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Helicobacter Pylori–Associated Peptic Ulcer Disease: Epidemiology, Antimicrobial Resistance, and Future Public-Health Strategies

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ABSTRACT

Helicobacter pylori remains a significant public health concern because of its association with chronic gastric infection, recurrent peptic ulcer disease (PUD), and increasing antimicrobial resistance (AMR). The review also considers socioeconomic inequalities, diagnostic limitations, and challenges in implementing effective eradication programmes. This narrative review synthesizes current evidence on the global and Indian epidemiology of *H. pylori*-associated PUD, antimicrobial resistance trends, treatment failures, and their implications for public health and healthcare services. Substantial geographical variation in resistance to metronidazole, clarithromycin, levofloxacin, and amoxicillin, particularly in India, has reduced the effectiveness of several empirical eradication regimens. Effective management requires antimicrobial stewardship, susceptibility-guided therapy, post-treatment confirmation of eradication, and equitable access to reliable diagnostic services. Emerging strategies include molecular resistance testing, vonoprazan-based therapies, adjunctive probiotics, evidence-based investigation of plant-derived antimicrobial compounds, urease inhibitors, and vaccine development. Coordinated clinical, diagnostic, public health, and research efforts are essential to reduce treatment failures, unnecessary antibiotic exposure, and the overall burden of *H. pylori* infection and associated PUD.

Keywords: *Helicobacter pylori*; Peptic ulcer disease; Antimicrobial resistance; Epidemiology; Antimicrobial stewardship

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INTRODUCTION

The high prevalence of *Helicobacter pylori* infection is associated with a variety of serious diseases of the stomach, such as chronic gastritis, peptic ulcer disease (PUD), gastric mucosa-associated lymphoid tissue lymphoma and gastric cancer, and *Helicobacter pylori* infection is still important in public health. Long term effects of *H. Pylori* chronic infection are beyond peptic ulcer disease. A recent systematic review and meta-analysis found that eradication therapy decreased the risk of gastric cancer in *H. pylori*-positive people without gastric neoplasia (RR 0.64, 95% CI 0.48–0.84) and also gastric-cancer mortality (RR 0.78, 95% CI 0.62–0.98). These results confirm early diagnosis and successful eradication of *H. pylori* as key elements of long-term prevention of gastric diseases [1].

The prevalence of *H. pylori* infection has declined in certain regions over recent decades; however, recent meta-analyses indicate that the global burden remains substantial, with considerable geographical variation and higher prevalence in low-income countries [2, 3]. Peptic ulcer disease (PUD) continues to represent a significant global health burden. According to the Global Burden of Disease (GBD) 2019 study, approximately 8.09 million prevalent cases of PUD were reported worldwide in 2019. Although the age-standardized prevalence rate declined from 143.4 per 100,000 population in 1990 to 99.4 per 100,000 in 2019, improvements were not uniformly observed across low- and lower-middle-sociodemographic-index regions [4].

Antimicrobial resistance (AMR) has emerged as a major challenge in the effective management and eradication of *H. pylori* infection. Resistance to commonly used antibiotics, including clarithromycin, metronidazole, and levofloxacin, reduces eradication success rates and contributes to treatment failure, repeated antibiotic exposure, increased healthcare costs, and persistent infection. Recent global evidence indicates that resistance to clarithromycin and levofloxacin exceeds clinically significant thresholds in several regions, emphasizing the need for continuous antimicrobial resistance surveillance and effective antimicrobial stewardship programmes [5]. In India, antimicrobial resistance in *H. pylori* represents a significant clinical challenge. A 2024 systematic review reported pooled primary resistance rates of 77.65% for metronidazole, 35.64% for clarithromycin, 32.80% for levofloxacin, and 37.78% for amoxicillin. Additionally, approximately 14.7% of isolates exhibited multidrug resistance. The review also identified substantial geographical variation in resistance patterns, highlighting the importance of regional antimicrobial resistance surveillance and susceptibility-guided eradication therapy [6].

