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HELICOBACTER PYLORI INFECTION IN CHILDREN AND ADOLESCENTS: AN UPDATE FROM THE LITERATURE

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Abstract – *Objective:* *Helicobacter pylori* (*H. pylori*) remains a significant global health concern in children and adolescents, associated with chronic active gastritis and potential long-term complications. Despite its clinical relevance, pediatric-specific data on prevalence, diagnosis, and treatment remain fragmented and inconsistent, with clinical management differing significantly from that of the adult population.
Materials and Methods: We performed a systematic review of original research on *H. pylori* infection in children and adolescents, published between January 1 and December 31 of 2024. Articles were identified via PubMed using MeSH and keyword-based search criteria and screened for relevance. Studies were categorized by primary research focus into four groups: epidemiology and clinical associations, diagnostics, treatment, and immunobiology.
Results: A total of 65 original publications were included. The majority focused on epidemiological trends and clinical associations or treatment strategies, while diagnostics and immunological insights were less represented. Significant geographic variation was observed in prevalence, diagnostic approaches, and adherence to treatment guidelines. High rates of antibiotic resistance were reported, while non-invasive methods, such as stool antigen and breath tests, remained widely used for diagnostics. Several studies emphasized the impact of nutritional status, particularly iron deficiency anemia, as well as socioeconomic factors, on diagnostic accuracy and treatment outcomes.
Conclusions: Despite growing interest in pediatric *H. pylori* research, recent literature highlights persistent gaps in diagnostic standardization, healthcare delivery, and our understanding of child-specific host-pathogen interactions. Continued efforts are needed to advance evidence-based management and address these challenges in pediatric populations.

Keywords: Pediatric *Helicobacter pylori*, Epidemiology, Diagnostic methods, Antibiotic resistance, Guideline adherence.

INTRODUCTION

H. pylori is a Gram-negative bacterium that colonizes the human stomach and is one of the most prevalent chronic infections worldwide[1,2]. While it is most commonly acquired during childhood[3,4], much of the clinical research and treatment guidelines have been derived from adult populations. In children, *H. pylori* infection can present with a wide spectrum of clinical outcomes, ranging from asymptomatic chronic active gastritis to dyspeptic complaints and, in rare cases, peptic ulcer disease[1]. Accumulating evidence has implicated *H. pylori* in broader systemic effects in children, particularly in association with iron deficiency anemia, growth impairment, and nutritional deficiencies[5-7].

Despite its early-life acquisition and long-term consequences, pediatric *H. pylori* infection remains underrecognized and underresearched. Due to the potential loss of the pathogen during adolescence and basic science findings highlighting the impact of *H. pylori* infection on immune system maturation[8], current guidelines do not recommend eradication in asymptomatic individuals or retesting once they reach adulthood[9]. Diagnostic algorithms are inconsistently applied in children, and eradication therapies (when indicated) often fail to meet efficacy targets due to rising antibiotic resistance, lack of susceptibility testing, and poor adherence to pediatric-specific guidelines[10]. Invasive diagnosis of *H. pylori* infection is rare compared to the adult cohort due to reserved endoscopic examinations in this age group. The immunological and microbiome-related consequences of infection and treatment in children are particularly underexplored, even as emerging research suggests distinct host responses in younger patients compared to adults[11-14].

In recent years, there has been a growing effort to address these gaps through targeted epidemiological studies, improved diagnostic methodologies, and more individualized treatment strategies in children. However, the pediatric literature remains fragmented, and regional data are sparse, especially from low- and middle-income countries where the burden is often highest. A structured synthesis of current pediatric-focused studies is needed to inform future research directions and clinical practice.

This review aims to provide a comprehensive overview of the current literature on *H. pylori* infection in children published between January 1 and December 31 of 2024, highlighting developments in epidemiology, diagnostics, treatment approaches, and immunobiological understanding. By focusing specifically on publications from the past year, we aim to highlight the urgent need for specific pediatric *H. pylori* research, particularly in light of the rising threat of gastric cancer in recent years[15], and to identify areas where research remains insufficient.

