Microbiota in Health and Disease
A Journal of the European Helicobacter & Microbiota Study Group

INSIGHTS AND NEW APPROACHES TO *H. PYLORI* DETECTION AND MANAGEMENT IN THE CONTEXT OF MICROBIOTA SCIENCE

M.M. Effat

Department of Microbiology and Immunology, The National Research Centre, Dokki, Giza, Cairo, Egypt

Corresponding Author: Mohammad M. Effat, Ph.D; email: mmeffaty@yahoo.com; mmeffatg@gmail.com

Abstract – Detection of *Helicobacter pylori* (*H. pylori*) has traditionally relied on two main approaches – invasive and noninvasive. The invasive approach involves gastroscopic examination with or without biopsy. When biopsy specimens are obtained, they are commonly followed by rapid urease testing (RUT), microbiological culture, and polymerase chain reaction (PCR). Noninvasive methods include serological assays, stool antigen tests (SAT), and the urea breath test (UBT). However, inherent limitations, methodological inconsistencies, and assay cross-reactivities compromise diagnostic validity, rendering many global and country-specific prevalence estimates – as well as test-driven treatment decisions – unreliable and in need of critical reassessment.

Therapeutically, the sequential use of single-, dual-, triple-, and quadruple-antibiotic regimens has failed to achieve consistent or durable eradication and has been associated with multiple unintended consequences. Collectively, these observations call for a fundamental reconsideration of the microbe-centric diagnostic paradigm and test-driven therapeutic strategies currently applied to *H. pylori*. Such reconsideration should be grounded in microbiota science to redefine the ecological role of *H. pylori* within the gastric ecosystem and to promote more balanced, ecology-based management strategies, including lifestyle modification and the rational use of herb-based dietary supplements.

Keywords: *Helicobacter pylori*, Prevalence, Endoscopy, Histopathology, RUT, Culture, PCR, UBT, Serology, SAT, Dysbiosis, Eradication, Restoration, Herbal infusion therapy, Antibiotic resistance, Lifestyle modification.

INTRODUCTION

Helicobacter pylori is a constituent of the human gastric microbiota, detected in a substantial proportion of the global population, frequently in the absence of clinical manifestations[1]. Its presence does not inherently indicate pathogenicity[2]; rather, its significance emerges under conditions of perturbation or dysbiosis, reflecting a context-dependent role within the gastric microbial ecosystem[2,3]. Like other members of the microbiota, *H. pylori* exhibits a context-dependent dualistic behavior, with its biological impact determined by host factors, microbial community structure, and environmental influences[3,4].

Clinical outcomes historically attributed to *H. pylori* are increasingly understood as consequences of altered host–microbiota–environment interactions rather than the effect of a single organism[3,5]. Under conditions of ecological imbalance or dysbiosis, shifts in microbial composition, host response, and environmental influences may contribute to a range of gastrointestinal disturbances, including gastritis, peptic ulceration, and, in specific contexts, neoplastic progression[5,6]. This perspective challenges reductionist, microbe-centered, test-driven interpretations and supports a context-level understanding of disease emergence[3,7].

Adding to this complexity, *H. pylori* demonstrates considerable genetic plasticity, driven by mutation and recombination, which facilitates continuous variation within the gastric environment[8,9]. Such variability influences its distribution, interaction with other microbial constituents, and functional expression, thereby limiting the interpretive value of detection strategies that rely solely on its identification[8,10].

Within this framework, the purpose of detection extends beyond confirming the presence of *H. pylori* to evaluating its relevance within a dynamic microbial and host context, yet conventional diagnostic approaches, largely based on presence–absence paradigms[10], may therefore fail to capture context-dependent microbial states or anticipate shifts in host–microbiota equilibrium[3,4].

Accordingly, this article critically re-examines current *H. pylori* detection methods through an ecological and integrative lens, highlighting their limitations and proposing a shift toward context-aware diagnostic interpretations that better reflect microbial dynamics and host–microbiota–environment equilibrium[3,4].

SOURCE SELECTION AND REVIEW APPROACH

This narrative review was based on a focused, interpretive assessment of the published literature on *H. pylori* detection, microbiota science, and gastric ecological homeostasis. Peer-reviewed articles were identified through searches of major biomedical databases, including PubMed and Google Scholar, using combinations of keywords related to *H. pylori*, diagnostic methods, microbiota, dysbiosis, and ecological approaches to disease management. Priority was given to studies that were recognized as scientifically relevant, methodologically clear, and conceptually contributive. Additional references were identified through manual screening of reference lists and the author's clinical and research expertise. No formal systematic inclusion or exclusion criteria were applied, consistent with the narrative review format.

GERM THEORY AND *HELICOBACTER PYLORI*: CONCEPTUAL FOUNDATIONS AND LIMITATIONS

Historically, under the classical germ theory paradigm, disease has been interpreted through a microbe-centric lens; accordingly, *H. pylori* was considered the primary causative agent of multiple gastric disorders, including dyspepsia, chronic gastritis, peptic and duodenal ulcer disease, gastric adenocarcinoma, and mucosa-associated lymphoid tissue (MALT) lymphoma[11,12]. In addition, *H. pylori* colonization has been associated with several extra-gastric conditions such as iron-deficiency anemia, immune thrombocytopenic purpura, gastro-esophageal reflux disease (GERD), inflammatory bowel disease (IBD), celiac disease, and, less consistently, colorectal adenomas[13-17]. This reductionist view, however, largely overlooks the presence of trillions of other microbial inhabitants of the stomach, including bacteria, viruses, fungi, and archaea, that coexist in complex, dynamic communities whose collective or individual roles remain incompletely characterized[18-22]. Moreover, non-microbial determinants such as host metabolism, immune status, psychological stress, dietary habits, medication exposure, and environmental exposures substantially influence gastric physiology and disease susceptibility[23].

With the discovery of the human microbiota, and the recognition that many healthy individuals harbor diverse microbial populations without overt pathology, mere microbial presence or colonization can no longer be equated with disease[24-26]. Accordingly, *H. pylori* – traditionally labeled as pathogens – are increasingly viewed as indigenous members, commensal or opportunistic, of the gastric microbial ecosystem, and their colonization is not inherently pathogenic but is context-dependent. The clinical outcomes are shaped by microbial community features and interactions, host factors, and environmental influences[2,27].

Current Approaches to *H. pylori* Detection: A Test-Driven Paradigm

Current diagnostic approaches to *H. pylori*-associated conditions remain largely microbe-centric and test-driven rather than context-driven. These approaches often fail to distinguish between colonization, infection (a special and context-dependent form of colonization), and clinical disease[3,28-31].

Limitations of Clinical Manifestations in the Detection of *H. pylori*

Common gastrointestinal symptoms – such as bloating, nausea, anorexia, belching, vomiting, and burning epigastric pain– are nonspecific and specifically unrelated to microbial colonization, occurring across a wide spectrum of gastric and systemic disorders[32].

"Gold Standard" *vs.* "Reliable Standard" in *H. pylori* Detection

In accordance with Marshall and Warren[11], histopathological detection of *H. pylori* represented the first novel reference standard[11,25]. Subsequently, each newly developed detection method was labeled a "gold standard" based on comparison with preceding techniques, rather than with an objectively reliable or ideal standard[26].

In this context, a gold standard test refers to the best available reference comparator at a given time, typically functioning as a substitute for a preceding reference method used to evaluate or validate other detection methods, regardless of its inherent reliability[26]. In contrast, a reliable standard test represents an ideal, universally trustworthy diagnostic tool, characterized by high sensitivity, specificity, accuracy, reproducibility, simplicity, rapidity, cost-effectiveness, context independence, and clinical relevance[26,27].

