RESEARCH PAPER

Virulence genotypes and antibiotic resistance patterns of *Helicobacter pylori*: A systematic review

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Abstract
Helicobacter pylori is a gastric bacterium with a wide global distribution and is recognized for its high genetic diversity, which influences both its virulence and its response to antibiotics. In recent years, the rise in antimicrobial resistance has compromised the effectiveness of empirical therapeutic regimens, highlighting the need to integrate molecular information into the clinical management of the infection. The objective of this systematic review was to analyze recent scientific evidence on the association between virulence genotypes and antibiotic resistance patterns in H. pylori. Methodology**:** A comprehensive search was conducted in the PubMed, Scopus, ScienceDirect, and Cochrane databases, including primary studies published between 2021 and 2025. After applying the inclusion and exclusion criteria, 24 studies were selected for qualitative analysis. The results showed a high prevalence of virulence genotypes, particularly cagA-positive and vacA s1/m1, which were frequently associated with greater clinical severity and, in several regional contexts, with resistance to first-line antibiotics. Resistance to clarithromycin and fluoroquinolones was mainly linked to mutations in 23S rRNA and gyrA, respectively, whereas resistance to metronidazole exhibited more heterogeneous genetic mechanisms. Conclusions: These findings support the implementation of molecular diagnostic approaches and personalized therapeutic strategies to optimize H. pylori eradication and contain antimicrobial resistance.

Key words: Helicobacter pylori, virulence, genotypes, CagA, VacA, BabA, iceA
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Introduction

Helicobacter pylori (*H. pylori*) is a Gram-negative, microaerophilic, spiral-shaped bacterium that persistently colonizes the gastric mucosa in humans. Its ability to survive in a highly acidic environment is mainly due to the production of urease, an enzyme that neutralizes the local pH and facilitates chronic colonization of the stomach [1]. *H. pylori* infection is typically acquired during childhood and affects more than 50% of the global population, with higher prevalence in low- and middle-income regions. From a clinical perspective, this bacterium is the primary etiological agent of chronic active gastritis and peptic ulcer disease and has been classified as a Group I carcinogen because of its causal association with gastric adenocarcinoma and lymphoma [2].

Since its discovery in the early 1980s, *H. pylori* has transformed the understanding of the pathogenesis of gastric diseases. Initially considered a commensal organism, accumulating evidence has demonstrated its crucial role in chronic gastric mucosal inflammation and progression toward malignant lesions. Subsequently, several virulence factors were identified to explain the clinical heterogeneity of infection, among which *cagA*, *vacA*, *babA*, and *iceA* are particularly notable. The *cagA* gene encodes an oncogenic protein associated with intense inflammation and an increased risk of gastric cancer, whereas the *vacA* s1/m1 alleles have been linked to greater cytotoxicity and tissue damage [3,4]Concurrently, the treatment of *H. pylori* infection has relied on empirical antibiotic regimens; however, over the past decade, increasing resistance to clarithromycin, metronidazole, and fluoroquinolones has been documented. This phenomenon has been attributed both to the indiscriminate use of antibiotics and to the high genetic plasticity of *H. pylori*. Recent studies have shown that specific mutations in genes such as 23S rRNA, *gyrA*, and *rdxA* account for a substantial proportion of the resistance observed worldwide, with marked regional differences [5,6,7]. Consequently, the interaction between virulence genotypes and antibiotic resistance patterns has become a central focus of contemporary research.

The analysis of *H. pylori* virulence genotypes and antibiotic resistance patterns is of great importance for public health and modern clinical practice. First, the persistence of high infection rates, together with the global increase in antibiotic resistance, jeopardizes the effectiveness of standard treatments and promotes therapeutic failure [8]. Understanding how virulence factors are associated with resistance profiles allows

for the identification of clinically high-risk strains and the optimization of therapeutic strategies. Second, evidence indicates that certain highly virulent genotypes are not nly associated with greater clinical severity but also with a higher likelihood of multidrug resistance, reinforcing the need for personalized therapeutic approaches based on molecular testing [13–15].

