Plant Archives Vol. 20, Supplement 2, 2020 pp. 1843-1848 **e-ISSN:2581-6063 (online), ISSN:0972-5210**

Review Article

A REVIEW ON *HELICOBACTER PYLORI* INFECTION IN CHILDREN

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Abstract

The infection of *Helicobacter pylori* is a public health issue for gastrointestinal. In developing countries, the infection is more severe than in developed countries. Initial infection is likely to arise at an early age and rise in incidence with age. The incidence of the infection is influenced by ethnic and racial influences, social background, and living environments. Geographical location, sex, ethnicity, educational level, health, and socio-economic status are among the factors affecting *Helicobacter pylori* infection. The infection is associated with some diseases such as iron deficiency anemia, B12 deficiency. There is proof of a link in children between Helicobacter pylori infection and antral gastritis, and duodenal ulcer disease. Invasive and non-invasive procedures may be used for treatment, while the gold standard is a GI tract biopsy specimen. The most frequent diagnosis in infanthood *Helicobacter pylori* infection is nodular gastritis. Treatment initiation is critical in children with an active helicobacter pylori infection (identified through histopathological examination). The best care for infants, though, isn't obvious. Patient behavior, care time, and vulnerability to *Helicobacter pylori* strain management regiments play a crucial role in clinical performance.

Keywords **:** *Helicobacter pylori,* Children, Infection.

Introduction

Helicobacter pylori were first identified in 1982 by Australian doctors Barry Marshall and Robin Warren who noticed it to be present in a person with recurrent gastritis and stomach ulcers, symptoms that were not commonly thought to have a microbial source. (Warren & Marshall, 1983) (Blaser & Berg, 2001). *Helicobacter pylori* were deemed a causative agent for gastric cancer by the International Health Organisation (WHO) in 1994 (Iwańczak, Buchner, & Iwańczak, 2017). *Helicobacter pylori* is a gram-negative spiral bacillus which in developing countries is more common than in industrialized ones (Salih *et al*., 2017). It has two to six flagella which enable it to survive during stomach contractions (Brown, 2000). The most growing reservoir for this agent is the human stomach, particularly the antrum (Salih *et al*., 2017). It may live in the acidic stomach atmosphere because this bacterium may generate urease(Salih *et al*., 2017). Such results rendered *Helicobacter pylori* deeply identified as a significant pathogen in pediatric gastroenterology**.**

Microbiological characteristics of *Helicobacter pylori*

Helicobacter pylori is a gram-negative and helically-shaped with 2-6 unipolar flagella characteristics usually found in the stomach (Figure 1). The bacterium has sharply rounded ends and reaches a length of 2.5-4.0 µm and a width of 0.5-1.0 µm. The cell wall is smooth and can be covered with a strong, up to 40 nm thick glycocalyx (Goodwin *et al*., 1989). The flagella have a length of 2.5µm and a thickness of around 30 nm and a characteristic terminal bulb (Goodwin & Worsley, 1993). The bacterium shows impressive motility in viscous liquids, and in this motility, the flagella perform a key function (Hazell, Lee, Brady, & Hennessy, 1986) and (Suerbaum, Josenhans, & Labigne, 1993). *Helicobacter pylori* is a microaerophilic that may be coccoid or U-shaped (Enroth *et al*., 1999). in some conditions. This occurs primarily inside the human and animal gastrointestinal tract (Fox, 2002). The bulk of *Helicobacter pylori* can be contained in the gastric mucosa in the stomach, but others are observed adhering to the epithelium of the gastric mucosal. The bacterium is strongly suited for life in the stomach's hostile climate, in which few other species can live. Even so, *H. Pylori* is considered an extra cellular bacteria, and there is proof that the bacteria have an intracellular invasion function (Kusters, van Vliet, & Kuipers, 2006).

Fig. 1: *H. pylori*. The curved bacillus with unipolar flagella is visualized

Epidemiology of *Helicobacter pylori*

Helicobacter pylori are spread out in developing countries in Africa, South America, and Asia. A documented increased prevalence of *Helicobacter pylori* infection among Korean, Chinese, and African populations (Goh, Chan, Shiota, & Yamaoka, 2011). *Helicobacter pylori* were typically obtained within the first five years of life (Daugule & Rowland, 2008). The prevalence of infection with *Helicobacter pylori* among children in developed countries is 1.2-12.2 percent, whereas *Helicobacter pylori* are the most frequently identified infectious agent in children in developing countries (Mourad-Baars, Verspaget, Mertens, & Mearin, 2007). (Mourad-Baars *et al*., 2007). Previous research has revealed, the factors that influence the prevalence of *H. pylori* infection is a geographic area, age, race, educational level, socio-economic status. (Brown, 2000).