Accordingly, no single, fully reliable, or ideal test for *H. pylori* detection currently exists. Each commonly used diagnostic modality – such as UBT, SAT, serological assays, histopathological findings, RUT, culture, and PCR – offers a combination of advantages and limitations which are summarized below[26,27].

Widely adopted strategies such as "test-and-treat," "screen-and-treat," and "test-treat-and-test" are fundamentally grounded in a microbe-centric, eradication-oriented paradigm rather than in pathophysiological relevance[32-35]. These approaches conflate microbial detectability with disease causation, often leading to unnecessary antimicrobial exposure. Routine screening for *H. pylori* in asymptomatic individuals lacks biological justification and confers no clinical benefit. Moreover, in symptomatic patients, indiscriminate testing offers limited diagnostic value given the nonspecific nature of gastrointestinal symptoms and the weak, inconsistent association between *H. pylori* detection and clinical outcomes[32-35].

Limitations of Endoscopy-Based Detection of *H. pylori*

Esophagogastroduodenoscopy (EGD) with gastric biopsy, although conventionally regarded as the invasive gold standard for *H. pylori* detection, is more appropriately viewed as an initial invasive assessment method[11]. It is susceptible to both false-negative and false-positive results. False positives may arise when nonspecific inflammatory or epithelial changes are misattributed to *H. pylori* without direct visualization of the organism[36]. False negatives arise primarily from sampling error, uneven or patchy colonization, and prior exposure to antibiotics, proton pump inhibitors, or bismuth compounds[37,38].

Histopathological evaluation – typically based on Giemsa and hematoxylin-eosin-stained sections – assesses mucosal features such as erythema, erosions, and peptic or duodenal ulcers, but these findings are not microbe-specific[36]. Rather, they reflect nonspecific host tissue responses and cannot reliably distinguish *H. pylori*-associated pathology from lesions caused by other factors[36]. Similar histopathological findings may result from chemical injury, mechanical stress, autoimmune gastritis, ischemia, NSAID-induced damage, bile reflux, or colonization by multiple bacterial or fungal species[36]. Consequently, histopathological assessment is invasive, insensitive, nonspecific, poorly reproducible, resource-intensive, and technically demanding, limiting its reliability as a definitive diagnostic reference for *H. pylori*[37].

Limitations of Culture-Based Detection of *H. pylori*

Culture of *H. pylori* performed after EGD is invasive, slow, costly, and technically demanding, with limited clinical relevance. It is insensitive and poorly reproducible, with frequent false negatives due to low bacterial density, patchy gastric distribution, prior antibiotic or acid-suppressive therapy, competing microbiota, and VBNC coccoid forms. Specificity is also compromised by potential contamination or misidentification of non-*pylori Helicobacter* species, particularly from extra-gastric sources. While valuable for research and targeted antibiotic susceptibility testing after eradication failure, culture is unreliable for routine *H. pylori* detection[39, 40].

Limitations of Molecular Detection of *H. pylori*

PCR-based detection of *H. pylori* from endoscopic biopsy specimens targets virulence genes, antibiotic resistance determinants, conserved loci (urease operon, 16S/23S rRNA, hsp60), or specific resistance mutations. In a highly diverse, panmictic organism, reliance on predefined targets is intrinsically limiting. PCR is costly, technically complex, and detects DNA rather than biological activity, failing to distinguish viable organisms from residual genetic material. False negatives may result from low bacterial density, VBNC states, inhibitors, or absent targets, while false positives can arise from conserved sequences shared with non-*pylori Helicobacter* species or homologous human DNA[41-45].

Genes traditionally labeled as virulence factors – *cagA*, *vacA*, *babA*, and *oipA* – are better understood as context-dependent determinants of microbial fitness and ecological adaptation. Their presence does not necessarily predict disease, nor does their absence imply benign behavior; pathogenic potential depends on the complex interplay between microbial genetic architecture, host susceptibility, immune responses, and environmental context[46,47].

Limitations of Immunology-Based Assays for *H. pylori* Detection

Immunological assays for *H. pylori*, including serological tests and stool antigen tests (SAT), rely on antigen–antibody interactions and on fixed, strain-dependent antigens, often derived from geographically restricted reference strains, which limits their universal applicability[20,48].

SEROLOGICAL ASSAYS

Serological tests predominantly detect IgG antibodies, as IgM responses are transient and generally uninformative in the context of long-term colonization. Host antibody profiles are highly context-dependent, shaped by microbial factors (strain diversity, bacterial load, and adaptive traits), host factors (genetic background, immune status, metabolism, and resident gastric microbiota), and environmental influences (gastric terrain, stressors, toxins, and nutrition). Multiple formats exist, including ELISA, immunochromatographic rapid tests, and immunoblotting[49-53]. Immunoblot analyses reveal heterogeneous antibody patterns directed against multiple *H. pylori* antigens, including surface and secreted components such as lipopolysaccharide (LPS), *CagA*, urease subunits, heat-shock proteins, catalase, and other enzymes[54].

Despite simplicity, low cost, rapidity, reproducibility, and high analytical sensitivity, serological assays are clinically nonspecific and inaccurate. IgG antibodies persist long after microbial suppression and cannot distinguish past exposure from active colonization, benign colonization from pathogenic activity, or colonization from ecosystem disruption. Both false positives and false negatives are common, limiting clinical relevance. Accordingly, the American College of Gastroenterology and the American Gastroenterological Association recommend against the use of serology for routine *H. pylori* detection[55,56].

Stool Antigen Tests (SAT; HpSAg)

SAT employs monoclonal or polyclonal antibodies in enzyme immunoassays (ELISA/EIA) or immunochromatographic formats (lateral flow) to detect *H. pylori* antigens noninvasively[57-66]. It is widely used for primary detection and post-treatment assessment, particularly in children as a noninvasive alternative to endoscopic testing[64]. Performance, however, is context-dependent and affected by stool consistency, antigen degradation, intermittent antigen shedding, cross-reactivity with non-*pylori Helicobacter* species or other intestinal microbes, pre-analytical handling, and recent use of antibiotics, proton pump inhibitors, or bismuth compounds[59]. While fecal immunochemical (FIT) tubes can standardize sample collection, storage, and transport, detection of stool antigen does not equate to a diagnosis of gastritis or peptic ulcer disease[67].

Limitations of Urease-Based Tests for *H. pylori* Detection

Both the urea breath test (UBT; noninvasive) and the rapid urease test (RUT; invasive) detect *H. pylori* indirectly by measuring urease activity rather than the organism itself. While UBT is highly sensitive, rapid, and reproducible, and RUT is simple, rapid, and low-cost, both tests are fundamentally nonspecific and context-dependent[68-73]. False positives may arise from urease-producing non-*pylori* microbiota, whereas false negatives occur with low bacterial load, altered gastric pH, recent use of proton pump inhibitors, antibiotics, bismuth compounds, or gastrointestinal bleeding[74-77]. Additionally, RUT false negatives are often due to patchy or uneven colonization, as the biopsy may miss colonized areas. Sensitivity is also influenced by bacterial form (spiral *vs.* coccoid) and interpretative variability[76]. Similar limitations are observed in post-gastrectomy patients and in conditions associated with altered gastric pH. Urease activity reflects a physiological buffering mechanism for local pH homeostasis rather than a pathogen-specific virulence trait. Collectively, these limitations render urease-based tests unreliable as standalone diagnostic tools, highlighting the need for critical reassessment of their clinical role[77] (Table 1).

