etiology is not overshadowed in patients with overlapping conditions. Chronic HBV and HCV infections influence lipid metabolism, insulin signaling, and inflammatory pathways, often exacerbating steatosis in individuals with metabolic risk factors. For example, patients with T2DM and chronic HCV infection demonstrate higher rates of hepatic steatosis compared to those with either condition alone [13]. Similarly, metabolic dysfunction in chronic HBV patients increases the risk of HCC [14]. By emphasizing this overlap, „MetVir" provides a framework for comprehensive therapeutic approaches targeting both metabolic and viral aspects, potentially improving outcomes.

In addition to its clinical implications, „MetVir" would enhance the accuracy of clinical trials and epidemiological studies. Currently, the absence of a term that captures the combined metabolic and viral etiology of steatosis complicates research interpretations and limits our understanding of disease mechanisms. Introducing „MetVir" would provide researchers with a standardized way to categorize and study this patient population. This, in turn, could catalyze studies investigating the effects of antiviral therapies on metabolic pathways and vice versa, potentially revealing novel treatment strategies [3].

Moreover, the term would encourage investigations into how viral hepatitis interacts with metabolic risk factors at the molecular level. For instance, chronic HBV and HCV infections are known to alter lipid metabolism, insulin resistance pathways, and inflammatory signaling cascades, creating a unique environment for steatosis development [15-19]. A refined classification system would enable studies to differentiate between metabolic-viral interactions and purely metabolic or viral drivers, leading to a more nuanced understanding of the disease.

The adoption of „MetVir" would promote collaboration among hepatologists, endocrinologists, infectious disease specialists, and other relevant experts. By fostering interdisciplinary care, we can more effectively address the multifactorial nature of hepatic steatosis in patients with coexisting metabolic and viral factors. Collaborative treatment plans, combining antiviral therapies, metabolic interventions, and lifestyle modifications, hold the potential to significantly improve outcomes.

For example, a patient with chronic HCV infection and metabolic syndrome may benefit from antiviral treatment combined with aggressive management of metabolic dysfunction, including weight loss, glucose control, and lipid-lowering therapies. Under the current terminology, such a patient might not receive adequately integrated care. The introduction of „MetVir" would encourage clinicians to view the patient's condition through a dual lens, ensuring both viral and metabolic components are addressed.

As the field of hepatology continues to expand, the terminology we use must evolve to capture the complexity of the conditions we treat. The proposal to introduce „MetVir"reflects a broader recognition of the diverse etiologies that contribute to hepatic steatosis. By bridging the current gap in nomenclature, „MetVir" would ensure that patients with metabolic and viral-associated steatotic liver disease are accurately categorized, appropriately managed, and thoroughly studied.

In conclusion, while the 2023 revisions to fatty liver disease nomenclature represent a significant advancement, they remain incomplete without a term that addresses mixed metabolic-viral etiologies. „MetVir" offers a necessary refinement, providing a clear and comprehensive way to describe and manage this unique subset of patients. By incorporating this term into clinical practice and research, we can advance patient care, improve outcomes, and drive the development of novel therapeutic strategies. We urge the hepatology community to consider its adoption, recognizing that accurate terminology is essential for addressing the complexities of modern liver disease.

Conflicts of interest: None to declare.

Authors' contribution: A.I. and D.L.D. conceived the manuscript. A.I. and S.L.P. collected data. A.I. drafted the manuscript. D.L.D revised the manuscript for its intellectual content. All the authors approved the final version of the manuscript.