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Investigating this topic provides direct benefits for the design of more effective treatment policies, reduces unnecessary exposure to ineffective antibiotics, and contributes to the containment of antimicrobial resistance. Moreover, from a research perspective, integrating virulence, genomic, and resistance data supports progress toward a precision medicine model for *H. pylori* eradication, with potential long-term impact on reducing gastric cancer incidence [9].

Numerous studies have been conducted worldwide. For example, a study carried out in Iceland compiled current evidence on geographic variations in *H. pylori*, focusing on differences between Eastern regions—East Asia—and Western regions (Europe and the Americas). The methodology involved systematically analyzing and comparing six fundamental domains: epidemiology and prevalence; transmission and reinfection; genetic diversity and population structure; clinical manifestations and disease risk; diagnostic approaches; and regional differences in treatment strategies and antibiotic resistance. The most relevant findings indicated that prevalence and disease burden are considerably higher in East Asia, with more virulent strains—such as Asian-type *cagA* and *vacA* s1/m1—associated with an increased risk of gastric cancer, pangastritis, and gastric ulcers, whereas in Western regions, less virulent strains, antral gastritis, and duodenal ulcers predominated [10].

In the same vein, a systematic review conducted in the United States of America sought to identify studies reporting antibiotic resistance in *H. pylori*; a total of 19 studies comprising 2,660 samples were included. Key findings showed high resistance rates to metronidazole (42.1%), levofloxacin (37.6%), and clarithromycin (31.5%), while resistance was low for amoxicillin (2.6%), tetracycline (0.87%), and rifabutin (0.17%). In addition, dual resistance to clarithromycin and metronidazole was identified in 11.7% of cases. These results highlight the need to avoid empirical treatments without knowledge of local resistance profiles and emphasize the importance of continuous and systematic surveillance, given the significant heterogeneity observed across studies [11].

In another review article conducted by researchers from the University of Lisbon, genomic, phenotypic, and epidemiological studies on *H. pylori* were analyzed with the aim of characterizing biomarkers of virulence and antibiotic resistance through the increasing use of next-generation sequencing (NGS) technologies. The most relevant findings included the high genetic and geographic variability of virulence factors such as CagA, VacA, and integrative and conjugative elements (ICEs), as well as mutations in target genes—such as 23S rRNA for clarithromycin, *gyrA* for levofloxacin, and *pbp1* for amoxicillin—that determine antibiotic resistance [12]

Based on this evidence, the following research question published scientific evidence on the association between virulence genotypes and antibiotic resistance patterns of Helicobacter pylori, considering its clinical and molecular impact.

1. Methodology

This review was based on a documentary research approach. For this purpose, four databases were used: Scopus, PubMed, ScienceDirect, and Cochrane. The initial search was conducted in each database according to the inclusion and exclusion criteria established for this review, using Boolean descriptors (AND, OR, NOT) and database-specific filters. The document search was performed by four professional reviewers listed as coauthors, and any doubts or disagreements were resolved through discussion among all members. Studies were included, if they used human samples and were primary articles, cross-sectional, longitudinal, observational, or interventional trials, available in full text, without language restrictions, and published between 2021 and 2025. Conversely, duplicate articles, repository-based articles, and review studies were excluded.

Article selection was carried out in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement. Subsequently, the selected studies were imported into the Rayyan platform to identify duplicates and, finally, for the screening and filtering of the documents to be evaluated.

Procedure

The analysis of the studies was carried out through the review of their titles and abstracts, as well as by full-text reading, excluding those that did not meet the inclusion criteria. The bibliographic search yielded a total of 166 articles, distributed as follows: 68 in PubMed, using the search strategy *("Helicobacter pylori"[MeSH] OR "H. pylori") AND ("Virulence Factors"[MeSH] OR cagA OR vacA OR babA2 OR "genotypes") AND ("Drug Resistance, Bacterial"[MeSH] OR "antibiotic resistance" OR "clarithromycin resistance" OR "metronidazole resistance") AND ("Polymerase Chain Reaction"[MeSH] OR PCR OR genotyping)*; 19 in ScienceDirect, using the search strategy *"Helicobacter pylori" AND "Virulence genotypes" AND ("CagA" OR "VacA" OR "BabA" OR "iceA") AND "antibiotic resistance"*; 30 in Scopus, using *"Helicobacter pylori" AND "Virulence genotypes" AND ("CagA" OR "VacA" OR "BabA" OR "iceA") AND "antibiotic resistance"*; and 49 in Cochrane, using the strategy *"Helicobacter pylori" AND "Virulence genotypes" AND ("CagA" OR "VacA" OR "BabA" OR "iceA") AND "antibiotic resistance" NOT "review"*. In the subsequent phase, 9 duplicate articles were identified, reducing the total to 157 documents. Subsequently, 86 studies were excluded