TABLE 1. COMPARATIVE CHARACTERISTICS OF *H. PYLORI* DETECTION TESTS.

Test	Principle	Practicality[1]	Invasive	Cost	Accuracy[2]	Reproducibility
Histological findings	Gastric tissue architecture, inflammation	↓	yes	↑	↑Sens / ↓Spec	↓
Microscopic *H. pylori* detection	Bacterial visualization in tissue sections (special stains)	↓	yes	↑	↑Sens / ↓Spec	↓
Microbial culture	Viable organism	↓	yes	↑	↓Sens / ↑Spec	↓
PCR[3]	Bacterial DNA detection	↓	yes	↑	↑Sens / Spec‡	↓
RUT	Urease activity	↓	yes	↑	↑Sens / ↓Spec	↓
UBT	Urease activity	↑	No	↔	↑Sens / ↓Spec	↔
Serological assays	Antibody detection	↑	No	↓	↑Sens / ↓Spec	↔
SAT	Antigen detection	↑↑	No	↓	↓Sens / ↑Spec	↓

[1]Practicality reflects rapidity, procedural simplicity, patient acceptability, resource requirements, and pre-test restrictions.
[2]Accuracy indicates the directional balance of sensitivity and specificity. Spec denotes specificity; Sens denotes sensitivity.
[3]PCR detects bacterial DNA of viable and nonviable organisms; genetic recombination or target sequence variation may lead to false negatives, even though analytical sensitivity and specificity are high.

Additional Notes on Reproducibility

Gastroscopy-based detection assays – including histopathological examination, microscopic *H. pylori* detection, microbial culture, PCR, and RUT – are of low reproducibility due to biopsy variability, patchy gastric colonization, sampling limitations, and operator-dependent interpretation, including pathologist expertise.

Immunology-based *H. pylori* detection assays, including serological tests (ELISA, immunochromatographic rapid tests, lateral flow, and immunoblotting) and SAT, show low reproducibility due to inter-individual antibody variability, assay differences, antibody persistence after eradication, intermittent antigen shedding, and post-treatment effects.

GLOBAL AND COUNTRY – SPECIFIC *H. PYLORI* PREVALENCE ESTIMATES: A NEED FOR REVISION

H. pylori is widely described as a long-standing human-associated gastric inhabitant and is frequently reported to colonize more than half of the global population[78,79]. Published prevalence estimates vary widely, typically ranging from approximately 35% to over 90% across populations[78]. Crucially, these values do not represent direct measurements of biological colonization but are largely determined by the diagnostic tools employed. In the setting of a highly diverse, panmictic organism characterized by extensive recombination and antigenic heterogeneity, diagnostic assays that focus on restricted antigenic or genetic targets inevitably fail to capture the full spectrum of circulating *H. pylori*. As a result, a substantial proportion of colonized individuals remain undetected, leading to systematic underestimation of true colonization prevalence. Consequently, actual *H. pylori* prevalence is likely higher than declared in both developed and developing regions[70,78-82].

Global and country-specific prevalence estimates of *H. pylori* are fundamentally microbe-centric and test-driven rather than context-driven constructs and should therefore be interpreted with caution. These estimates rely on heterogeneous invasive and noninvasive assays that routinely conflate analytical detectability with true biological presence or clinical relevance, converting methodological outputs into epidemiological claims. Epidemiological studies frequently report higher *H. pylori* prevalence in developing regions than in developed ones, attributing this difference to age, socioeconomic status, hygiene, overcrowding, sanitation, and water quality[80]. However, the majority of colonized individuals remain asymptomatic throughout life, and several regions reporting very high prevalence exhibit low incidences of peptic ulcer disease and gastric cancer. Conversely, some regions classified as low-prevalence – particularly in Western Europe and North America – demonstrate disproportionately higher incidences of peptic ulcer disease and gastric cancer. Such apparent geographic differences are therefore more plausibly explained by diagnostic methodology, assay selection, and study design than by genuine biological or epidemiological disparities. Accordingly, the clinical expression of *H. pylori*-associated disorders appears to be primarily shaped by host and environmental factors rather than by microbial presence alone. Lifestyle and contextual factors – including diet, sleep disruption, psychosocial stress, metabolic status, immune regulation, and mucosal resilience – modulate gastric physiology and influence whether colonization remains silent or progresses to symptomatic disease; thus, microbial detectability in isolation is insufficient to explain disease patterns[83,84].

Phylogeographic and evolutionary inferences regarding the antiquity and global spread of *H. pylori* are similarly constrained. Such conclusions depend predominantly on molecular detection and comparative genomic analyses.

H. PYLORI AND GASTRIC CANCER: AN EPIDEMIOLOGICAL PARADOX

H. pylori colonization has been consistently associated with an increased risk of gastric adenocarcinoma, particularly non-cardia gastric cancer, through epidemiological, meta-analytic, and mechanistic studies[85-91].

H. pylori colonizes over half of the global population, yet gastric cancer (GC) develops in only 1-2% of colonized individuals. Relative risk estimates for GC among *H. pylori*-positive individuals are modest (≈1.4-4.2-fold), and geographic patterns are inconsistent: regions with >90% colonization, such as India and much of Africa, show low GC incidence, whereas Western Europe and the U.S. exhibit lower colonization but higher GC rates[92-94].

These observations indicate that colonization alone is insufficient for carcinogenesis. Host genetics, diet, environmental exposures, and microbial co-colonization are critical modulators. *H. pylori* virulence factors do not directly induce mutagenesis, and their presence or absence is not determinative of cancer[95].

While implicated in peptic ulcer disease and non-cardia gastric adenocarcinoma, *H. pylori* may protect against GERD, Barrett's esophagus, esophageal adenocarcinoma, and inflammatory bowel disease[96-99]. Eradication can disrupt the gastric microbiota, sometimes leading to persistent ecological imbalance, whereas inverse associations with pro-inflammatory bacteria suggest regulatory roles within the gut ecosystem[94-97].

Viewed as an indigenous gastric inhabitant, typically acquired in early childhood, *H. pylori* may confer physiological benefits, including modulation of leptin and ghrelin signaling and protection against allergic, autoimmune, and inflammatory disorders[97,100-102].

THE FALLACY OF *H. PYLORI* NEGATIVITY: BIOLOGICAL ORIGINS OF VARIABLE DIAGNOSTIC OUTCOMES

The human microbiota represents a dynamic ecosystem under continuous adaptive modulation, constantly reshaped by diet, stress, medication, host immunity, and environmental pressures. This macro-level dynamism implies ongoing compositional and functional fluctuations of microbial communities. In parallel, a micro-level dynamism operates within individual microbial species, enabling members to sense and adapt to their immediate microenvironment[103].

Pervasive intra-host and inter-strain diversification in *H. pylori* arises exclusively from pre-existing lineages through extensive homologous recombination, the principal driver of allelic reshuffling, alongside horizontal gene transfer and point mutations that further expand genomic diversity. In panmictic populations, frequent recombination generates highly mosaic genomes in which antigenic determinants, including surface antigens and traditionally defined virulence factors, may differ substantially from those of parental strains. Consequently, a single human host may harbor multiple coexisting or newly recombined *H. pylori* variants that are functionally distinct with respect to immune recognition, diagnostic detectability, and epidemiological classification[104-109].