REFERENCES

1. Rinella ME, Lazarus JV, Ratziu V, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. Hepatology 2023;78:1966-1986. doi:10.1097/HEP.0000000000000520
2. Chen L, Tao X, Zeng M, Mi Y, Xu L. Clinical and histological features under different nomenclatures of fatty liver disease: NAFLD, MAFLD, MASLD and MetALD. J Hepatol 2024;80:e64-e66. doi:10.1016/j.jhep.2023.08.021
3. Yeh ML, Yu ML. From nonalcoholic steatohepatitis, metabolic dysfunction-associated fatty liver disease, to steatotic liver disease: Updates of nomenclature and impact on clinical trials. Clin Mol Hepatol 2023;29:969-972. doi:10.3350/cmh.2023.0359
4. Hong S, Hao Y, Sun L, et al. Prevalence and risk factors of significant fibrosis in chronic hepatitis B patients with concurrent metabolic dysfunction-associated steatotic liver disease. Ann Hepatol 2024;30:101589. doi:10.1016/j.aohep.2024.101589
5. Younossi ZM, Henry L, P Ong J, et al. Systematic review with meta-analysis: extrahepatic manifestations in chronic hepatitis C virus-infected patients in East Asia. Aliment Pharmacol Ther 2019;49:644-653. doi:10.1111/apt.15131
6. Jang TY, Lin YH, Liang PC, et al. Amelioration of glucose intolerance through directly acting antiviral agents in chronic hepatitis C cirrhotic patients without overt diabetes. Kaohsiung J Med Sci 2022;38:897-906. doi:10.1002/kjm2.12563
7. Huang CF, Dai CY, Yeh ML, et al. Cure or curd: Modification of lipid profiles and cardio-cerebrovascular events after hepatitis C virus eradication. Kaohsiung J Med Sci 2020;36:920-928. doi:10.1002/kjm2.12275
8. Wong YJ, Nguyen VH, Yang HI, et al. Impact of fatty liver on long-term outcomes in chronic hepatitis B: a systematic review and matched analysis of individual patient data meta-analysis. Clin Mol Hepatol 2023;29:705-720. doi: 10.3350/cmh.2023.0004
9. Li J, Yang HI, Yeh ML, et al. Association Between Fatty Liver and Cirrhosis, Hepatocellular Carcinoma, and Hepatitis B Surface Antigen Seroclearance in Chronic Hepatitis B. J Infect Dis 2021;224:294-302. doi:10.1093/infdis/jiaa739
10. Huang SC, Su TH, Tseng TC, et al. Distinct effects of hepatic steatosis and metabolic dysfunction on the risk of hepatocellular carcinoma in chronic hepatitis B. Hepatol Int 2023;17:1139-1149. doi:10.1007/s12072-023-10545-6
11. Enjoji M, Kohjima M, Kotoh K, Nakamuta M. Metabolic disorders and steatosis in patients with chronic hepatitis C: metabolic strategies for antiviral treatments. Int J Hepatol 2012;2012:264017. doi:10.1155/2012/264017
12. Cheng YM, Hsieh TH, Wang CC, Kao JH. Impact of HBV infection on clinical outcomes in patients with metabolic dysfunction-associated fatty liver disease. JHEP Rep 2023;5:100836. doi:10.1016/j.jhepr.2023.100836
13. Asselah T, Rubbia-Brandt L, Marcellin P, Negro F. Steatosis in chronic hepatitis C: why does it really matter? Gut 2006;55:123-130. doi:10.1136/gut.2005.069757
14. Adali G, Aykut H, Bilgic NM, Yilmaz Y. Chronic hepatitis B and metabolic dysfunction-associated steatotic liver disease: Metabolic risk factors are key drivers of hepatocellular carcinoma. Heliyon 2024;10:e37990. doi:10.1016/j.heliyon.2024.e37990
15. Bose SK, Ray R. Hepatitis C virus infection and insulin resistance. World J Diabetes 2014;5:52-58. doi:10.4239/wjd.v5.i1.52
16. Machado MV, Cortez-Pinto H. Insulin resistance and steatosis in chronic hepatitis C. Ann Hepatol 2009;8 Suppl 1:S67-S75. doi:10.1016/S1665-2681(19)31829-0
17. Gastaldi G, Goossens N, Clément S, Negro F. Current level of evidence on causal association between hepatitis C virus and type 2 diabetes: A review. J Adv Res 2017;8:149-159. doi:10.1016/j.jare.2016.11.003
18. Su TC, Lee YT, Cheng TJ, Chien HP, Wang JD. Chronic hepatitis B virus infection and dyslipidemia. J Formos Med Assoc 2004;103:286-291.
19. Rivera-Esteban J, Muñoz-Martínez S, Higuera M, et al. Phenotypes of Metabolic Dysfunction-Associated Steatotic Liver Disease-Associated Hepatocellular Carcinoma. Clin Gastroenterol Hepatol 2024;22:1774-1789.e8. doi:10.1016/j.cgh.2024.03.028