arises: what is the association between virulent genotypes and antibiotic resistance patterns of H. pylori reported in recent literature? Therefore, the objective of this review is to systematically analyze the currentafter title screening, 37 after abstract review, and 10 following full-text assessment (4 that included pediatric patients and 6 that did not report the sample used), resulting in a final inclusion of 24 articles.

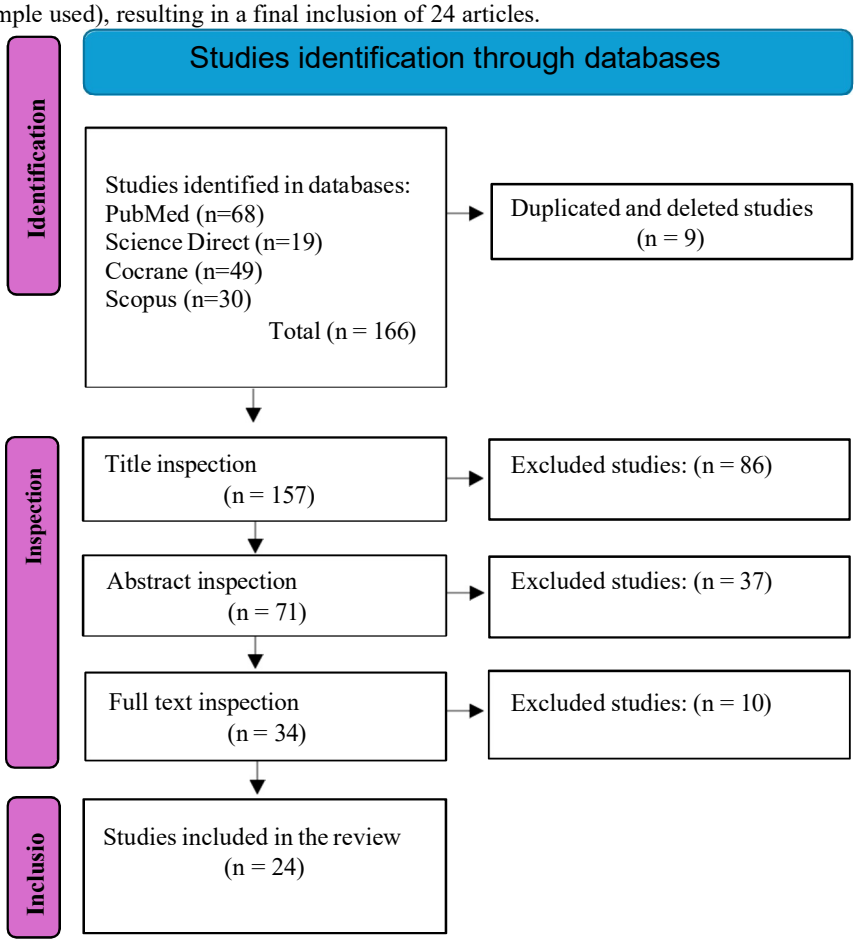

Figure 1. *Diagram for identifying, selecting, and including articles.*

2. Results

Table 1. *Helicobacter pylori virulence genotypes and their association with antibiotic resistance.*