In a previous study conducted the prevalence of *Helicobacter pylori* among 2-4-year-old children in Ethiopia was stated to be 48 %, whereas in Nigeria and Mexico it was 82 % and 43 % among 5-9-year-old children respectively. (Hunt *et al*., 2011). Of the 327 children they examined, Rowland *et al*. confirmed the existence of *Helicobacter pylori* in 28 (Rowland *et al*., 2006). In Sudan, children recorded a prevalence of around 56 percent of Helicobacter pylori infection (13 percent in subjects under 36 months and 40.6 percent in those over 109 months) (Salih *et al*., 2017). Other African nations, such as Uganda, Kenya, and Cameroon, accounted for 44%, 45%, and 37% respectively(Abdallah, Mohammed, Mohammed, & Ali, 2014) (Langat, Ogutu, Kamenwa, & Simiyu, 2006). In Sweden, the recorded incidence of *Helicobacter pylori* infection was 13.6 percent in children aged between 18 and 24 months, while concentrations were 8.6 percent and 2.4 percent respectively in Irish and German research (Granström, Tindberg, & Blennow, 1997) (Weyermann, Adler, Brenner, & Rothenbacher, 2006) .

Previous studies in Iran reported a prevalence of 57-82%, *Helicobacter pylori* infection in children aged 9 months and 15 years. (Alborzi *et al*., 2006). Two prior findings have shown that the incidence of infection with *Helicobacter pylori* has decreased in recent decades, in comparison to a study from Denmark (Rosenstock, Jørgensen, Andersen, & Bonnevie, 2000). Patients with peptic ulcers and MALT gastric lymphoma constitute a high-risk group. Infection with H. pylori and may gain from a diagnosis and treatment strategy (Chey, Leontiadis, Howden, & Moss, 2017). Recent findings have shown that the incidence of *Helicobacter pylori* infection has decreased in recent years in some Asian countries such as Japan, Iran, and China (Kusano, Gotoda, Ishikawa, & Moriyama, 2017; Shu, Ping, Yin, & Jiang, 2017).

Prevalence of *Helicobacter pylori* infection

Helicobacter pylori infection has been recognized as a public health concern impacting about 50 percent of the world's population (Bener *et al*., 2007) and (Sachs & Scott, 2012). Most of the previous studies on the spread of infection indicate that people are infected with H. pylori virus in early childhood (<5 years) and that the risk of infection decreases rapidly after that. The incidence of *Helicobacter pylori* antibodies was observed in communities in the developing countries more than 70 percent (Nurgalieva *et al*., 2002) and (Stasi & Provan, 2008). On the opposite, in the developed countries, *Helicobacter pylori* infection is less common in young children and increases with age and reaches 50% by adulthood (Lane *et al*., 2006) and (Zhou *et al*., 2012). The prevalence sum of *H. Pylori* in Texas children is 12.2% and 55.9% in India (Mishra *et al*., 2008). The prevalence of *H. pylori* Infection within the Gaza Strip is (72.2%) (Yassin, Altibi, & El-Shanti, 2011). Particularly during childhood the infection penetrates and persists for life.

Transmission of Helicobacter pylori

A) Transmission from one person to another

Humans are the only known significant reservoir of *H. pylori* (Afana, 2016). Transmission from one person to another is believed to be the primary route of transmission *H. pylori* infection in developed and developing nations. Close-up touch, especially within the family counting mother/parent to an infant, kin to kin, and life partner to life partner, was reliably demonstrated as an opportunity for contamination transmission. (Escobar & Kawakami, 2004) & (Khalifa, Sharaf, & Aziz, 2010)

B) Transmission on oral

Helicobacter pylori deoxyribonucleic acid (DNA) has been detected in the saliva of *H. pylori*-positive subjects by polymerase chain reaction (PCR) (Khalifa *et al*., 2010) and (Afana, 2016). *Helicobacter pylori* bacteria were also effectively isolated from contaminated individuals' dental plaque (De, Vásquez, Velasco, & Parlapiano, 2006) and (Rasmussen *et al*., 2010). In general, though, isolation was not universally effective, possibly as a consequence of *Helicobacter pylori's* intermittent existence in the oral cavity or low detection capacity arising from several other bacteria co-occurring in the oral cavity.