Therefore, *H. pylori* infection should be recognized not only as a gastroenterological concern but also as a major public health challenge. Persistent infection is influenced by multiple factors,

including a substantial disease burden, inappropriate empirical antibiotic use, limited availability of antimicrobial susceptibility testing, treatment failures, socioeconomic inequalities, and unequal access to effective diagnostic and therapeutic services. Additionally, plant-derived antibacterial and antiulcer agents, along with urease inhibitors, are being investigated as potential complementary therapeutic strategies to address the growing challenges associated with antimicrobial resistance [7, 8]. This narrative review explores the global and Indian epidemiology of PUD associated with *H. pylori,* the escalating problem of antimicrobial resistance, difficulties in treatment and the public health and health services implications. It also covers future priorities of surveillance, antimicrobial stewardship, susceptibility-guided therapy, prevention and evidence-based complementary and emerging strategies.

Review Approach

This article presents a narrative review of the published literature concerning *Helicobacter pylori* infection, antimicrobial resistance, epidemiology, therapeutic strategies, public health burden, and emerging approaches to the management of *H. pylori*-associated peptic ulcer disease. Relevant evidence was selected from published original research articles, systematic reviews, meta-analyses, clinical practice guidelines, scientific reports, and other scholarly publications addressing the objectives of this review. No restrictions were imposed on the publication dates of the included literature.

Particular emphasis was placed on recent studies addressing global and Indian epidemiology, antimicrobial resistance patterns, treatment recommendations, antimicrobial stewardship, susceptibility-guided therapy, and emerging therapeutic approaches, with special consideration of their relevance to India. Earlier publications were also considered to provide relevant background information, mechanistic insights, and supporting scientific evidence. The selected literature was synthesized narratively and organized into major themes, including epidemiology, antimicrobial resistance, public health implications, current treatment considerations, and future management strategies.

Global and Indian Epidemiology of *Helicobacter pylori*-Associated Peptic Ulcer Disease

Helicobacter pylori remains one of the most prevalent chronic bacterial infections worldwide. According to a global systematic review and meta-analysis, the prevalence of H. pylori infection declined from approximately 52.6% before 1990 to 43.9% among adults during 2015–2022. During the same period, the estimated prevalence among children and adolescents was approximately 35.1% [2]. Another global systematic review and meta-analysis reported an overall prevalence of *H. pylori* infection of 43.1% during 2011–2022. The study also highlighted

the influence of sanitation, household overcrowding, socioeconomic conditions, and childhood acquisition on infection prevalence [3].

In India, the prevalence of *H. pylori* infection varies considerably across geographical regions, partly reflecting differences in socioeconomic conditions. A cross-sectional study involving 2,998 patients with dyspepsia in Karnataka reported an *H. pylori* prevalence of 43.2%. The study also identified a significant association between district-level infection prevalence and the Multidimensional Poverty Index [9]. These findings highlight geographical differences in the burden of *H. pylori* infection and suggest that national prevalence estimates alone may not adequately represent regional variations. Therefore, region-specific epidemiological surveillance and targeted public health interventions should be considered.

Recent evidence from India indicates a substantial and geographically heterogeneous burden of *H. pylori* infection. A 2025 systematic review and meta-analysis comprising 52 studies conducted across 15 Indian states reported a pooled prevalence of 54% among individuals with suspected gastrointestinal disease and 61% among those without clinically diagnosed gastrointestinal disease. Regional prevalence estimates ranged from 9% in Gujarat to 70% in Rajasthan [10]. These findings emphasize that *H. pylori* infection may occur in individuals without clinically diagnosed gastrointestinal disease and that infection prevalence should not be equated with the prevalence of peptic ulcer disease. Nevertheless, *H. pylori* is a well-established etiological factor in both gastric and duodenal ulcers and therefore represents an important target for the prevention of ulcer-related complications.

H. pylori infection also represents a substantial health burden among children and adolescents, particularly in low- and middle-income countries. A global systematic review and meta-analysis involving 198 studies and 152,650 children reported an overall paediatric prevalence of 32.3% [11]. The prevalence was significantly higher in low- and middle-income countries than in high-income countries (43.2% versus 21.7%). Important associated factors included poverty, household overcrowding, inadequate sewage facilities, consumption of untreated or unboiled drinking water, and *H. pylori* infection among close family members [11].