Author, Year, Country	Title	Study design /sample	Virulance genes	Resistance profile	Findings
Alarcón-Millán et al. (2023) Mexico [13]	*Helicobacter pylori* Virulence Factors and Clarithromycin Resistance-Associated Mutations in Mexican Patients	Cross-sectional study, 117 patients	*cagA*, *vacA*	Clarithromycin	Predominance of vacA s1m1/cagA+ (44.8%); clarithromycin resistance rate of 19.8%, associated with A2143G and A2142G mutations.
Othman & Jalal (2025) Iraq [14]	Investigation of new *Helicobacter pylori* variants among cagA positive strains using MLST typing method in Iraq	Cross-sectional observational study, 120 isolates	*cagA*, *vacA*, *babA*, *iceA*	Metronidazole, clarithromycin	High coexistence of virulence genes and elevated resistance to first-line antibiotics.
Chang-Jun et al. (2025) China [15]	Detection of virulence genes in *Helicobacter pylori* and its correlation with drug resistance by polymerase chain reaction	Cross-sectional observational study, 56 strains	*cagA*, *vacA*, *babA2*, *iceA*	Multiple antibiotics	No significant association was found between virulence profiles and antibiotic resistance.

Asaad et al. (2023) Egypt [16]	Susceptibility patterns and virulence genotypes of *Helicobacter pylori* affecting eradication therapy outcomes among Egyptian patients with gastroduodenal diseases	Cross-sectional observational study, 100 patients	*cagA*, *vacA*, *babA*	Metronidazole, clarithromycin	Predominance of cagA+ and vacA s1m1 genotypes; association with greater clinical severity.
Saruuljavkhlan et al. (2023) Japan [17]	Study of *Helicobacter pylori* Isolated from a High-Gastric-Cancer-Risk Population: Unveiling the Comprehensive Analysis of Virulence-Associated Genes including Secretion Systems, and Genome-Wide Association Study	Cross-sectional observational study, 96 isolates	*cagA*, *vacA*, *babA*, *iceA*	Clarithromycin, metronidazole	Highly virulent genotypes were associated with multidrug antibiotic resistance.

Table 2. *Genetic determinants of antibiotic resistance and genomic profiles.*

Author, Year, Country	Title	Isolates	Resistance mutations	Antibiotics	Findings
Alkharsah et al. (2022) Saudi Arabia [18]	Molecular characterization of *Helicobacter pylori* clinical isolates from Eastern Saudi Arabia	92	23S rRNA (A2143G, A2142G)	Clarithromycin	All strains were cagA+; clarithromycin resistance reached up to 29%.
Imane et al. (2022) Morocco [19]	*Helicobacter pylori* resistance to metronidazole and its association with virulence factors in a Moroccan population	111	*rdxA*	Metronidazole	High resistance to metronidazole; association with cagA+ and vacA s1m1.
Cong et al. (2023) China [20]	RdxA Diversity and Mutations Associated with Metronidazole Resistance of *Helicobacter pylori*	150	*rdxA*	Metronidazole	High genetic diversity of rdxA is associated with resistance.
Hu et al. (2023) China [21]	Long-Read- and Short-Read-Based Whole-Genome Sequencing Reveals the Antibiotic Resistance Pattern of *Helicobacter pylori*	104	23S rRNA, *gyrA*	Clarithromycin, levofloxacin	High genotype–phenotype concordance.
Kumar et al. (2022) India [22]	Region-specific genomic signatures of multidrug-resistant *Helicobacter pylori* isolated from East and South India	48	*rdxA*, 23S rRNA, *gyrA*	Multiple	Regional genomic signatures associated with multidrug resistance.
Li et al. (2021) China [23]	Genotyping *Helicobacter pylori* antibiotic resistance and virulence-associated genes in patients with gastric cancer in Wenzhou, China	101	23S rRNA, *gyrA*, *rdxA*, *pbp1*	Metronidazole, levofloxacin	High resistance in strains associated with gastric cancer.

Schubert et al. (2024) Australia [24]	Genomic analysis of *Helicobacter pylori* in Australia: Antimicrobial resistance, phylogenetic patterns, and virulence factors	82	23S rRNA, *gyrA*, *rdxA*	Clarithromycin, metronidazole	Multidrug resistance in 59% of isolates; high genomic concordance.
Wang et al. (2026) China [25]	Genomic insights into antibiotic resistance, virulence traits and phylogenetic lineages of 141 clinical *Helicobacter pylori* isolate from Eastern China	141	23S rRNA (A2143G), *gyrA* (N87K)	Metronidazole, levofloxacin	Very high resistance; predominance of highly virulent genotypes.
Yakubu et al. (2024) África; [26]	Pangenome Analysis of *Helicobacter pylori* Isolates from Selected Areas of Africa Indicated Diverse Antibiotic Resistance and Virulence Genes	34	Genes AMR múltiples	Multiple	High genetic diversity; coexistence of virulence and AMR genes.