Commonly used detection methods – including antibody-based serodiagnostic assays, stool antigen tests (SAT), immunoblotting, and molecular approaches such as polymerase chain reaction (PCR) – depend on the recognition of fixed antigenic or genetic targets. However, the marked genomic and phenotypic diversity generated by continuous recombination and progressive antigenic diversification precludes any single antigenic or genetic marker from universally representing all circulating strains. Apparent variability, inaccuracy, or even "negativity" in detection outcomes therefore reflects the biological reality of pervasive genetic mixing and antigenic divergence rather than true absence, eradication, or methodological failure alone. If *H. pylori* is regarded as an indigenous gastric inhabitant rather than a primary pathogen, routine detection itself becomes biologically questionable. Under such a paradigm, diagnostic efforts should shift away from mere microbial presence toward evaluation of host-microbiota interactions and the ecological state of the gastric environment.

CLINICAL MANAGEMENT AND THERAPEUTIC STRATEGIES OF *H. PYLORI*

Because of the interconnected nature of the human body and the current era of frequent antibiotic exposure, the use of antibiotics – whether appropriately or misused – can disrupt the gut microbial ecosystem (dysbiosis). This occurs whether antibiotics are administered directly to control *H. pylori* colonization, using broad-spectrum antibiotics in single, dual, triple, or even quadruple regimens, or indirectly to treat other conditions. Such practices can also promote the horizontal transfer of antibiotic resistance genes among resident gut microbiota, including *H. pylori*. Consequently, the emergence of multidrug-resistant *H. pylori* strains has become increasingly common, and unfortunately, *H. pylori* may shift toward a pathogenic behavior[110].

In line with emerging microbiota-based therapeutic strategies, *H. pylori* should be viewed not solely as a pathogen to be eliminated, but rather as a long-standing gastric resident whose biological behavior is strongly influenced by its surrounding ecosystem. Accordingly, therapeutic strategies should shift from an eradication-centered approach to one that restores and rehabilitates gastric microbial balance.

In this context, a patent-submitted herbal formulation composed of anise, cumin, black cumin (*Nigella sativa*), peppermint, caraway, sage, fennel, chamomile, dill, and rosemary has demonstrated efficacy in alleviating nonspecific gastrointestinal symptoms commonly misattributed to *Helicobacter* *pylori* in clinical practice. When prepared as an infusion by steeping the herbal mixture in boiled water for approximately ten minutes, the formulation was associated with symptomatic improvement and good tolerability, without clinical evidence of adverse gastrointestinal effects. These observations support the concept that targeted microbial rehabilitation, rather than eradication, may represent a safer and more sustainable alternative to conventional antibiotic-based strategies.

Possible Mechanisms of Action of the Herbal Formulation

The observed benefits of this multi-herbal formulation may be attributed to the synergistic bioactivities of its constituent plants. Key phytochemicals – including anethole (anise, fennel, and dill), carvone and limonene (caraway), rosmarinic acid (rosemary, sage, and peppermint), flavonoids, terpenes, and volatile oils (chamomile and cumin), and thymoquinone (black cumin) – exhibit antioxidant, anti-inflammatory, cytoprotective, mucosal-protective, and immunomodulatory properties, with reported antimicrobial and anticancer activities[111-114]. Chamomile exhibits solely antioxidant, antibacterial, antifungal, anticancer, antidiabetic, antiparasitic, anti-inflammatory, antidepressant, antipyretic, anti-allergic, and analgesic activities[115].

BARLEY PORRIDGE (AT-TALBINA): A NUTRIENT-DENSE FUNCTIONAL FOOD

At-Talbina is a traditional barley-based food prepared from whole-grain barley flour cooked with milk and sometimes sweetened with honey. In Muslim culture, it has been described as alleviating sadness, soothing the heart, and easing gastric discomfort, a description biologically compatible with current insights into gut-brain interactions, dietary fiber biology, and microbiota-mediated metabolic and neuroimmune pathways[116-118].

Barley is rich in dietary fiber – particularly β-glucan – and contains bioactive compounds with anti-inflammatory and antioxidant properties, while milk contributes high-quality proteins, minerals, and vitamins. Barley also provides tryptophan, a precursor of serotonin, offering a plausible biological basis for its traditional association with emotional comfort and mood regulation[119,120].

Β-Glucan functions as a soluble prebiotic fiber that enhances gut microbial fermentation and short-chain fatty acid production, supporting intestinal barrier integrity and immune modulation. Regular β-glucan intake is associated with improved glycemic control, cholesterol reduction, enhanced satiety, reduced cardiovascular risk, and potential protection against gastrointestinal malignancies[121-125]. Insoluble fiber fractions further promote bowel regularity and gastrointestinal health.

THE IMPACT OF DAILY LIFESTYLE MODIFICATIONS ON GASTRIC ECOLOGICAL HOMEOSTASIS, INCLUDING *H. PYLORI*

Daily lifestyle modifications influence gastric ecological homeostasis by shaping host physiology, mucosal integrity, immune regulation, and microbial balance, including *H. pylori* behavior. Balanced dietary patterns, appropriate meal timing, adequate hydration, regular moderate physical activity, sufficient sleep, and avoidance of harmful external influences modulate gastric acidity, epithelial defense, and microbiota stability. Intermittent fasting practices, including Ramadan fasting, have been associated with improved metabolic regulation, reduced inflammation, and activation of cellular repair pathways such as autophagy, indirectly supporting gastric ecological balance. Moderate physical activity enhances gastrointestinal motility, microbial diversity, and immune homeostasis. Adequate sleep (7-9 hours) and circadian alignment are essential for maintaining microbial equilibrium and limiting inflammation, whereas sleep disruption is associated with dysbiosis and an increased risk of gastrointestinal disease. Collectively, these factors shift clinical focus from microbial presence toward host-ecosystem resilience as the primary determinant of gastric health. Equally important, rational antibiotic use represents a critical modifiable determinant of gastric ecological stability. Unnecessary or inappropriate antibiotic exposure should be avoided, and when antibiotics are clinically indicated, they should be prescribed judiciously, at recommended doses and durations, without extension beyond the prescribed course. Limiting antibiotic use to clear clinical indications helps preserve microbial diversity, prevent ecological disruption, and reduce selective pressures that may alter *H. pylori* behavior within the gastric ecosystem[126,127].

CONCLUSIONS

The current paradigm concerning *Helicobacter pylori* remains constrained by assumptions that equate detection with pathogenicity and prevalence with disease burden. A critical re-evaluation of commonly employed diagnostic modalities, including gastroscopy, histopathology, PCR-based methods, microbial culture, rapid urease testing, serological assays, stool antigen testing, and urea breath testing reveals important limitations related to practicality, reproducibility, specificity, sensitivity, and contextual interpretation. None of these approaches, in isolation, can reliably distinguish colonization from clinically relevant infection.

Furthermore, global prevalence estimates of *H. pylori* are frequently misinterpreted as direct indicators of disease risk, overlooking well-documented epidemiological paradoxes such as the African and Indian enigma, where high colonization rates do not correspond to proportional increases in gastric malignancy. These observations underscore that this organism should not be viewed as a uniform pathogen, but rather as a context-dependent component of a complex gastric ecosystem shaped by host factors, microbial factors, environmental and lifestyle determinants.

Accordingly, management strategies should move beyond indiscriminate eradication toward individualized, ecologically informed approaches that prioritize restoration and rehabilitation through targeted lifestyle and dietary modifications supporting gastric and microbial homeostasis. The development of novel, non-antibiotic modalities, including microbiome-modulating formulations, represents a promising direction for safer and more sustainable intervention. Collectively, these considerations support a necessary shift from detection-driven and eradication-dependent paradigms toward context-aware, patient-centered, and restorative management of *Helicobacter pylori*.