MATERIALS AND METHODS

A systematic literature search was conducted in PubMed to identify original research articles related to *H. pylori* infection in pediatric populations. The search and analysis parameters were based on the referred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[16]. The following search query was used: ("Helicobacter pylori"[MeSH Terms] OR "Helicobacter pylori"[All Fields]) AND ("Infant"[MeSH Terms] OR "Child"[MeSH Terms] OR "Adolescent"[MeSH Terms] OR child*[All Fields] OR pediatric*[All Fields]).

This search yielded 250 articles. Titles and abstracts were screened for relevance, and articles were included if they met the following criteria:

– Focused on *H. pylori* infection in individuals aged 0-18 years;
– Published between January 1, 2024, and December 31, 2024;
– Reported original research data.

The following types of publications were excluded: reviews, meta-analyses, guidelines, single case reports, conference abstracts or posters, and non-English language articles. After applying these criteria, 65 original research articles were included in the final review.

RESULTS

A total of 65 publications from the year 2024 focusing on *H. pylori* in pediatric populations were identified and reviewed. These studies were systematically grouped into four major thematic categories based on their primary research focus. Each article could be assigned to one or more categories depending on its content. 39 publications addressed epidemiology and clinical associations, followed by 30 on treatment, 15 on diagnostics, and 8 on immunobiology. These totals reflect that several articles were assigned to multiple categories, with the most frequent overlap occurring among studies combining themes of epidemiology, diagnostics, and treatment. The resulting classification is illustrated in Figure 1, which presents a Euler diagram summarizing the aforementioned overlap between categories.

Figure 1. Euler diagram depicting the 65 selected publications from the year 2024 categorized based on their main research focus (Epidemiology and Clinical Associations, Treatment, Diagnostics, Immunobiology) and their overlap. The diagram visually conveys both the relative size of each thematic group and the degree of overlap, with circle intersections representing multi-focus studies.

Epidemiology and Clinical Associations

Recent studies from 2024 highlight a substantial global variation in the prevalence of *H. pylori* infection among children. Exceptionally high prevalence rates were reported in endoscopy-based cohorts of symptomatic children, with 80.3% among Moroccan patients[17] and 81.3% among Vietnamese children[18]. In contrast, population-based screening using stool antigen testing, e.g., in Slovenian children, revealed a much lower prevalence of 10.9%[19]. Additionally, longitudinal and retrospective analyses from countries such as Turkey[20], China[21], and Taiwan[22] indicate a declining trend in pediatric *H. pylori* prevalence over recent years, although the decrease appears less pronounced than in adults. In contrast, a recent global meta-analysis by Chen et al[23], which included 1,748 studies from 111 countries, found that while the prevalence of *H. pylori* in adults declined substantially (from 52.6% before 1990 to 43.9% between 2015 and 2022), the prevalence in children and adolescents remained relatively high at 35.1% during the same period, without evidence of significant reduction across WHO regions.

Several studies investigated associations between *H. pylori* and comorbid conditions. A potential link with cerebral palsy was noted[24], as well as with non-alcoholic fatty liver disease[25]. Common risk factors for *H. pylori* infection identified across these studies include older age, a positive family history, and poor hygiene practices. A seemingly evident yet impactful finding was that handwashing with soap significantly reduced the risk of infection (OR 0.35)[18].

Multiple studies found strong associations between *H. pylori* infection and iron deficiency anemia, with notable improvements in hemoglobin, ferritin, and other hematological markers following eradication therapy and iron supplementation[26,27].

Coinfections were another point of focus: *H. pylori* was commonly found alongside intestinal parasites, such as *Giardia lamblia,* in children from the Middle East and East Africa hospitalized for gastrointestinal symptoms, though these associations were also influenced by underlying socioeconomic and hygiene factors[28,29].