Table 3. *Molecular mechanisms of antibiotic resistance, virulence, and diagnostic approaches in Helicobacter pylori.*

Author, Year, Country	Tìtle	Study type	Molecular approach	Evaluated resistance	Findings
Ashkar et al. (2024) Israel [27]	Associations between biofilm formation and virulence factors among clinical *Helicobacter pylori* isolates	Cross-sectional	Biofilm + PCR	Clarithromycin	Resistant strains exhibited a significantly higher capacity for biofilm formation.
Dai et al. (2021) China [28]	Reduce, reinforce, and replenish: safeguarding the early-life microbiota to reduce intergenerational health disparities	Observacional	PCR reverse dot blot	Clarithromycin, levofloxacin	A2143G and gyrA mutations were the strongest predictors of antibiotic resistance.
Ferdaus et al. (2024) Bangladesh [29]	The Prevalence, Risk Factors, and Antimicrobial Resistance Determinants of *Helicobacter pylori* Detected in Dyspeptic Patients in North–Central Bangladesh	Metodológico	PCR multiplex	Clarithromycin	High sensitivity for the simultaneous detection of virulence and resistance markers.
Hallur et al. (2022) India [30]	Low clarithromycin resistance in virulent *Helicobacter pylori* from dyspeptic patients at a tertiary care centre in Odisha	Observacional	PCR + E-test	Clarithromycin	Low levels of resistance despite a high prevalence of virulent genotypes.
Haumaier et al. (2022) Germany [31]	Rapid Detection of Quinolone Resistance Mutations in gyrA of *Helicobacter pylori* by Real-Time PCR	Experimental	RT-PCR (FRET)	Quinolones	Rapid and reliable detection of gyrA resistance-associated mutations.
Hemeda et al. (2025) Egypt [32]	Investigation of metronidazole resistance-associated mutations and virulence genotypes in *Helicobacter pylori* isolates from the Egyptian population: A cross-sectional study	Observacional	Secuenciación *rdxA/frxA*	Metronidazole	Resistance was associated with cagA+/vacA s1 strains.

Hu et al. (2023) China [33]	Long-Read- and Short-Read-Based Whole-Genome Sequencing Reveals the Antibiotic Resistance Pattern of *Helicobacter pylori*	Multicéntrico	Secuenciación Sanger	Metronidazole	High resistance rates with low concordance with rdxA mutations.
Kekić (2024) Serbia [34]	Genetic Determinants of Clarithromycin and Fluoroquinolones Resistance in *Helicobacter pylori* in Serbia	Observacional	PCR + secuenciación	Clarithromycin	The A2143G mutation was identified as the main resistance determinant.
Martínez-Martínez et al. (2026) France [35]	Genomic determinants of antibiotic resistance for *Helicobacter pylori* treatment: a retrospective phenotypic and genotypic observational study	Retrospectivo	Análisis de 1011 genomas	Clarithromycin, levofloxacin	High genotype–phenotype sensitivity and specificity, with marked regional differences.
Tran et al. (2024) Vietnam [36]	Current status of *Helicobacter pylori* resistance to clarithromycin and levofloxacin in Vietnam: Results from molecular analysis of gastric biopsy specimens	Observacional	DNA-strip technology	Clarithromycin, levofloxacin	High rates of dual resistance, with A2143G as the predominant mutation.

2.1. Virulence genotypes and their association with antibiotic resistance

The studies summarized in Table 1 analyzed the distribution of the main *H. pylori* virulence genotypes (*cagA, vacA, babA,* and *iceA*) and their association with antibiotic resistance and gastric clinical manifestations. In most samples, a high prevalence of genotypes considered highly virulent was observed, particularly *cagA*-positive and *vacA* s1m1. These genotypes were frequently reported in patients with active gastritis, intestinal metaplasia, and greater histopathological severity. Several studies demonstrated the coexistence of multiple virulence genes within the same isolate, which was particularly notable in samples from Asia, the Middle East, and Latin America. Regarding antibiotic resistance, some studies identified significant associations between highly virulent genotypes—mainly *cagA*+/ *vacA* s1m1—and resistance to clarithromycin or metronidazole, whereas others did not find significant associations between virulence and resistance. Overall, the results revealed marked geographic heterogeneity both in the distribution of virulence genotypes and in their relationship with antimicrobial resistance.