C) Fecal-oral route

Fecal- oral is the primary transmission path of *Helicobacter pylori*, PCR has identified *Helicobacter pylori* in feces through culture and its DNA (Delport & van der Merwe, 2007; Mishra *et al*., 2008) and (Momtaz, Souod, Dabiri, & Sarshar, 2012)**.**

D) Iatrogenic transmission

Owing to inadequate disinfection during treatments, endoscopes used regularly in upper gastrointestinal treatments can be the cause of iatrogenic infection (Brown, 2000).

Mechanisms of infection with *Helicobacter pylori*

In the stomach, the majority of *Helicobacter pylori* can be found in the gastric mucosa; however, a few are found adhered to the gastric mucosal epithelium. The bacterium is highly adapted to survive in the hostile environment of the stomach where few other organisms can survive. And so, *H. Pylori* is thought to be an extracellular bacteria and there is proof that the bacteria have an intracellular invasion process (Kusters *et al*., 2006). The human gut is colonized by the *Helicobacter pylori*. It colonizes over half of the world's people, and its gastric mucosa infection has been linked with numerous upper gastrointestinal tract diseases such as persistent gastritis, peptic ulcer, mucosa-related lymphoma, and gastric adenocarcinoma (Suharsono *et al*., 2019). *Helicobacter pylori* are usually liable for asymptomatic gastric infection. Recognized effects of this condition include

persistent gastritis, peptic ulcer disease, and atrophic gastritis. While *Helicobacter pylori* infection induces gastric inflammation in virtually all infected subjects, most infected subjects remain asymptomatic while atrophic gastritis develops in certain subsets of patients(Sebastian Suerbaum & Michetti, 2002) (Figure 2).