Some studies reported no significant associations between *H. pylori* infection and other chronic conditions. There was no correlation found with inflammatory bowel disease or its activity level in children[30], and no association was observed between *H. pylori* and atopic diseases[31]. Both studies focused on an Italian patient cohort. A study from China found that recurrent abdominal pain (RAP) in children was not associated with *H. pylori* infection but was strongly linked to low physical activity (less than one hour per day) and academic stress[32].

Finally, potential transmission routes were explored. Thorat et al[33] proved vertical mother-to-child transmission as a likely mode of early-life *H. pylori* acquisition.

Diagnostics

Current guidelines stress that the primary aim of evaluating gastrointestinal symptoms in children should be to determine their underlying cause, rather than simply establishing *H. pylori* status[9]. Testing is recommended only in cases of gastric or duodenal ulcers, where infection should be confirmed by endoscopic biopsy with histopathology plus either molecular testing or culture as the gold standard. Despite this, clinical practice often diverges: in many pediatric settings, diagnosis relies on non-invasive methods, such as stool antigen testing, serology, or a single rapid urease test (RUT). This shortcut approach, while convenient, risks reduced diagnostic accuracy and inconsistent adherence to evidence-based care[34]. To address concerns about both sensitivity and feasibility, several studies have further evaluated non-invasive techniques, including the urea breath test (UBT), stool antigen assays, and real-time PCR for *H. pylori* detection in children.

Recognizing that culturing *H. pylori* remains time-consuming and resource-intensive, Wu et al[35] assessed the diagnostic value of gastric nodularity observed during endoscopy, reporting high sensitivity and specificity, which increased further when combined with RUT.

Similarly, Semwal et al[36] demonstrated that narrow band imaging (NBI) enhanced the endoscopic identification of *H. pylori*-positive gastritis, showing strong concordance with histopathology-based gold standards.

Price et al[37] evaluated the PyloPlus UBT in a pediatric population aged 3-17 years and demonstrated equivalent diagnostic performance to the established, FDA-approved BreathTek UBT, supporting its use as a reliable, non-invasive tool for diagnosing *H. pylori* infection in children.

Meanwhile, Moreno Trigos et al[38] employed advanced molecular methods for non-invasive stool-based detection, including Deep Amplicon Sequencing (DAS), Real-Time PCR, and Fluorescence in Situ Hybridization (FISH). These approaches showed broad superiority over traditional culture and antigen testing, offering greater sensitivity and the ability to detect viable organisms and multiple Helicobacter species.

Treatment

Treatment-related publications from 2024 addressed eradication efficacy, antibiotic resistance, and adjunctive or personalized strategies for managing *H. pylori* infection in children and adolescents.

Standard triple therapy continues to be widely used. However, alarming levels of antibiotic resistance were reported, with clarithromycin resistance exceeding 90% and metronidazole resistance surpassing 70% in populations from Vietnam[39] or in Chinese children[40]. In another Chinese comparative trial, Miao et al[41] found that none of the tested regimens (standard triple, bismuth quadruple, or sequential therapy) achieved ideal eradication rates. In contrast, Barakat et al[42] reported that a ciprofloxacin-based triple therapy achieved the highest eradication rate at 90% in their pediatric population from Egypt.

Several studies emphasized the importance of tailored treatment approaches. Zhou et al[43] highlighted the benefits of selecting regimens based on antimicrobial susceptibility and genetic

polymorphisms, recommending resistance testing prior to initiating therapy. Thuy et al[44] identified one host genetic factor (the MDR1 C3435T polymorphism) that influences the absorption and metabolism of proton pump inhibitors (PPIs), a crucial component of eradication therapy, and highlighted these as potential risk factors for treatment failure.

In a preliminary study, Yan et al[45] explored probiotic therapy (*Clostridium butyricum* and *Bacillus coagulans*) without antibiotics, reporting modest eradication effects, symptom improvement, and gut microbiota modulation. While not a replacement for antibiotics, these findings suggest a potential supportive role for probiotics even in children.