The global burden of peptic ulcer disease (PUD) has declined over recent decades; however, substantial inequalities persist across countries and regions in terms of disease incidence, mortality, and disability-adjusted life years (DALYs). According to the Global Burden of Disease (GBD) 2019 study, the age-standardized incidence rate of PUD decreased from 63.84 per 100,000 population in 1990 to 44.26 per 100,000 in 2019. The age-standardized mortality rate also declined significantly during this period. Nevertheless, persistent socioeconomic

inequalities highlight the need for improved prevention, early diagnosis, and equitable access to timely and effective treatment, particularly in resource-limited settings [12].

Table 1: Global and Indian epidemiological comparison of *Helicobacter pylori* infection. Source: Compiled from published epidemiological studies [2, 3, 10, 11].

Indicator	Global evidence	Indian evidence
Recent overall/adult prevalence	~43-44%	~54% in people with GI disorders
Children/adolescents	~35%	34% in children with GI diseases (95% CI: 5–68%)
Important determinants	Income, sanitation, crowding, health coverage	Marked regional and socioeconomic variation
Public-health implication	Persistent global reservoir	High burden with regional heterogeneity

***Helicobacter pylori*, Peptic Ulcer Disease And Antimicrobial Resistance**

Recurrent *Helicobacter pylori*-associated peptic ulcer disease (PUD) remains a significant clinical concern, and successful eradication of *H. pylori* is essential for reducing ulcer recurrence. However, the increasing prevalence of antimicrobial resistance (AMR) has compromised the effectiveness of several conventional eradication regimens. Resistance to commonly used antibiotics, particularly clarithromycin, metronidazole, and levofloxacin, represents a major challenge to first-line and rescue therapies. Antimicrobial resistance is a global concern, with clarithromycin resistance exceeding 15% in 24 of 31 countries and levofloxacin resistance exceeding 15% in 18 countries, according to the evidence summarized in reference [5].

The global magnitude of antimicrobial resistance in *H. pylori* was further demonstrated in a systematic review and meta-analysis by Yu et al., which included 163 studies involving 47,002 *H. pylori* isolates from 36 countries. The analysis identified geographical variations in primary antibiotic resistance and an overall increasing trend during 2013–2023. Resistance rates were generally higher among adults than among children. These findings emphasize the importance of regional antimicrobial resistance surveillance and the use of local resistance patterns to guide appropriate eradication regimens [13].

The situation is particularly concerning in India. A 2024 systematic review of studies published between 2000 and May 2023 reported pooled primary resistance rates of 77.65% for metronidazole, 35.64% for clarithromycin, 32.80% for levofloxacin, 37.78% for amoxicillin, 12.03% for furazolidone, and 11.63% for tetracycline. Approximately 14.7% of the *H. pylori* isolates exhibited multidrug resistance. The review also demonstrated considerable regional

heterogeneity, persistently high resistance to metronidazole, and an increasing trend in levofloxacin resistance in recent years [6].

The clinical consequences of antimicrobial resistance are reflected in reduced *H. pylori* eradication success rates. A systematic review and meta-analysis involving 120 studies and 28,707 patients demonstrated that resistance to clarithromycin, metronidazole, and levofloxacin significantly reduced the effectiveness of first-line eradication therapy. The adverse effect was particularly evident in cases involving clarithromycin resistance and combined clarithromycin–metronidazole resistance. These findings highlight antimicrobial resistance as an important determinant of treatment failure and emphasize the need to consider resistance patterns when selecting empirical eradication regimens [14].

Evidence from South Asia further highlights the growing challenge of antimicrobial resistance in *H. pylori*. A systematic review and meta-analysis comprising 23 studies involving 6,357 patients and 3,294 *H. pylori* isolates reported pooled resistance rates of 69% for metronidazole, 27% for clarithromycin, 34% for levofloxacin, 23% for amoxicillin, 16% for tetracycline, 12% for ciprofloxacin, and 14% for furazolidone. Temporal analyses indicated increasing resistance to several commonly used antibiotics, particularly in India, Pakistan, and Bangladesh [15].

