

# Response to Article “Effect of Helicobacter Pylori Infection on Glucose Metabolism, Lipid Metabolism and Inflammatory Cytokines in Nonalcoholic Fatty Liver Disease Patients” [Letter]

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## Dear editor

We have read the article by Xiao et al about “Effect of Helicobacter Pylori Infection on Glucose Metabolism, Lipid Metabolism and Inflammatory Cytokines in Nonalcoholic Fatty Liver Disease Patients”.<sup>1</sup> This study investigates the impact of *Helicobacter pylori* infection on glucose metabolism, lipid metabolism, and inflammatory cytokines in patients with nonalcoholic fatty liver disease (MASLD). Nonalcoholic fatty liver disease, now known as metabolic-dysfunction-associated steatotic liver disease (MASLD), is a leading cause of chronic liver disease worldwide. The global prevalence of MASLD has been increasing over time, with a recent meta-analysis estimating that MASLD afflicts 32% of the adult population.<sup>2</sup> Since the initial report of *H. pylori* DNA being detected in the liver of non alcoholic fatty liver disease patients, numerous studies have investigated the relationship between *H. pylori* infection and this disease.<sup>3</sup>

The authors have utilized diagnostic criteria from the “Prevention and Treatment Guidelines for Nonalcoholic Fatty Liver Disease” which may not be readily accessible to an international audience due to the language barrier. The retrospective nature of the study implies reliance on diagnostic standards that have since been updated, as noted in the June 2023 revision by Rinella et al.<sup>4</sup> The study’s methodology, particularly the use of the 14C-urea breath test to diagnose *H. pylori* infection, has inherent limitations. Future investigations could enhance diagnostic accuracy through molecular techniques, such as PCR, to detect *H. pylori* and its virulence factors, including variations in the cytotoxin-associated gene A (Cag A) status.<sup>3</sup>

There is a direct association between *H. pylori* infection and insulin resistance and dyslipidemia, both presently recognized as factors contributing to the development of MASLD. Several studies revealed a positive correlation between *H. pylori* infection and MASLD, similar to this study, while some clinical studies negate this conclusion.<sup>3</sup> This may be due to variability in *H. pylori* strains, inconsistent *H. pylori* diagnostic methods, updated MASLD diagnostic criteria, and regional differences in race, genetics, lifestyle, and dietary habits. A possible mechanism of interaction between *H. pylori* infection and MASLD involves fetuin-A or alpha 2-HS glycoprotein (AHSG). Higher serum fetuin-A levels in *H. pylori*-positive patients have been reported to correlate with impaired insulin sensitivity and glucose tolerance.<sup>5</sup> Fetuin-A also acts as an endogenous adaptor protein for free fatty acid-mediated activation of TLR4 in mice. This might reflect the presence of a broad panel of inflammatory mediators (c-reactive protein, TNF- $\alpha$ , IL-6, IL-1 $\beta$ ) in patients suffering from *H. pylori* infection.<sup>6</sup> Future research should employ large-scale and multi-center randomized controlled trials to objectively and effectively assess the influence of *H. pylori* infection in MASLD patients.

We acknowledge and appreciate this study’s contribution to the field of hepatology and gastroenterology, highlighting the extragastric influence of *H. pylori* on metabolic diseases. It lays a foundation for future research to explore the

relationships between *H. pylori* infection, metabolic dysregulation, and MASLD more deeply, potentially leading to improved patient outcomes.

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## Disclosure

The authors have disclosed no conflicts of interest in this communication.

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