Acknowledgments
Artificial intelligence-based tools were used only for polishing and stylistic refinement. All the scientific concepts, data interpretations, and opinions are entirely those of the author.

Ethics Approval and Informed Consent
Not applicable due to the type of article.

Conflict of Interest
The author declares no conflicts of interest.

Funding
This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data Availability
No datasets were generated or analyzed during this study.

ORCID ID
Mohammad M. Effat: 0000-0001-5519-3194

REFERENCES

1. Marshall BJ, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. Lancet 1984; 1: 1311-1315.
2. NIH Consensus Conference. Helicobacter pylori in peptic ulcer disease. NIH Consensus Development Panel on Helicobacter pylori in Peptic Ulcer Disease. JAMA 1994; 272: 65-69.
3. Valiyaveettil AN, Hamide A, Bobby Z, Krishnan R. Effect of anti-Helicobacter pylori therapy on outcome of iron-deficiency anemia: a randomized, controlled study. Indian J Gastroenterol 2005; 24: 155-157.
4. Franceschi F, Gasbarrini A. Helicobacter pylori and extragastric diseases. Best Pract Res Clin Gastroenterol 2007; 21: 325-334.

5. Franceschi F, Gasbarrini A, Polyzos SA, Kountouras J. Extragastric Diseases and Helicobacter pylori. Helicobacter 2015; 20: 40-46.
6. Pellicano R, Ianiro G, Fagoonee S, Settanni CR, Gasbarrini A. Review: Extragastric diseases and Helicobacter pylori. Helicobacter 2020; 25: e12741.
7. Gravina AG, Zagari RM, De Musis C, Romano L, Loguercio C, Romano M. Helicobacter pylori and extragastric diseases: A review. World J Gastroenterol 2018; 24: 3204-3221.
8. Bik EM, Eckburg PB, Gill SR, Nelson KE, Purdom EA, Francois F, Perez-Perez G, Blaser MJ, Relman DA. Molecular analysis of the bacterial microbiota in the human stomach. Proc Natl Acad Sci U S A 2006; 103: 732-737.
9. Delgado S, Cabrera-Rubio R, Mira A, Suárez A, Mayo B. Microbiological survey of the human gastric ecosystem using culturing and pyrosequencing methods. Microb Ecol 2013; 65: 763-772.
10. Yang I, Nell S, Suerbaum S. Survival in hostile territory: the microbiota of the stomach. FEMS Microbiol Rev 2013; 37: 736-761.
11. Turnbaugh PJ, Ley RE, Hamady M, Fraser-Liggett CM, Knight R, Gordon JI. The human microbiome project. Nature 2007; 449: 804-810.
12. Human Microbiome Project Consortium. Structure, function and diversity of the healthy human microbiome. Nature 2012; 486: 207-214.
13. Karl JP, Hatch AM, Arcidiacono SM, Pearce SC, Pantoja-Feliciano IG, Doherty LA, Soares JW. Effects of Psychological, Environmental and Physical Stressors on the Gut Microbiota. Front Microbiol 2018; 9: 2013.
14. Casanova JL. From second thoughts on the germ theory to a full-blown host theory. Proc Natl Acad Sci U S A 2023; 120: e2301186120.
15. Carlsson F, Råberg L. The germ theory revisited: A noncentric view on infection outcome. Proceedings of the National Academy of Sciences of the United States of America. 2024; 121: e2319605121.
16. Dubos RJ. Second thoughts on the germ theory. Scientific American 1955; 192: 31–35.
17. Blaser MJ, Atherton JC. Helicobacter pylori persistence: biology and disease. J Clin Invest 2004; 113: 321-333.
18. Bernardo-Cravo AP, Schmeller DS, Chatzinotas A, Vredenburg VT, Loyau A. Environmental Factors and Host Microbiomes Shape Host-Pathogen Dynamics. Trends Parasitol 2020; 36: 616-633.
19. Mohammadian T, Ganji L. The Diagnostic Tests for Detection of Helicobacter pylori Infection. Monoclon Antib Immunodiagn Immunother 2019; 38: 1-7.
20. Bordin DS, Voynovan IN, Andreev DN, Maev IV. Current Helicobacter pylori Diagnostics. Diagnostics (Basel) 2021; 11: 1458.
21. Zheng D, Liwinski T, Elinav E. Interaction between microbiota and immunity in health and disease. Cell Res 2020; 30: 492-506.
22. Mégraud F, Lehours P. Helicobacter pylori detection and antimicrobial susceptibility testing. Clin Microbiol Rev 2007; 20: 280-322.
23. Mégraud F. Advantages and disadvantages of current diagnostic tests for the detection of Helicobacter pylori. Scand J Gastroenterol Suppl 1996; 215: 57-62.
24. Talley NJ, Ford AC. Functional Dyspepsia. N Engl J Med 2015; 373: 1853-1863.
25. Pajares-García JM. Diagnosis of Helicobacter pylori: invasive methods. Ital J Gastroenterol Hepatol 1998; 30: S320-323.
26. Patel SK, Pratap CB, Jain AK, Gulati AK, Nath G. Diagnosis of Helicobacter pylori: what should be the gold standard? World J Gastroenterol 2014; 20: 12847-12859.
27. Charach L, Perets TT, Gingold-Belfer R, Huta Y, Ashorov O, Levi Z, Dickman R, Boltin D. Comparison of Four Tests for the Diagnosis of Helicobacter pylori Infection. Healthcare (Basel) 2024; 12: 1479.
28. Graham DY, Fischbach L. Helicobacter pylori treatment in the era of increasing antibiotic resistance. Gut 2010; 59: 1143-1153.
29. Vakil N, Megraud F. Eradication therapy for Helicobacter pylori. Gastroenterology 2007; 133: 985-1001.
30. Graham DY, Lew GM, Malaty HM, Evans DG, Evans DJ Jr, Klein PD, Alpert LC, Genta RM. Factors influencing the eradication of Helicobacter pylori with triple therapy. Gastroenterology 1992; 102: 493-496.
31. Thung I, Aramin H, Vavinskaya V, Gupta S, Park JY, Crowe SE, Valasek MA. Review article: the global emergence of Helicobacter pylori antibiotic resistance. Aliment Pharmacol Ther 2016; 43: 514-533.
32. Leung WK, Cheung KS, Sham PCO, Tang RSY, Loo CK, Hsu ASJ, Cheung TK, Lam LY, Chiu BCF, Wu JCY. Consensus recommendations for the screening, diagnosis, and management of Helicobacter pylori infection in Hong Kong. Hong Kong Med J 2023; 29: 532-541.
33. Leja M, Dumpis U. What Would the Screen-and-Treat Strategy for Helicobacter pylori Mean in Terms of Antibiotic Consumption? Dig Dis Sci 2020; 65: 1632-1642.
34. Moayyedi P, Malfertheiner P, Yuan Y, Rokkas T, Ford AC. Current evidence from randomized controlled trials of the benefits and harms of population-based Helicobacter pylori screen-and-treat strategies for gastric cancer prevention and review of the existing recommendations, consensus reports, and guidelines. In: Park JY, editor. Population-Based Helicobacter pylori Screen-and-Treat Strategies for Gastric Cancer Prevention: Guidance on Implementation. Lyon (FR): International Agency for Research on Cancer; 2025. Chapter 2. Available from: https://www.ncbi.nlm.nih.gov/books/NBK615778/35
35. Bomme M, Hansen JM, Wildner-Christensen M, Hallas J, Schaffalitzky de Muckadell OB. Effects of Community Screening for Helicobacter pylori: 13-Year Follow-Up Evaluation of a Randomized Controlled Trial. Clin Gastroenterol Hepatol 2017; 15: 1715-1723.e7.
36. Molyneux AJ, Harris MD. Helicobacter pylori in gastric biopsies--should you trust the pathology report? J R Coll Physicians Lond 1993; 27: 119-120.