Similar concerns have been reported across the Asia-Pacific region. An updated systematic review and meta-analysis reported resistance rates of approximately 30% for clarithromycin, 61% for metronidazole, and 35% for levofloxacin. In contrast, resistance rates to tetracycline and amoxicillin were comparatively lower, at approximately 4% and 6%, respectively [16]. These findings emphasize the importance of local antimicrobial resistance surveillance and caution against adopting uniform empirical treatment strategies across populations with differing resistance patterns.

The need to optimize *H. pylori* eradication regimens in the context of increasing antimicrobial resistance is further illustrated by recent clinical evidence from India. A 2025 randomized controlled trial conducted at the Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, enrolled 148 patients with *H. pylori*-positive peptic ulcer disease or gastritis. Participants were randomized to receive either 14-day concomitant therapy or reverse hybrid therapy. The intention-to-treat eradication rates were 79.7% and 83.7%, respectively, while the per-protocol eradication rates were 92.2% and 92.5%, respectively. No statistically significant difference was observed between the two treatment regimens. These findings highlight the importance of appropriate regimen selection, treatment adherence, and post-treatment confirmation of eradication in optimizing therapeutic outcomes [17].

Contemporary treatment guidelines increasingly emphasize the importance of antimicrobial resistance when selecting *H. pylori* eradication regimens. The 2024 American College of Gastroenterology (ACG) guideline recommends 14-day optimized bismuth quadruple therapy as the preferred empirical treatment for treatment-naïve patients when antimicrobial susceptibility is unknown. Clarithromycin- and levofloxacin-containing salvage regimens should generally be reserved for patients with confirmed susceptibility to the respective antibiotics [18]. These recommendations are consistent with the Maastricht VI/Florence Consensus Report, which emphasizes that empirical *H. pylori* eradication therapy should be guided by local antimicrobial resistance patterns. In regions where clarithromycin resistance exceeds 15% or resistance data are unavailable, bismuth quadruple therapy is recommended as a first-line treatment option [19]. The consensus further supports antimicrobial susceptibility-guided treatment and molecular resistance testing, particularly following eradication treatment failure or when resistance patterns remain uncertain [19].

Table 2: Antimicrobial resistance of *Helicobacter pylori*: comparison of India and the Asia-Pacific region. Source: Compiled from Dutta et al. (2024) [6] and Hong et al. (2024) [16].

Antibiotic	India (%)	Recent Asia-Pacific (%)	Public-health implication
Metronidazole	77.65	61	Very high resistance; empirical effectiveness may be compromised
Clarithromycin	35.64	30	Exceeds the level at which empirical clarithromycin therapy becomes problematic
Levofloxacin	32.80	35	Limits empirical rescue therapy
Amoxicillin	37.78	6	Marked Indian heterogeneity requires confirmation and surveillance
Tetracycline	11.63	4	Comparatively lower resistance

Public-Health and Health-Services Impact of *H. Pylori*-Associated PUD and AMR

The consequences of antimicrobial resistance in *Helicobacter pylori* infection extend beyond the immediate failure of eradication therapy. Unsuccessful empirical treatment may necessitate repeated clinical consultations, additional courses of antibiotics, endoscopic examinations, prolonged acid-suppressive therapy, and further diagnostic investigations. Eradication failure is associated with important clinical and economic consequences. A review conducted in the United States highlighted that unsuccessful *H. pylori* eradication may increase the risk of complications associated with persistent infection and repeated treatment, whereas successful eradication reduces the likelihood of recurrent or complicated peptic ulcer disease. The review also emphasized the substantial healthcare expenditures associated with *H. pylori*-related

complications, including hospitalization, medication costs, outpatient consultations, and the management of complicated peptic ulcer disease and gastric cancer [20].