2.2. Genetic determinants of antibiotic resistance

Table 2 summarizes the studies focused on the genetic determinants of antibiotic resistance and the genomic profiles of *H. pylori*. Most investigations reported a high frequency of mutations in the 23S rRNA gene—particularlyA2143G and A2142G—which are associated with clarithromycin resistance, as well as mutations in *gyrA* (N87 and D91) linked to fluoroquinolone resistance. Resistance to metronidazole exhibited considerable genetic heterogeneity, frequently associated with multiple mutations and truncations in *rdxA*. Studies based on whole-genome sequencing and pangenomic analyses demonstrated high concordance between genotypic and phenotypic resistance profiles for clarithromycin and levofloxacin, whereas this concordance was variable for metronidazole. In addition, significant regional differences in resistance patterns were identified, with frequent coexistence of virulence and resistance genes in multidrug-resistant strains. These findings reflect extensive genetic diversityand regional adaptation of *H. pylori* under antibiotic selective pressure.

2.3. Mechanisms of resistance

Studies summarized in Table 3 evaluated the molecular mechanisms contributing to antibiotic resistance, their relationship with virulence factors, and the development or validation of diagnostic techniques. Several studies confirmed that molecular identification of specific mutations in 23S rRNA and *gyrA* enables reliable prediction of resistance to clarithromycin and fluoroquinolones, respectively. In contrast, resistance to metronidazole exhibited more complex and less predictable mechanisms, involving multiple genes and mutations. Some studies examined additional factors, such as biofilm formation, observing a greater biofilm-forming capacity in multidrug-resistant strains. Moreover, the studies demonstrated that rapid molecular techniques—including multiplex PCR, RT-PCR, and pyrosequencing—show high sensitivity and specificity for the simultaneous detection of virulence and resistance genes.

3. Discussion

This review provides a comprehensive analysis of

recent evidence on the association between virulence genotypes and antibiotic resistance patterns in H. pylori, addressing a central focus of contemporary research in gastroenterology and clinical microbiology. Altogether, the findings confirm that H. pylori infection is characterized by marked genetic and phenotypic heterogeneity, with important clinical, therapeutic, and epidemiological implications.

3.1. Virulence genotypes, clinical severity and antibiotic resistance

The included studies demonstrate a high prevalence of genotypes considered highly virulent, particularly cagA-positive and vacA s1/m1, across different geographic regions. This pattern is consistent with findings from previous epidemiological studies, in which these genotypes have been associated with a more intense inflammatory response, greater epithelial damage, and an increased risk of gastric adenocarcinoma [10].

In line with the comparative review between Eastern and Western regions conducted by Namikawa et al. [10], studies from Asia and the Middle East (China, Japan,

Iraq) report a more frequent coexistence of multiple virulence genes and greater clinical severity, in contrast to some studies from Latin America and Europe, where virulence expression showed greater variability [13–17]. These differences may be explained, at least in part, by the population structure of *H. pylori*, host–bacterium coevolution, and environmental factors such as diet and early-life exposure to infection.

Regarding antibiotic resistance, several studies have identified significant associations between highly virulent genotypes (cagA+/vacA s1m1) and resistance to clarithromycin or metronidazole [13,14,16,17]. These findings support the hypothesis that more virulent strains may exhibit greater adaptive capacity under antibiotic pressure, either through higher rates of genetic recombination or prolonged persistence within the gastric mucosa. However, other studies did not demonstrate a statistically significant association between virulence and resistance [15], suggesting that this relationship is not universal and may depend on contextual factors.

The observed discrepancies may be attributed to methodological differences, sample size, sample type (isolates vs. biopsies), the molecular detection techniques employed (conventional PCR vs. multiplex methods), and the criteria used to define resistance (phenotypic or genotypic). In addition, local patterns of antibiotic use and prescribing policies play a decisive role in shaping the resistance profiles observed [11].