Additional influencing factors and confounders were reported. In the cohort analyzed by Andrews et al[46], weight-based dosing significantly influenced eradication outcomes. Appropriate dosing of PPIs was associated with an eradication rate of 78.8%, compared to 62.2% with suboptimal dosing. Similarly, correct weight-based dosing of amoxicillin achieved an eradication rate of 81.0%, whereas inadequate dosing resulted in a substantially lower rate of 53.8%. Le Thi et al[47] analyzed data from the EuroPedHp registry, including 1,165 treatment-naïve children with endoscopically confirmed *H. pylori* infection across 17 European countries, to identify factors influencing treatment decisions. They found that older children were more likely to receive eradication therapy in the absence of comorbidities, whereas those with gastrointestinal comorbidities such as eosinophilic esophagitis (EoE), inflammatory bowel disease (IBD), or celiac disease (CeD) were significantly less likely to be treated. For example, only 43% of children with celiac disease underwent eradication therapy. In children without comorbidities, factors favoring treatment included being overweight, the presence of symptoms, endoscopic findings, such as erosions or antral nodularity, and the availability of antibiotic susceptibility testing. Abdelgalil et al[48] showed that *H. pylori* eradication in children with idiopathic generalized epilepsy treated with valproic acid was associated with increased serum valproic acid levels and improved seizure control, suggesting a possible anticonvulsive effect linked to eradication therapy.

Nutritional status may also affect treatment outcomes. Liu et al[49] reported that children with low serum ferritin, hemoglobin, and serum iron levels experienced lower *H. pylori* eradication rates and higher recurrence. They noted that serum ferritin was particularly important, as patients with lower levels were more likely to relapse after treatment. The authors suggest that poor iron status may reduce the effectiveness of eradication therapy and contribute to the persistence or return of infection.

Despite these promising strategies, real-world adherence to treatment guidelines remains inconsistent. Vernon-Roberts et al[34] observed that even in high-quality healthcare settings, recommendations regarding endoscopic confirmation and eradication are often not followed. In the multicenter study by Kotilea et al[50], the authors analyzed 3,890 children undergoing upper endoscopy for suspected CeD, IBD, or EoE. *H. pylori* was identified in 9% of cases overall, with similar prevalence across disease groups. Marked regional differences were observed, with prevalence ranging from 4 to 6% in Europe to 26.6% in the Middle East. Endoscopic findings included nodular gastritis (61.0%), erosions (21.3%), and ulcers (6.3%), while nearly one-third of infected children had a normal gastric mucosa. Despite these findings, eradication therapy was prescribed in fewer than 40% of patients, most often when erosions, ulcers, or nodular gastritis were present, and more frequently in centers from low-prevalence regions. Children with incidental infection but no ulcer disease were often left untreated, particularly in high-prevalence regions, which contributed to the overall low treatment rates observed.

Immunobiology

Immunobiological studies in 2024 deepened our understanding of host-pathogen interactions in pediatric *H. pylori* infection. Infected children exhibited elevated inflammatory markers, including salivary IL-8, ND-1, and TLR-2[51]. Gastric histopathology revealed that nodular gastritis was associated with higher inflammation scores but did not indicate a genotoxic microbial community, according to a study by Zheng et al[52].

Microbiome analyses identified significant disruptions following eradication therapy; however, microbial diversity and richness were shown to fully recover within one year, suggesting the long-term safety of *H. pylori t*reatment in children with peptic ulcers[11]. Amrousy et al[53] reported

that adolescents with *H. pylori* infection showed gut dysbiosis, characterized by reduced levels of beneficial bacteria such as *Lactobacillus spp.* and increased counts of *Clostridium difficile* and *Salmonella spp.* Post-eradication changes were not assessed.

