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Letter to the Editor

Impact of *Helicobacter pylori*-related Microbial Dysbiosis in the Pathogenesis of Metabolic Syndrome and Gastrointestinal Dysmotility Disorders

TO THE EDITOR: Singh et al[1] reviewed data on gut dysbiosis and/or interactions involved in the pathogenesis of gastrointestinal tract (GIT) dysmotility and metabolic syndrome (MetS) conditions including irritable bowel syndrome (IBS), functional dyspepsia (FD), and type 2 diabetes mellitus (T2DM). They concluded that MetS is greatly influenced by the gut, thereby metabolic disorders could begin there.

In this respect, *Helicobacter pylori* infection, a global high burden, induces GIT dysmotility (mainly abnormal gastric emptying).[2] Likewise, *H. pylori*-associated MetS conditions are related with dysmotility-stimulated gastrointestinal microbial overgrowth, potentially leading to bacteremia with systemic conditions.[3] As mentioned by the authors,[1] MetS occurs commonly in patients with small intestinal bacterial overgrowth (SIBO).[3] Gut microbiota has been connected with MetS parameters, and *H. pylori*-related T2DM, a parameter of MetS, provokes diabetic gastroparesis which may contribute to hepatic encephalopathy (HE) by altering GIT motility and inducing SIBO and subsequent bacterial translocation.[4] *H. pylori*-associated insulin resistance (IR), the main MetS key component,[5] may further provoke diabetic gastroparesis, and IR-associated diabetes is linked with bacteremia and sepsis triggering subsequent systemic conditions. In this respect, dysbiosis of the GIT microbiome, including oral and gastric *H. pylori* bacteria and several non-*H. pylori* microorganisms, is related with systemic inflammatory processes and conditions, including HE. In the setting of defensins, also mentioned by the authors,[1] the upregulation of human β defensin-1 (hBD-1) may present a biomarker of bacterial translocation involved in the pathogenesis of HE.[6] Moreover, *H. pylori* infection appears to induce hBD-1 mRNA expression,[6] which also may contribute to the pathophysiology of the central nervous system pathologies, by altering both innate and adaptive immune system reactions.[7]

Regarding *H. pylori* and MetS-related FD accompanied by GIT dysbiosis, *H. pylori* eradication may reduce the risk of MetS criteria in FD patients.[8] Likewise, *H. pylori* and MetS-related IBS may be associated with dysbiosis, and *H. pylori* eradication therapy may decrease the risk of IBS. Interestingly, *H. pylori* infection and MetS-related dysbiosis may represent major risk indicators of Parkinson's disease (PD).[5] In this respect, *H. pylori* infection may affect the bioavailability of L-dopa, a dopamine precursor used for therapy of PD, by injuring the duodenal mucosa, the main place of L-dopa main absorption. On the other hand, *H. pylori* eradication seems to improve L-dopa onset plus duration time, and PD's GIT motor fluctuations. Besides, MetS and *H. pylori* infection are connected with systemic sclerosis (SSc).[9] SSc, by inducing GIT dysmotility and SIBO, may trigger the development of complications with high morbidity/mortality. Moreover, SSc is associated with multiple sclerosis, the latter of which is also connected with dysbiosis. Eradication of *H. pylori* infection may influence the pathophysiology of SSc and multiple sclerosis, at least in certain populations.[10] Important to note, however, is that the relationship between *H. pylori* infection and the aforementioned chronic diseases has not been established yet, and, thus, further large-scale studies are needed.

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1. Singh R, Zogg H, Wei L, et al. Gut microbial dysbiosis in the pathogenesis of gastrointestinal dysmotility and metabolic disorders. J Neurogastroenterol Motil 2021;27:19-34.
2. Gümürdülü Y, Serin E, Ozer B, et al. The impact of B_{12} treatment on gastric emptying time in patients with *Helicobacter pylori* infection. J Clin Gastroenterol 2003;37:230-233.
3. Fialho A, Fialho A, Thota P, McCullough AJ, Shen B. Small intestinal bacterial overgrowth is associated with non-alcoholic fatty liver disease. J Gastrointestin Liver Dis 2016;25:159-165.
4. Ampuero J, Ranchal I, del Mar Díaz-Herrero M, del Campo JA, Bautista JD, Romero-Gómez M. Role of diabetes mellitus on hepatic encephalopathy. Metab Brain Dis 2013;28:277-279.
5. Franceschi F, Gasbarrini A, Polyzos SA, Kountouras J. Extragastric diseases and *Helicobacter pylori*. Helicobacter 2015;20(suppl 1):40-46.
6. Kountouras J, Zavos C, Polyzos SA, Deretzi G. Potential impact of *Helicobacter pylori*-related human beta-defensin-1 on hepatic encephalopathy and neurodegeneration. Ann Gastroenterol 2016;29:99.
7. Kountouras J, Deretzi G, Gavalas E, et al. A proposed role of human defensins in *Helicobacter pylori*-related neurodegenerative disorders. Med Hypotheses 2014;82:368-373.
8. Kountouras J, Gavalas E, Papaefthymiou A, et al. Trimebutine maleate monotherapy for functional dyspepsia: a multicenter, randomized, double-blind placebo controlled prospective trial. Medicina 2020;56:339.
9. Radićc M, Kaliterna DM, Bonacin D, et al. Is *Helicobacter pylori* infection a risk factor for disease severity in systemic sclerosis? Rheumatol Int 2013;33:2943-2948.
10. Kountouras J, Zavos C, Gavalas E, et al. *Helicobacter pylori* may be a common denominator associated with systemic and multiple sclerosis. Joint Bone Spine 2011;78:222-223, author reply 223.

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