37. Lee JY, Kim N. Diagnosis of Helicobacter pylori by invasive test: histology. Ann Transl Med 2015; 3: 10.
38. Adu-Aryee NA, Aabakken L, Dedey F, Nsaful J, Kudzi W. Comparison of endoscopic based diagnosis with Helicobacter urease test for Helicobacter pylori infection. BMC Res Notes 2016; 9: 421.
39. De Korwin JD. Avantages et inconvénients des différentes méthodes diagnostiques de l'infection à H. pylori [Advantages and limitations of diagnostic methods for H. pylori infection]. Gastroenterol Clin Biol 2003; 27: 380-390.
40. Leszczyńska K, Namiot A, Namiot Z, Leszczyńska JK, Jakoniuk P, Chilewicz M, Namiot DB, Kemona A, Milewski R, Bucki R. Patient factors affecting culture of Helicobacter pylori isolated from gastric mucosal specimens. Adv Med Sci 2010; 55: 161-166.
41. Di Bonaventura G, Neri M, Angelucci D, Rosini S, Piccolomini M, Piccolomini R. Detection of Helicobacter pylori by PCR on gastric biopsy specimens taken for CP test: comparison with histopathological analysis. Int J Immunopathol Pharmacol 2004 17: 77-82.
42. Ho SA, Hoyle JA, Lewis FA, Secker AD, Cross D, Mapstone NP, Dixon MF, Wyatt JI, Tompkins DS, Taylor GR, et al. Direct polymerase chain reaction test for detection of Helicobacter pylori in humans and animals. J Clin Microbiol 1991; 29: 2543-2549.
43. Clayton C, Kleanthous K, Tabaqchali S. Detection and identification of Helicobacter pylori by the polymerase chain reaction. J Clin Pathol 1991; 44: 515-516.
44. Makristathis A, Pasching E, Schütze K, Wimmer M, Rotter ML, Hirschl AM. Detection of Helicobacter pylori in stool specimens by PCR and antigen enzyme immunoassay. J Clin Microbiol 1998; 36: 2772-2774.
45. Schabereiter-Gurtner C, Hirschl AM, Dragosics B, Hufnagl P, Puz S, Kovách Z, Rotter M, Makristathis A. Novel real-time PCR assay for detection of Helicobacter pylori infection and simultaneous clarithromycin susceptibility testing of stool and biopsy specimens. J Clin Microbiol 2004; 42: 4512-4518.
46. Yamaoka Y. Mechanisms of disease: Helicobacter pylori virulence factors. Nat Rev Gastroenterol Hepatol 2010; 7: 629-641.
47. Dundon WG, de Bernard M, Montecucco C. Virulence factors of Helicobacter pylori. Int J Med Microbiol 2001; 290: 647-658.
48. Vaira D, Holton J, Menegatti M, Ricci C, Landi F, Ali' A, Gatta L, Acciardi C, Farinelli S, Crosatti M, Berardi S, Miglioli M. New immunological assays for the diagnosis of Helicobacter pylori infection. Gut 1999; 45(Suppl 1): I23-127.
49. Hahn M, Fennerty MB, Corless CL, Magaret N, Lieberman DA, Faigel DO. Noninvasive tests as a substitute for histology in the diagnosis of Helicobacter pylori infection. Gastrointest Endosc 2000; 52: 20-26.
50. Loy CT, Irwig LM, Katelaris PH, Talley NJ. Do commercial serological kits for Helicobacter pylori infection differ in accuracy? A meta-analysis. Am J Gastroenterol 1996; 91: 1138-1144.
51. Laheij RJ, Straatman H, Jansen JB, Verbeek AL. Evaluation of commercially available Helicobacter pylori serology kits: a review. J Clin Microbiol 1998; 36: 2803-2809.
52. Leal YA, Flores LL, García-Cortés LB, Cedillo-Rivera R, Torres J. Antibody-based detection tests for the diagnosis of Helicobacter pylori infection in children: a meta-analysis. PLoS One 2008; 3: e3751.
53. Burucoa C, Delchier JC, Courillon-Mallet A, de Korwin JD, Mégraud F, Zerbib F, Raymond J, Fauchère JL. Comparative evaluation of 29 commercial Helicobacter pylori serological kits. Helicobacter 2013; 18: 169-179.
54. Raymond J, Sauvestre C, Kalach N, Bergeret M, Dupont C. Immunoblotting and serology for diagnosis of Helicobacter pylori infection in children. Pediatr Infect Dis J 2000; 19: 118-121.
55. Chey WD, Wong BC; Practice Parameters Committee of the American College of Gastroenterology. American College of Gastroenterology guideline on the management of Helicobacter pylori infection. Am J Gastroenterol 2007; 102: 1808-1825.
56. Xu AA, Graham DY. Things We Do for No Reason™: Serum Serologic Helicobacter pylori testing. J Hosp Med 2021; 16: 691-693.
57. Kayali S, Aloe R, Bonaguri C, Gaiani F, Manfredi M, Leandro G, Fornaroli F, Di Mario F, De' Angelis GL. Non-invasive tests for the diagnosis of Helicobacter pylori: state of the art. Acta Biomed 2018; 89: 58-64.
58. Dore MP, Negrini R, Tadeu V, Marras L, Maragkoudakis E, Nieddu S, Simula L, Cherchi GB, Massarelli G, Realdi G. Novel monoclonal antibody-based Helicobacter pylori stool antigen test. Helicobacter 2004; 9: 228-232.
59. Gisbert JP, Pajares JM. Diagnosis of Helicobacter pylori infection by stool antigen determination: a systematic review. Am J Gastroenterol 2001; 96: 2829-2838.
60. Vaira D, Malfertheiner P, Mégraud F, Axon AT, Deltenre M, Hirschl AM, Gasbarrini G, O'Morain C, Garcia JM, Quina M, Tytgat GN. Diagnosis of Helicobacter pylori infection with a new non-invasive antigen-based assay. HpSA European study group. Lancet 1999; 354: 30-33.
61. Calik Z, Karamese M, Acar O, Aksak Karamese S, Dicle Y, Albayrak F, Can S, Guvendi B, Turgut A, Cicek M, Yazgi H. Investigation of Helicobacter pylori antigen in stool samples of patients with upper gastrointestinal complaints. Braz J Microbiol 2016; 47: 167-171.
62. El-Shabrawi M, El-Aziz NA, El-Adly TZ, Hassanin F, Eskander A, Abou-Zekri M, Mansour H, Meshaal S. Stool antigen detection versus 13C-urea breath test for non-invasive diagnosis of pediatric Helicobacter pylori infection in a limited resource setting. Arch Med Sci 2018; 14: 69-73.
63. Vaira D, Vakil N. Blood, urine, stool, breath, money, and Helicobacter pylori. Gut 2001; 48: 287-289.
64. Sabbi T, De Angelis P, Colistro F, Dall'Oglio L, di Abriola GF, Castro M. Efficacy of noninvasive tests in the diagnosis of Helicobacter pylori infection in pediatric patients. Arch Pediatr Adolesc Med 2005;159: 238-241.
65. Van Leerdam ME, van der Ende A, ten Kate FJ, Rauws EA, Tytgat GN. Lack of accuracy of the noninvasive Helicobacter pylori stool antigen test in patients with gastroduodenal ulcer bleeding. Am J Gastroenterol 2003; 98: 798-801.