Repeated antibiotic exposure may further promote antimicrobial resistance, creating a cycle of treatment failure, retreatment, additional antibiotic use, and increased selection pressure for resistant *H. pylori* strains. Consequently, contemporary management increasingly emphasizes antimicrobial stewardship and susceptibility-guided treatment rather than repeated empirical therapy, particularly in regions with high antimicrobial resistance rates. Recent comparative evidence supports resistance-informed treatment as an important component of antimicrobial stewardship. A systematic review and meta-analysis comparing susceptibility-guided therapy with empirical first-line treatment reported generally higher *H. pylori* eradication rates with susceptibility-guided approaches, particularly when compared with conventional empirical regimens other than bismuth quadruple therapy. These findings support the selective incorporation of antimicrobial susceptibility testing into clinical practice, especially in settings with substantial resistance to commonly prescribed antibiotics. However, the additional benefit of susceptibility-guided therapy may be less pronounced when highly effective empirical bismuth quadruple therapy is already employed [21].

This issue is particularly relevant to India, where substantial geographical variation in *H. pylori* antimicrobial resistance has been documented. Given the high pooled resistance rates to metronidazole, clarithromycin, and levofloxacin, reliance on a uniform empirical eradication strategy across the country may be inappropriate [6]. Key health-service priorities include strengthening regional antimicrobial resistance surveillance, expanding laboratory capacity for culture-based and molecular susceptibility testing, developing treatment algorithms informed by local resistance patterns, promoting rational antibiotic use, and ensuring post-treatment confirmation of *H. pylori* eradication [6].

Post-treatment confirmation of *Helicobacter pylori* eradication is essential because symptomatic improvement alone does not reliably indicate successful microbiological eradication. Current clinical guidelines recommend confirmation of eradication in all patients treated for *H. pylori* infection, preferably using a urea breath test, stool antigen test, or another validated non-serological diagnostic method. Testing should generally be performed at least four weeks after completion of eradication therapy, with proton pump inhibitors (PPIs) withheld for approximately two weeks before testing to minimize the risk of false-negative results [18, 19].

These recommendations align with broader antimicrobial resistance control initiatives in India, which emphasize integrated surveillance, antimicrobial stewardship, and strengthening of

healthcare systems [22]. Despite successful initial eradication, recurrence of *H. pylori* infection remains an important public health concern. A systematic review and meta-analysis involving 31 studies and 16,797 participants reported an overall recurrence rate of 9% and an annual recurrence rate of approximately 4%. The risk of recurrence increased with time following eradication and varied according to geographical region, treatment regimen, and Human Development Index. These findings suggest that long-term control requires not only effective initial eradication therapy but also strategies to prevent recrudescence and reinfection [23].

Socioeconomic inequalities significantly influence the transmission, persistence, and management of *H. pylori* infection. Household overcrowding, inadequate sanitation, unsafe drinking water, financial barriers to healthcare, limited health literacy, and restricted access to diagnostic and therapeutic services may contribute to persistent infection and adverse clinical outcomes. Recent evidence further supports the association between social determinants of health and the risk of *H. pylori* infection. A systematic review and meta-analysis comprising 57 studies and 387,956 participants reported a significant association between household overcrowding and increased infection risk (odds ratio [OR] 1.38; 95% confidence interval [CI] 1.03–1.85). Occupational instability and lower educational attainment were also associated with increased infection risk. Inadequate drinking-water sources, unfavorable housing conditions, and poor hygiene practices generally showed associations with increased infection risk, although considerable heterogeneity was observed across studies [24].

Reducing the burden of *H. pylori*-associated disease requires a comprehensive approach integrating effective eradication therapy, infection prevention, early diagnosis, equitable healthcare access, rational antibiotic use, and strengthened public health infrastructure. Infection prevention and antimicrobial stewardship are also important components of broader global strategies promoted by the World Health Organization (WHO) to address antimicrobial resistance and reduce its impact on healthcare systems [25].

