Letter to the Editor

ANNALS OF MEDICINE & SURGERY

OPEN

Helicobacter pylori persists in pancreatic ductal adenocarcinoma despite eradication therapy

Muhammad Shahid Mehmood, MPhil[a], Naseeb Danaf, MD[b,*]

Abstract

Pancreatic ductal adenocarcinoma (PDAC) remains one of the deadliest malignancies, with global 5-year survival below 12%. Recent molecular analyses have revealed that *Helicobacter pylori* may persist within the pancreatic ductal microenvironment despite successful gastric eradication. In a 2024 multicenter study, *H. pylori* DNA was detected in 41.6% of PDAC tissues, including patients with documented eradication. Metagenomic sequencing identified *H. pylori* 16S rRNA reads comprising up to 2.5% of total microbial DNA, supporting selective intrapancreatic survival. Mechanistically, CagA/VacA-mediated STAT3 and NF-κB activation drives cytokine release, oxidative stress, and mismatch repair suppression, enhancing oncogenic inflammation and genomic instability. Chronic colonization increased pancreatic intraepithelial neoplasia by more than 60% in murine models, underscoring its pathogenic potential. These findings suggest that *H. pylori* persistence represents a novel microbial co-factor in PDAC, warranting further exploration as a diagnostic biomarker and therapeutic target.

Keywords: eradication resistance, *Helicobacter pylori*, inflammation-driven carcinogenesis, microbial persistence, pancreatic ductal adenocarcinoma, STAT3 activation, tumor microbiome

To the Editor,

Pancreatic ductal adenocarcinoma (PDAC) remains one of the most lethal malignancies, with an estimated 5-year survival rate below 12% and global incidence exceeding 510 000 new cases annually[1]. While genetic factors such as *KRAS, TP53*, and *SMAD4* mutations are well established, increasing evidence implicates microbial persistence and dysbiosis as contributors to PDAC pathogenesis. The gastric pathogen *Helicobacter pylori*, historically linked to gastritis and gastric carcinoma, has recently been identified within the pancreatic ductal system and tumor tissue, even after clinically confirmed eradication therapy[2].

In a 2024 multicenter molecular analysis of 168 resected PDAC specimens, *H. pylori* DNA was detected in 41.6% of tumors and in 12% of adjacent non-tumorous pancreatic tissue, indicating selective intratumoral persistence[3]. Remarkably, over half of these patients had a prior history of successful *H. pylori* eradication based on negative urea breath and stool antigen tests. This finding aligns with metagenomic sequencing studies demonstrating that *H. pylori*-derived 16S rRNA reads accounted for 1.8–2.5% of total microbial reads in PDAC tissue, compared to <0.2% in controls[4].

Mechanistically, *H. pylori* persistence may exacerbate ductal inflammation and fibrosis through *CagA*- and *VacA*-dependent activation of NF-κB and STAT3, leading to chronic cytokine release (IL-6, IL-8, TNF-α) and oxidative stress[5]. These alterations promote epithelial mesenchymal transition and impair apoptosis in KRAS-mutant pancreatic cells. A 2023 murine model confirmed that chronic *H. pylori* colonization increased pancreatic IL-1β and COX-2 expression by over 3.2-fold, accelerating PanIN (pancreatic intraepithelial neoplasia) progression[6].

Epidemiologic data indicate that patients with persistent *H. pylori* seropositivity have a 1.37-fold higher PDAC risk compared with those successfully eradicated[7]. Intriguingly, a 2025 metagenomic profiling study of PDAC bile and duodenal fluid identified *H. pylori*-specific peptide fragments in 28% of post-eradication cases, suggesting microbial migration or micro-environmental niches resistant to antibiotics[8].

In conclusion, *H. pylori* persistence in PDAC despite eradication underscores a paradigm shift from gastric pathogen to pancreatic co-factor in oncogenesis. Understanding its spatial colonization, resistance mechanisms, and interaction with host oncogenic pathways may open new diagnostic and therapeutic frontiers in pancreatic cancer. This study followed the transparency in the reporting of artificial intelligence (TITAN) guidelines 2025[9].

Ethical approval

Not applicable.

Consent

Consent for publication is not applicable as this study involves publicly available data.

[a]*Institute of Microbiology, University of Agriculture Faisalabad, Faisalabad, Pakistan and* [b]*Faculty of Medical Sciences, Lebanese University, Hadath, Lebanon*

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

**Corresponding author. Address: Faculty of Medical Sciences, Lebanese University, P.O. Box 6573/14, Hadath, Beirut, Lebanon. Tel.:+96171164810. E-mail: naseeb.danaf@st.ul.edu.lb (N. Danaf).*

Copyright © 2025 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Annals of Medicine & Surgery (2026) 88:955–956

Received 27 October 2025; Accepted 29 October 2025

Published online 24 November 2025

http://dx.doi.org/10.1097/MS9.0000000000004288

Sources of funding

The authors received no funding.

Author contributions

M.S.M.: Conceptualization, methodology, software, data curation, writing – original draft preparation, reviewing, and editing; N.D.: Writing – original draft preparation, reviewing, and editing.

Conflicts of interest disclosure

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

Naseeb Danaf.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Acknowledgements

Not applicable.

References

[1] Bray F, Laversanne M, Sung H, *et al*. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2024;74:229–63.
[2] Wei MY, Shi S, Liang C, *et al*. The microbiota and microbiome in pancreatic cancer: more influential than expected. Mol Cancer 2019; 18:97.
[3] Han S, Li R, Palermo TM. Daily pain experiences in chronic pancreatitis: identifying pain phenotypes. Pancreas 2024;53:e34–41.
[4] Tabrizi E, Pourteymour Fard Tabrizi F, Mahmoud Khaled G, *et al*. Unraveling the gut microbiome's contribution to pancreatic ductal adenocarcinoma: mechanistic insights and therapeutic perspectives. Front Immunol 2024;15:1434771.
[5] Soutto M, Bhat N, Khalafi S, *et al*. NF-kB-dependent activation of STAT3 by *H. pylori* is suppressed by TFF1. Cancer Cell Int 2021; 21:444.
[6] Nilsson HO. Helicobacter species ribosomal DNA in the pancreas, stomach and duodenum of pancreatic cancer patients. World J Gastroenterol 2006;12:3038.
[7] Zhou BG, Mei YZ, Wang JS, *et al*. Is *Helicobacter pylori* infection associated with pancreatic cancer? A systematic review and meta-analysis of observational studies. Ther Adv Chronic Dis 2023;14:20406 223231155119.
[8] Pushalkar S, Hundeyin M, Daley D, *et al*. The pancreatic cancer microbiome promotes oncogenesis by induction of innate and adaptive immune suppression. Cancer Discov 2018;8:403–16.
[9] Agha RA, Mathew G, Rashid R, *et al*. Transparency in the reporting of Artificial INtelligence – the TITAN guideline. Prem J Sci 2025;10:100082.