66. Alfau M, Delgado A, Reyes C, Durán D, Arbaje D, García A. Accuracy of Stool Antigen Test in the Diagnosis of Helicobacter pylori Infection in the Dominican Republic. Cureus 2023; 15: e44290.
67. Nieuwenburg SAV, Mommersteeg MC, Wolters LMM, van Vuuren AJ, Erler N, Peppelenbosch MP, Fuhler GM, Bruno MJ, Kuipers EJ, Spaander MCW. Accuracy of H. pylori fecal antigen test using fecal immunochemical test (FIT). Gastric Cancer 2022; 25: 375-381.
68. Savarino V, Vigneri S, Celle G. The 13C urea breath test in the diagnosis of Helicobacter pylori infection. Gut 1999; 45(Suppl 1): I18-122.
69. Corvaglia L, Bontems P, Devaster JM, Heimann P, Glupczynski Y, Keppens E, Cadranel S. Accuracy of serology and 13C-urea breath test for detection of Helicobacter pylori in children. Pediatr Infect Dis J 1999; 18: 976-969.
70. Gisbert JP, Pajares JM. Review article: 13C-urea breath test in the diagnosis of Helicobacter pylori infection -- a critical review. Aliment Pharmacol Ther 2004; 20: 1001-1117.
71. Deslandres C. 13C urea breath testing to diagnose Helicobacter pylori infection in children. Can J Gastroenterol 1999; 13: 567-570.
72. Graham DY, Klein PD. Accurate diagnosis of Helicobacter pylori. 13C-urea breath test. Gastroenterol Clin North Am 2000; 29: 885-893.
73. Leal YA, Flores LL, Fuentes-Pananá EM, Cedillo-Rivera R, Torres J. 13C-urea breath test for the diagnosis of Helicobacter pylori infection in children: a systematic review and meta-analysis. Helicobacter 2011; 16: 327-337.
74. Osaki T, Mabe K, Hanawa T, Kamiya S. Urease-positive bacteria in the stomach induce a false-positive reaction in a urea breath test for diagnosis of Helicobacter pylori infection. J Med Microbiol 2008; 57: 814-819.
75. Ferwana M, Abdulmajeed I, Alhajiahmed A, Madani W, Firwana B, Hasan R, Altayar O, Limburg PJ, Murad MH, Knawy B. Accuracy of urea breath test in Helicobacter pylori infection: meta-analysis. World J Gastroenterol 2015; 21: 1305-1314.
76. Losurdo G, Francioso F, Pricci M, Girardi B, Russo F, Riezzo G, D'Attoma B, Bleve MA, Iannone A, Celiberto F, Ierardi E, DI Leo A. A prospective study on Helicobacter pylori rapid urease test false negativity: is it time for its use in restricted situations? Minerva Gastroenterol (Torino) 2023; 69: 382-387.
77. Seo JH, Park JS, Rhee KH, Youn HS. Limitations of urease test in diagnosis of pediatric Helicobacter pylori infection. World J Clin Pediatr 2015; 4: 143-147.
78. Hooi JKY, Lai WY, Ng WK, Suen MMY, Underwood FE, Tanyingoh D, Malfertheiner P, Graham DY, Wong VWS, Wu JCY, Chan FKL, Sung JJY, Kaplan GG, Ng SC. Global Prevalence of Helicobacter pylori Infection: Systematic Review and Meta-Analysis. Gastroenterology 2017; 153: 420-429.
79. Hunt RH, Xiao SD, Megraud F, Leon-Barua R, Bazzoli F, van der Merwe S, Vaz Coelho LG, Fock M, Fedail S, Cohen H, Malfertheiner P, Vakil N, Hamid S, Goh KL, Wong BC, Krabshuis J, Le Mair A; World Gastroenterology Organization. Helicobacter pylori in developing countries. World Gastroenterology Organisation Global Guideline. J Gastrointestin Liver Dis 2011; 20: 299-304.
80. Zamani M, Ebrahimtabar F, Zamani V, Miller WH, Alizadeh-Navaei R, Shokri-Shirvani J, Derakhshan MH. Systematic review with meta-analysis: the worldwide prevalence of Helicobacter pylori infection. Aliment Pharmacol Ther 2018; 47: 868-876.
81. Go MF. Review article: natural history and epidemiology of Helicobacter pylori infection. Aliment Pharmacol Ther 2002; 16: 3-15.
82. Gisbert JP, Pajares JM. Stool antigen test for the diagnosis of Helicobacter pylori infection: a systematic review. Helicobacter. 2004 Aug;9(4):347-368.
83. Zhang ZH, Ke HF, ShangGuan XY, Zhao NJ, Hu X, Li B, Cai MN, Chen MQ, Liu JH, Wu JL, Yang SY. Association of co-occurrence of gastrointestinal, sleep, and affective symptoms with Helicobacter pylori infection: a monocentric cross-sectional study in China. Front Endocrinol (Lausanne) 2025; 16: 1234567.
84. He S, He X, Duan Y, Luo Y, Li Y, Li J, Li Y, Yang P, Wang Y, Xie J, Liu M, Sk Cheng A. The impact of diet, exercise, and sleep on Helicobacter pylori infection with different occupations: a cross-sectional study. BMC Infect Dis 2024; 24: 692.
85. Huang JQ, Sridhar S, Chen Y, Hunt RH. Meta-analysis of the relationship between Helicobacter pylori seropositivity and gastric cancer. Gastroenterology 1998; 114: 1169-1179.
86. Uemura N, Okamoto S, Yamamoto S, Matsumura N, Yamaguchi S, Yamakido M, Taniyama K, Sasaki N, Schlemper RJ. Helicobacter pylori infection and the development of gastric cancer. N Engl J Med 2001; 345: 784-789.
87. Fox JG, Wang TC. Inflammation, atrophy, and gastric cancer. J Clin Invest 2007; 117: 60-69.
88. Engstrand L, Lindberg M. Helicobacter pylori and the gastric microbiota. Best Pract Res Clin Gastroenterol 2013; 27: 39-45.
89. Peek RM Jr, Blaser MJ. Helicobacter pylori and gastrointestinal tract adenocarcinomas. Nat Rev Cancer 2002; 2: 28-37.
90. Plummer M, Franceschi S, Vignat J, Forman D, de Martel C. Global burden of gastric cancer attributable to Helicobacter pylori. Int J Cancer 2015; 136: 487-490.
91. Huang JQ, Sridhar S, Chen Y, Hunt RH. Meta-analysis of the relationship between Helicobacter pylori seropositivity and gastric cancer. Gastroenterology 1998; 114: 1169-1179.
92. Holcombe C. Helicobacter pylori: the African enigma. Gut 1992; 33: 429-431.
93. Gordon D. Solving the African enigma: parasites may have their place. Gastroenterology 2000; 119: 611.
94. Graham DY, Lu H, Yamaoka Y. African, Asian or Indian enigma, the East Asian Helicobacter pylori: facts or medical myths. J Dig Dis 2009; 10: 77-84.