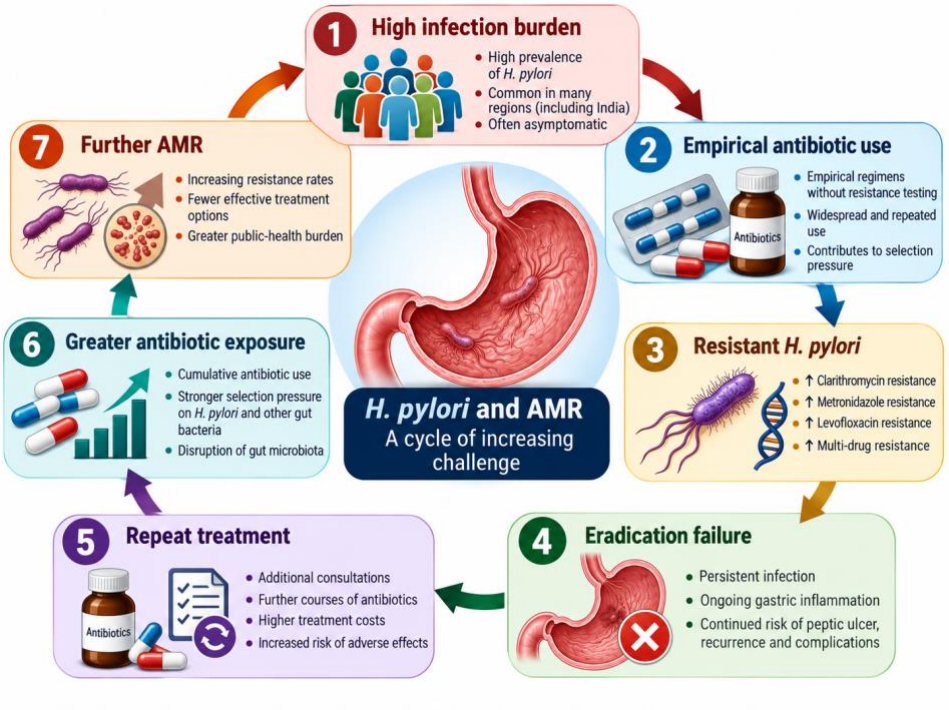


Figure 1: Public-health cycle linking *Helicobacter pylori* infection, antimicrobial resistance, treatment failure, and increased healthcare burden. Original conceptual illustration developed by the author based on published evidence [2, 5, 6, 14, 18, 20, 25].

Future Perspectives and Emerging Strategies

The management of *Helicobacter pylori*-associated peptic ulcer disease should increasingly incorporate precision-based therapeutic strategies, antimicrobial resistance surveillance, preventive measures, and antimicrobial stewardship, rather than relying solely on empirical antibiotic treatment. Considerable geographical variation in antibiotic resistance patterns exists across countries and among different regions of India. Greater integration of culture-based antimicrobial susceptibility testing and molecular techniques for detecting resistance-associated mutations may facilitate more appropriate selection of antibiotic regimens before initiating eradication therapy.

Recent advances in molecular diagnostics have expanded opportunities for susceptibility-guided *H. pylori* eradication therapy. Molecular assays can identify specific resistance-associated genetic mutations in gastric biopsy specimens and, increasingly, in stool samples, particularly those associated with clarithromycin and levofloxacin resistance [26]. Compared with conventional culture-based susceptibility testing, molecular diagnostic methods may provide more rapid identification of selected resistance-associated mutations and support rational antibiotic prescribing. However, their clinical implementation remains limited by factors such as

cost, availability, differences in diagnostic performance across antibiotics, and the need for further validation [26].

Contemporary clinical guidelines increasingly support susceptibility-guided treatment and discourage the empirical use of clarithromycin- or levofloxacin-containing regimens when susceptibility to these antibiotics has not been confirmed [18].

Clinical evidence also supports the potential benefits of genotype-guided *H. pylori* eradication therapy. A 2023 systematic review and single-arm meta-analysis involving 35 studies and 4,626 patients reported pooled eradication rates of 86.9% in intention-to-treat analyses and 91.5% in per-protocol analyses for genotype-guided *H. pylori* treatment [27]. These findings suggest that molecularly informed treatment strategies may improve eradication outcomes and reduce unnecessary exposure to potentially ineffective antibiotics, particularly in regions with high rates of clarithromycin and levofloxacin resistance [27].

