Letter to the Editor

The validity of serum ferritin levels in predicting cardiovascular events of metabolic dysfunction-associated steatotic liver disease patients may need more consideration

Jie Yang[1,2], Qing Liu[1,2], Jie Li[3]*, Chao Sun[1,2]*

[1]Department of Gastroenterology, Tianjin Medical University General Hospital Airport Hospital, Tianjin, China; [2]Department of Gastroenterology and Hepatology, Tianjin Medical University General Hospital, Tianjin, China; [3]Department of Infectious Diseases, Nanjing Drum Tower Hospital, Affiliated Hospital of Medical School, Nanjing University, Nanjing, China

*These authors contributed equally to this work.

Correspondence to: Jie Li, MD, PhD. Department of Infectious Diseases, Nanjing Drum Tower Hospital, Affiliated Hospital of Medical School, Nanjing University, No. 321 Zhongshan Road, Gulou District, Nanjing 210008, China. Email: lijier@nju.edu.cn; Chao Sun, MD, PhD. Department of Gastroenterology, Tianjin Medical University General Hospital Airport Hospital, Tianjin, China; Department of Gastroenterology and Hepatology, Tianjin Medical University General Hospital, Anshan Road 154, Heping District, Tianjin 300052, China. Email: chaosun@tmu.edu.cn.

Comment on: Armandi A, Sanavia T, Younes R, *et al.* Serum ferritin levels can predict long-term outcomes in patients with metabolic dysfunction-associated steatotic liver disease. Gut 2024;73:825-34.

Keywords: Metabolic dysfunction-associated steatotic liver disease (MASLD); serum ferritin; cardiovascular events

Submitted Apr 18, 2024. Accepted for publication Jul 02, 2024. Published online Jul 22, 2024.
doi: 10.21037/hbsn-24-217
View this article at: https://dx.doi.org/10.21037/hbsn-24-217

We read with great interest the informative study by Armandi *et al.*, which shed light on the potential role of serum ferritin in predicting the long-term prognosis of patients with metabolic dysfunction-associated steatotic liver disease (1). However, there remain certain facets requiring in-depth investigation and interpretation.

First of all, the study found that integrating stepwise increased ferritin thresholds (215.5 and 272 μg/L) into predictive models can improve the performance of fibrosis-4 (FIB-4) and Non-Alcoholic Fatty Liver Disease Fibrosis Score (NFS) in the longitudinal risk assessment of liver-related events and overall mortality. However, it has been suggested that metabolic hyperferritinaemia (MHF) appears to exhibit a male predominance (2,3). Since the study primarily comprised male participants (65%), it raises the query of whether the ferritin threshold based on the entire population can accurately predict risks within female patients. Therefore, a sex-specific analysis is warranted to ensure a more precise evaluation.

Furthermore, we find the exclusion criteria did not address advanced cancer, active infection, or active inflammatory disease. These conditions can significantly impact the baseline serum ferritin levels, potentially compromising the accuracy of mortality prediction.

Currently, there are several different methods to determine ferritin levels, including labelled radiometric (immunoradiometric assay and radioimmune assay), labelled nonradiometric (fluorimetric, enzyme linked immunosorbent assay, chemiluminescent, microparticle enzyme immunoassay and radial partition immunoassay), agglutination (turbidimetric, nephelometric and latex photometric immunoassay), and others (4). It is also reported that the enzyme linked immunosorbent assay has poor agreement with microparticle enzyme immunoassay or chemiluminescent assay (5). Considering the maximum follow-up period of up to 540 months in this multi-center study, it is critical to clarify the precise measurement of ferritin across different centers. Consequently, the following concerns were raised: Firstly, were the assays utilized consistent across different centers, or sufficiently aligned for horizontal comparison? Secondly, did the results demonstrate continuity over the past 45 years for longitudinal comparison, taking the developments in assays, testing reagents, and measuring accuracy into consideration?

This study demonstrated that serum ferritin levels cannot accurately predict cardiovascular events. On the contrary, several studies have implicated significant associations between ferritin and risk factors pertinent to cardiovascular events, such as dyslipidemia, atheromatous plaque formation, hypertension and insulin resistance (6-8). The latest consensus has also highlighted the relationship between hyperferritinaemia and cardiovascular events (9). Notably, numerous medications have been developed and applied to manage abnormal low-density lipoprotein, hypertension, and vascular plaque over the course of the study. For instance, it has been proven that widely prescribed statins were capable of reducing serum ferritin levels (10). Therefore, it is pivotal to take into account the potential impact of medication on the predictive performance of baseline serum ferritin levels in relation to cardiovascular events.

Acknowledgments

Funding: This work was supported by the grant from Beijing iGandan Foundation (iGandanF-1082024-LG013).

Footnote

Provenance and Peer Review: This article was a standard submission to the journal. The article did not undergo external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://hbsn.amegroups.com/article/view/10.21037/hbsn-24-217/coif). The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Armandi A, Sanavia T, Younes R, et al. Serum ferritin levels can predict long-term outcomes in patients with metabolic dysfunction-associated steatotic liver disease. Gut 2024;73:825-34.
2. Liu WY, Lian LY, Zhang H, et al. A Population-Based and Clinical Cohort Validation of the Novel Consensus Definition of Metabolic Hyperferritinemia. J Clin Endocrinol Metab 2024;109:1540-9.
3. Suresh D, Li A, Miller MJ, et al. Associations between metabolic hyperferritinaemia, fibrosis-promoting alleles and clinical outcomes in steatotic liver disease. Liver Int 2024;44:389-98.
4. Garcia-Casal MN, Peña-Rosas JP, Urrechaga E, et al. Performance and comparability of laboratory methods for measuring ferritin concentrations in human serum or plasma: A systematic review and meta-analysis. PLoS One 2018;13:e0196576.
5. Karakochuk CD, Whitfield KC, Rappaport AI, et al. Comparison of four immunoassays to measure serum ferritin concentrations and iron deficiency prevalence among non-pregnant Cambodian women and Congolese children. Clin Chem Lab Med 2017;55:65-72.
6. Zhou B, Liu S, Yuan G. Combined Associations of Serum Ferritin and Body Size Phenotypes With Cardiovascular Risk Profiles: A Chinese Population-Based Study. Front Public Health 2021;9:550011.
7. Medisetty MK, Runwal K, Phalgune DS. Relation between Serum Ferritin Level and the Risk of Acute Myocardial Infarction. J Assoc Physicians India 2022;70:11-2.
8. Zhang Z, Li X, Zhou X, et al. Association of gestational hypertriglyceridemia, diabetes with serum ferritin levels in early pregnancy: a retrospective cohort study. Front Endocrinol (Lausanne) 2023;14:1067655.
9. Valenti L, Corradini E, Adams LA, et al. Consensus Statement on the definition and classification of metabolic hyperferritinaemia. Nat Rev Endocrinol 2023;19:299-310.
10. Zacharski LR, DePalma RG, Shamayeva G, et al. The statin-iron nexus: anti-inflammatory intervention for arterial disease prevention. Am J Public Health 2013;103:e105-12.

Cite this article as: Yang J, Liu Q, Li J, Sun C. The validity of serum ferritin levels in predicting cardiovascular events of metabolic dysfunction-associated steatotic liver disease patients may need more consideration. HepatoBiliary Surg Nutr 2024;13(4):755-756. doi: 10.21037/hbsn-24-217