Further studies demonstrated that immunoglobulin levels, T-cell subset distributions, and both oral and gut microbiota composition differed significantly between infected and non-infected children. Teng et al[54] investigated immune function in children with peptic ulcer disease and its relationship to *H. pylori* infection. They found that children with ulcers had lower CD3+, CD4+, and CD4+/CD8+ ratios compared with healthy controls, along with higher IgG levels, indicating both cellular and humoral immune alterations. Among ulcer patients, those who were *H. pylori*-positive showed higher CD3+, CD4+, and CD8+ counts but a lower CD4+/CD8+ ratio than *H. pylori*-negative cases. The authors concluded that the infection could stimulate expansion of T-lymphocyte subsets and that the development of peptic ulcer in children is closely linked to disruptions in immune regulation. Ogaya et al[55] analyzed the oral microbiome in children and adults with and without *H. pylori* detected in the oral cavity. Using 16S rRNA sequencing, the authors found that microbial diversity patterns differed depending on infection status and age. In children, *H. pylori*-positive saliva samples showed significant differences in β-diversity compared with negative samples, indicating distinct community composition. At the genus level, Porphyromonas was the only taxon consistently enriched in both infected children and adults relative to uninfected controls.

DISCUSSION

Recent work on *H. pylori* in children and adolescents has focused mainly on prevalence, clinical associations, and treatment outcomes, while in comparison, little attention has been given to diagnostic strategies or the immunobiology of infection. This imbalance leaves important gaps in our understanding of host-pathogen interactions in childhood and the unique diagnostic challenges of pediatric populations. A common methodological limitation was the lack of well-defined control groups with confirmed infection status. Few studies included adult controls to account for age-related differences in microbiome or immune responses, and histopathology-confirmed diagnoses were rarely applied in larger pediatric cohorts. On top of that, although local studies indicate a downward trend in pediatric infections, global data do not yet confirm a consistent decline.

There have been advances in diagnostics and personalized treatment strategies, yet there are major discrepancies between guideline recommendations and actual clinical practice. This is aggravated by socioeconomic imbalance, unequal access to diagnostic tools, and limited incorporation of evidence-based standards into routine pediatric care. For example, in the analysis provided by Kotilea et al[50], only a minority of children in their cohort met the strict criteria for treatment. The fact that many children were tested and treated for other diagnostic indications and that eradication was still considered in incidental cases showcases how guideline-based recommendations and real-world pediatric practice do not overlap, and treatment decisions are shaped by endoscopic appearance and local epidemiology rather than guidelines alone. Rising antibiotic resistance and the underuse of susceptibility-guided regimens (even within well-resourced healthcare systems) further aggravate the challenge, leaving a notable proportion of infected children untreated and exposing weaknesses in existing care pathways. Future strategies must clearly distinguish between adult and pediatric indications, ensuring that therapeutic decisions in children are grounded in pediatric evidence rather than generalized from adult oncology-driven practice.

Taken together, these findings point to the need for standardized research approaches, region-specific implementation strategies, and policy measures to improve the diagnosis and management of *H. pylori* infection in children and adolescents.

CONCLUSIONS

This literature review summarizes pediatric *H. pylori* research published in 2024. Interest in pediatric aspects of *H. pylori* infection is clearly growing, but progress will depend on more refined

studies addressing diagnostic accuracy, implementation in healthcare systems, and the biological mechanisms underlying infection in children. Improving evidence-based care requires separating children and adolescents from adults in disease management, given the distinct challenges in pediatric patients.

Conflict of Interests

The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

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Authors' Contributions

L.G. and B.T. formulated the study concept, contributed to all stages of the review process, performed the literature search and data extraction, wrote the first draft of the manuscript, and acted as first reviewers. C.S. oversaw the review conceptualization and execution and acted as a second reviewer. B.T. acted as a third reviewer for discrepancies and revisions of the manuscript. All authors contributed equally to preparing the final version of the manuscript. All authors have read and agreed to the published version of the manuscript.

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Data Availability Statement

The data supporting the findings of this review are derived from the published research articles cited within the manuscript. No new datasets were generated.

Ethics Statement and Informed Consent

As this manuscript is a review, it does not involve original research with human participants. Therefore, informed consent was not required. The paper synthesizes and analyses the existing literature on the subject, ensuring compliance with all relevant ethical guidelines for review articles.

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