Advances in gastric acid suppression offer promising opportunities to improve *Helicobacter pylori* eradication outcomes. Potassium-competitive acid blockers (P-CABs), particularly vonoprazan, provide rapid and sustained suppression of gastric acid secretion and have emerged as important components of selected *H. pylori* eradication regimens. A 2024 systematic review and meta-analysis involving 27 randomized controlled trials reported pooled *H. pylori* eradication rates of 82.8% for Vonoprazan–amoxicillin dual therapy, 89.1% for Vonoprazan–amoxicillin–clarithromycin triple therapy, and 91.8% for Vonoprazan-based bismuth-containing quadruple therapy [28]. Vonoprazan-containing triple and quadruple regimens generally demonstrated favorable eradication outcomes compared with conventional proton pump inhibitor (PPI)-based regimens in the studies reviewed. However, optimal treatment selection should consider antibiotic susceptibility, treatment duration, local resistance patterns, and the available clinical evidence [28].

Probiotics have also been investigated as adjuncts to conventional *H. pylori* eradication therapy. A 2024 umbrella review reported that probiotic supplementation may modestly improve eradication rates and reduce treatment-related adverse effects. However, the methodological quality of the available evidence varied across the included studies [29]. Further evidence from an umbrella meta-analysis comprising 18 eligible meta-analyses and 47,278 patients indicated that probiotic supplementation was associated with improved *H. pylori* eradication outcomes, with a pooled relative risk (RR) of 1.13 (95% confidence interval [CI] 1.11–1.14) [30].

Higher probiotic doses and mixed-strain formulations were associated with greater benefits in the reviewed evidence. Nevertheless, probiotics should be considered adjunctive interventions and

should not replace established antibiotic-based *H. pylori* eradication therapy [30]. Plant-derived bioactive compounds represent another emerging area of investigation for the management of *H. pylori*-associated diseases. Several natural products have demonstrated potential antibacterial, anti-inflammatory, antioxidant, anti-adhesion, and urease-inhibitory activities in experimental studies. Recent reviews have identified numerous plant-derived compounds exhibiting these pharmacological activities. However, most supporting evidence remains preclinical, and substantial variability in plant extracts, active constituents, dosages, and experimental models limits direct translation into routine clinical practice. Further standardized investigations and well-designed clinical trials are necessary to establish their efficacy and safety [7].

Urease inhibition represents a promising therapeutic approach against *Helicobacter pylori*, as urease is a major virulence-associated enzyme that enables the bacterium to survive in the acidic gastric environment by catalyzing the hydrolysis of urea into ammonia and carbon dioxide. Recent reviews of synthetic urease inhibitors have described various classes of compounds exhibiting urease-inhibitory activity and have examined their structure–activity relationships and molecular interaction patterns. These findings may facilitate the development of more potent and selective urease inhibitors [8]. However, most urease inhibitors remain at the experimental or preclinical stage of development. Further investigations are required to establish their efficacy, safety, pharmacokinetic properties, and clinical applicability before they can be considered for routine *H. pylori* eradication therapy [8].

Previous investigations of medicinal plants and plant-derived bioactive compounds have provided a scientific foundation for further research into their potential anti-*H. pylori* and gastroprotective activities [7, 8]. Nevertheless, these investigational approaches should not replace established, evidence-based eradication regimens until their clinical efficacy, optimal dosage, safety, potential drug interactions, and effects on antimicrobial resistance have been adequately evaluated through well-designed clinical trials.

The development of an effective vaccine against *H. pylori* remains an important long-term public health objective. Although considerable progress has been made in antigen selection, vaccine delivery systems, adjuvant development, and optimization of immune responses, several scientific and clinical challenges remain unresolved [31]. A 2025 review of *H. pylori* subunit vaccine development highlighted advances in adjuvant formulations, antigen delivery systems, immunization strategies, and the identification of promising vaccine candidate antigens [32]. Although several vaccine candidates have demonstrated protective effects in preclinical models, no *H. pylori* vaccine has yet been approved for routine clinical use. Further research should focus

on inducing effective mucosal immune responses, optimizing antigen delivery and adjuvant systems, and evaluating promising vaccine candidates in well-designed human clinical trials [32].