3.2. Genetic determinants of resistance

The results confirm that clarithromycin resistance is strongly associated with point mutations in the 23S rRNA gene, particularly A2143G and A2142G, consistent with what has been documented in the literature [11,12]. The high genotype–phenotype concordance observed across multiple genomic studies reinforces the clinical utility of molecular testing to guide empirical treatment strategies [21,24,35].

In the case of fluoroquinolones, mutations in gyrA (N87 and D91) showed a consistent association with levofloxacin resistance, particularly in studies conducted in Asia and Europe [21–25,34,36]. These findings align with the genomic analysis performed by Vital et al. [12], which highlights the predictive capacity of these molecular markers.

In contrast, resistance to metronidazole demonstrated greater genetic complexity, involving multiple mutations and truncations in rdxA and, in some cases, low genotype–phenotype concordance [20,33]. This variability is consistent with findings reported by Mladenova [5], who indicates that metronidazole resistance is influenced by redundant mechanisms and by microenvironmental conditions such as oxygen tension.

The regional differences identified, including specific genomic signatures and multidrug resistance patterns in India, China, Africa, and Australia [22,24–26], reflect the evolutionary adaptation of H. pylori to local antibiotic pressure contexts, reinforcing the need for therapeutic strategies based on regional surveillance.

3.3. Resistance mechanisms

The studies expand the understanding of resistance mechanisms by incorporating additional factors such as biofilm formation and the development of advanced molecular diagnostic methods. The association between antibiotic resistance and an increased capacity for biofilm formation reported by Ashkar et al. [27] suggests a complementary mechanism of bacterial persistence, which may contribute to therapeutic failure even in the absence of classical resistance mutations.

Likewise, methodological and diagnostic studies demonstrate that techniques such as multiplex PCR, RT-PCR, DNA-strip technology, and targeted sequencing enable rapid and simultaneous detection of virulence and resistance genes with high sensitivity and specificity [29,31,34,36]. These findings are consistent with recent proposals to move toward a precision medicine model for the eradication of *H. pylori* [9,12].

3.4. Limitations and future perspectives

Although this review provides a broad and up-to-date overview, it has several limitations. Methodological heterogeneity among the included studies, variability in resistance criteria, and the lack of longitudinal clinical data in some reports limit direct comparison of results. In addition, most studies employed cross-sectional designs, which precludes the establishment of causal relationships.

Future research should prioritize multicenter studies with standardized methodologies, integrate genomic analyses, and prospectively explore the relationship between virulence, antibiotic resistance, and therapeutic response. Such approaches will help advance more effective eradication strategies for this bacterium.

4. Conclusions

The collected evidence demonstrates that highly virulent *H. pylori* genotypes, particularly cagA-positive and vacA s1/m1, predominate across diverse geographic regions and are consistently associated with greater clinical severity of gastric disease. In several population contexts, these genotypes have also been linked to resistance to first-line antibiotics such as clarithromycin and metronidazole; however, the heterogeneity of the findings suggests that this association is influenced by regional, methodological, and evolutionary factors, precluding the establishment of a universal relationship between virulence and antibiotic resistance.

Genomic studies confirm that antibiotic resistance in *H. pylori* is primarily driven by well-characterized mutations in genes such as 23S rRNA for clarithromycin and gyrA for fluoroquinolones, with high genotype–phenotype concordance. In contrast, resistance to metronidazole involves more complex and variable genetic mechanisms, reflecting substantial regional and adaptive diversity. These findings underscore the importance of local molecular surveillance and the use of genomic approaches to guide more precise and effective therapeutic strategies.The integration of additional molecular mechanisms, such as biofilm formation, together with the development of rapid and sensitive molecular diagnostic techniques, highlights that antibiotic resistance in *H. pylori* is a multifactorial phenomenon that extends beyond classical mutations. The application of tools such as multiplex PCR, RT-PCR, and targeted sequencing enables the simultaneous detection ofvirulence and resistance determinants, constituting a fundamental pillar for advancing toward a precision medicine model in the eradication of *H. pylori* and in reducing therapeutic failure.

Conflict of interest

Authors declare that there is no conflict of interest

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