95. Clemente JC, Ursell LK, Parfrey LW, Knight R. The impact of the gut microbiota on human health: an integrative view. Cell. 2012; 148: 1258-1270.
96. Rokkas T, Gisbert JP, Niv Y, O'Morain C. The association between Helicobacter pylori infection and inflammatory bowel disease based on meta-analysis. United European Gastroenterol J 2015; 3: 539-550.
97. Arnold IC, Hitzler I, Müller A. The immunomodulatory properties of Helicobacter pylori confer protection against allergic and chronic inflammatory disorders. Front Cell Infect Microbiol 2012; 2: 10.
98. Rubenstein JH, Inadomi JM, Scheiman J, Schoenfeld P, Appelman H, Zhang M, Metko V, Kao JY. Association between Helicobacter pylori and Barrett's esophagus, erosive esophagitis, and gastroesophageal reflux symptoms. Clin Gastroenterol Hepatol 2014; 12: 239-345.
99. Islami F, Kamangar F. Helicobacter pylori and esophageal cancer risk: a meta-analysis. Cancer Prev Res (Phila) 2008; 1: 329-338.
100. Schubert JP, Rayner CK, Costello SP, Roberts-Thomson IC, Forster SC, Bryant RV. Helicobacter pylori: Have potential benefits been overlooked? JGH Open. 2022; 6: 735-737.
101. Sadighi A, Aghamohammadpour Z, Heravi FS, Somi MH, Nezhad KM, Hosseini S, Soufiani KB, Leylabadlo HE. The protective effects of Helicobacter pylori: A comprehensive review. Journal of Research in Clinical Medicine. 2024; 12: 1-3.
102. Francois F, Roper J, Joseph N, Pei Z, Chhada A, Shak JR, de Perez AZ, Perez-Perez GI, Blaser MJ. The effect of H. pylori eradication on meal-associated changes in plasma ghrelin and leptin. BMC Gastroenterol. 2011; 11-37.
103. Lozupone CA, Stombaugh JI, Gordon JI, Jansson JK, Knight R. Diversity, stability and resilience of the human gut microbiota. Nature. 2012; 489: 220-230.
104. Suerbaum S, Smith JM, Bapumia K, Morelli G, Smith NH, Kunstmann E, Dyrek I, Achtman M. Free recombination within Helicobacter pylori. Proc Natl Acad Sci U S A 1998; 95: 12619-12624.
105. Wilkinson DJ, Dickins B, Robinson K, Winter JA. Genomic diversity of Helicobacter pylori populations from different regions of the human stomach. Gut Microbes 2022; 14: 2152306.
106. Falush D, Kraft C, Taylor NS, Correa P, Fox JG, Achtman M, Suerbaum S. Recombination and mutation during long-term gastric colonization by Helicobacter pylori: estimates of clock rates, recombination size, and minimal age. Proc Natl Acad Sci U S A 2001; 98: 15056-15061.
107. Suerbaum S, Josenhans C. Helicobacter pylori evolution and phenotypic diversification in a changing host. Nat Rev Microbiol 2007; 5: 441-452.
108. Suerbaum S, Achtman M. Evolution of Helicobacter pylori: the role of recombination. Trends Microbiol 1999; 7: 182-184.
109. Achtman M, Azuma T, Berg DE, Ito Y, Morelli G, Pan ZJ, Suerbaum S, Thompson SA, van der Ende A, van Doorn LJ. Recombination and clonal groupings within Helicobacter pylori from different geographical regions. Mol Microbiol 1999; 32: 459-470.
110. Zou Y, Qian X, Liu X, Song Y, Song C, Wu S, An Y, Yuan R, Wang Y, Xie Y. The effect of antibiotic resistance on Helicobacter pylori eradication efficacy: A systematic review and meta-analysis. Helicobacter 2020; 25: e12714.
111. Vale FF, Oleastro M. Overview of the phytomedicine approaches against Helicobacter pylori. World J Gastroenterol 2014; 20: 5594-5609.
112. McKay DL, Blumberg JB. A review of the bioactivity and potential health benefits of peppermint tea (Mentha piperita). Phytother Res 2006; 20: 619-633.
113. Jadid N, Widodo AF, Ermavitalini D, Sa'adah NN, Gunawan S, Nisa C. The medicinal Umbelliferae plant Fennel (Foeniculum vulgare Mill.): cultivation, traditional uses, phytopharmacological properties, and application in animal husbandry. Arabian Journal of Chemistry 2023; 16: 104541.
114. Khan MA, Chen HC, Tania M, Zhang DZ. Anticancer activities of Nigella sativa (black cumin). Afr J Tradit Complement Altern Med 2011; 8: 226-232.
115. El Mihyaoui A, Esteves da Silva JCG, Charfi S, Candela Castillo ME, Lamarti A, Arnao MB. Chamomile (Matricaria chamomilla L.): A Review of Ethnomedicinal Use, Phytochemistry and Pharmacological Uses. Life (Basel) 2022; 12: 479.
116. Al-Bukhari MI. Sahih al-Bukhari. Translated by Khan MM. Riyadh: Darussalam; 1997. Book 76, Kitab al-Tibb (Book of Medicine).
117. Badrasawi MM, Shahar S, Abd Manaf Z, Haron H. Effect of Talbinah food consumption on depressive symptoms among elderly individuals in long term care facilities, randomized clinical trial. Clin Interv Aging 2013; 8: 279-285.
118. Lahouar L, Achour L, Latiri I. Talbina as a functional food and a source of health-beneficial ingredients: a narrative review. North Afr J Food Nutr Res 2021; 5: 139-151.
119. Slavin J. Whole grains and human health. Nutr Res Rev 2004; 17: 99-110.
120. Aune D, Chan DS, Lau R, Vieira R, Greenwood DC, Kampman E, Norat T. Dietary fibre, whole grains, and risk of colorectal cancer: systematic review and dose-response meta-analysis of prospective studies. BMJ 2011; 343: d6617.
121. AbuMweis SS, Jew S, Ames NP. β-glucan from barley and its lipid-lowering capacity: a meta-analysis of randomized, controlled trials. Eur J Clin Nutr 2010; 64: 1472-1480.
122. Miyamoto J, Watanabe K, Taira S, Kasubuchi M, Li X, Irie J, Itoh H, Kimura I. Barley β-glucan improves metabolic condition via short-chain fatty acids produced by gut microbial fermentation in high fat diet fed mice. PLoS One 2018; 13: e0196579.

123. Ho HV, Sievenpiper JL, Zurbau A, Blanco Mejia S, Jovanovski E, Au-Yeung F, Jenkins AL, Vuksan V. A systematic review and meta-analysis of randomized controlled trials of the effect of barley β-glucan on LDL-C, non-HDL-C and apoB for cardiovascular disease risk reduction. Eur J Clin Nutr 2016; 70: 1239-1245.
124. Kim YI. AGA technical review: impact of dietary fiber on colon cancer occurrence. Gastroenterology 2000; 118: 1235-1257.
125. Makki K, Deehan EC, Walter J, Bäckhed F. The Impact of Dietary Fiber on Gut Microbiota in Host Health and Disease. Cell Host Microbe 2018; 23: 705-715.
126. Singh RK, Chang HW, Yan D, Lee KM, Ucmak D, Wong K, Abrouk M, Farahnik B, Nakamura M, Zhu TH, Bhutani T, Liao W. Influence of diet on the gut microbiome and implications for human health. J Transl Med 2017; 15: 73.
127. Thaiss CA, Zeevi D, Levy M, Zilberman-Schapira G, Suez J, Tengeler AC, Abramson L, Katz MN, Korem T, Zmora N, Kuperman Y, Biton I, Gilad S, Harmelin A, Shapiro H, Halpern Z, Segal E, Elinav E. Transkingdom Control of microbiota diurnal oscillations promotes metabolic homeostasis. Cell 2014; 1593: 514-429.