Key future priorities for India include strengthening regional antimicrobial resistance surveillance, improving access to antimicrobial susceptibility testing, promoting antimicrobial stewardship, ensuring post-treatment confirmation of *H. pylori* eradication, harmonizing evidence-based treatment guidelines, and expanding multicentre clinical research. Integrating these national priorities with global antimicrobial resistance surveillance initiatives may help reduce treatment failures, improve eradication outcomes, and generate region-specific evidence to inform future clinical guidelines.

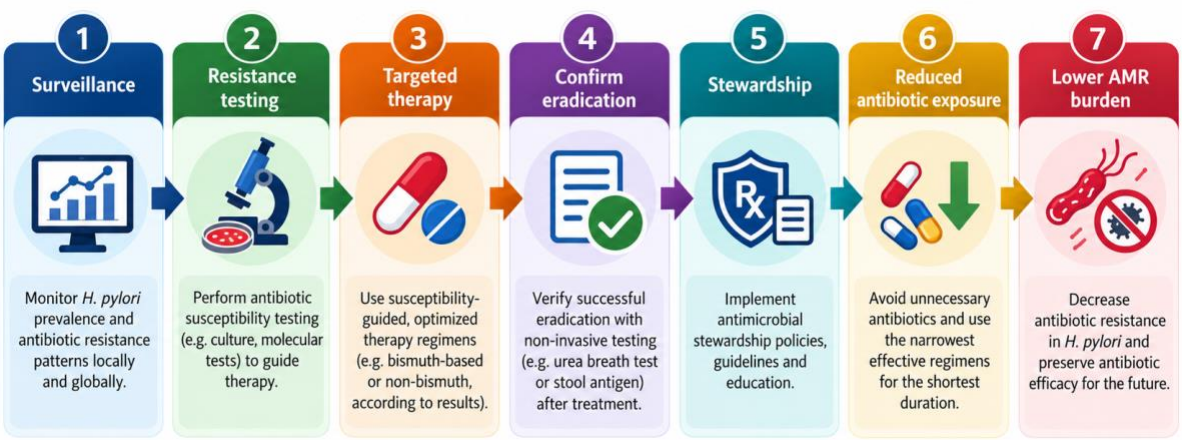


Figure 2: Integrated future strategies for controlling *Helicobacter pylori* infection and antimicrobial resistance through susceptibility-guided therapy, antimicrobial stewardship, improved diagnostics, and emerging therapeutic approaches. Original conceptual illustration developed by the author based on published evidence [18, 19, 21, 22, 25, 26, 27].

CONCLUSION

Helicobacter pylori-associated peptic ulcer disease (PUD) remains a significant global public health concern, particularly in regions characterized by a high prevalence of infection, increasing antimicrobial resistance, and limited access to diagnostic services. Increasing resistance to commonly prescribed antibiotics, particularly clarithromycin, metronidazole, and levofloxacin, has compromised the effectiveness of several empirical eradication regimens, contributing to treatment failures, repeated antibiotic exposure, additional treatment courses, and increased healthcare costs.

Substantial regional variations in antimicrobial resistance patterns further complicate the selection of effective eradication regimens in India, emphasizing the importance of regional

resistance surveillance and susceptibility-guided therapy. Future control strategies should prioritize rational antibiotic use, post-treatment confirmation of eradication, accessible and reliable diagnostic services, antimicrobial stewardship, and strengthened public health surveillance systems.

Emerging approaches, including Vonoprazan-based eradication regimens, adjunctive probiotics, molecular resistance testing, plant-derived antimicrobial and gastroprotective compounds, urease inhibitors, and vaccine development, offer opportunities to improve future management strategies. However, investigational approaches require further clinical validation before their routine use can be recommended. Coordinated clinical, diagnostic, surveillance, research, and preventive efforts at national and international levels are essential to reduce the burden of *H. pylori* infection, associated peptic ulcer disease, and antimicrobial resistance.

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