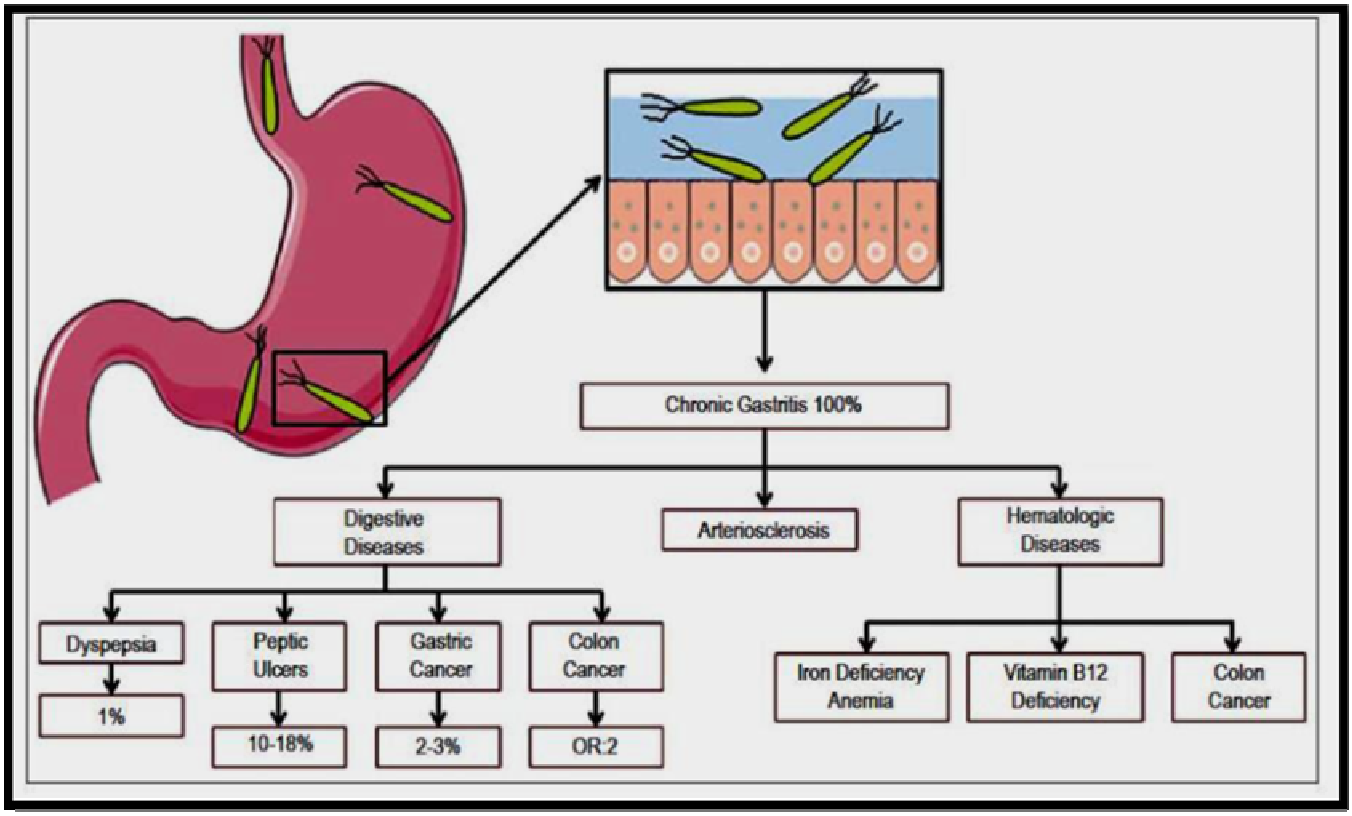

Fig. 2: Diseases produced by *H. pylori*: Chronic gastritis, digestive disease, arteriosclerosis, hematologic disease, dyspepsia, peptic ulcers, gastric cancer, colon cancer, iron deficiency anemia, and vitamin B12 deficiency.

The disorder can have many symptoms during its progression, including acute gastritis, persistent atrophic gastritis, intestinal metaplasia, dysplasia, development deficiency, starvation and eventually cancer (Akcam *et al*., 2007) and (Windle, Kelleher, & Crabtree, 2007). *Helicobacter pylori* are the main cause of histological gastritis and also plays a significant part in the production of peptic ulcers, stomach ulcers, stomach carcinoma, and primary gastric B-cell lymphoma (DIXON, 1991) and (Tytgat, Noach, & Rauws, 1993). The etiology of atrophic gastritis and gastric cancer has been rewritten since the detection of *Helicobacter pylori* during the 1980s. It is now known that the major cause of atrophic gastritis is an infection with *Helicobacter pylori*, which normally occurs in early childhood and persists lifelong if left untreated (Sebastian Suerbaum & Michetti, 2002) . One severe consequence of atrophic gastritis is the malabsorption of cobalamin (vitamin B12), which is frequent in the elderly due to hypo- or achlorhydria with subsequent bacterial overgrowth, and reduced production and secretion of intrinsic factor(Carmel, 1997). It has been proposed that infection with *Helicobacter pylori* can play an important role in reducing acid output, reducing intrinsic factor secretion, and therefore the development of deficiency of vitamin B12 (Carmel, 1997). *H. Pylori* colonizes the whole gastric epithelium and has a strong urease function contributing to the development of ammonia to defend itself against gastric acidity. It also develops certain enzymes, such as phospholipase A2 and C, and glycosulfatase, which play a role in the production of gastric mucosal damage(Dzierzanowska-Fangrat & Dzierzanowska, 2006). *H. Pylori* causes an immune reaction to pro-inflammatory cytokines such as interleukin 1β and interleukin 8 via the gastric epithelium. Any *H. Pylori* genotypes, in particular certain positive vacuolated toxin A (Vac-A) and cytotoxin-associated gene A (Cag-A), are correlated with enhanced pathogenicity and more serious disease. Positive Cag-A strains induce a stronger inflammatory response of gastric mucosa, with enhanced pro-inflammatory cytokine output. Genetically encoded in any is the VacA gene, which contributes to the vacuolization and apoptosis of gastric epithelial cells. *H. Pylori* strain, although it appears phenotypically in just 60 percent of them(Yamaoka, 2010). *H. Pylori* is correlated etiologically with non-atrophic, atrophic gastritis, and peptic ulcer (especially duodenal ulcer). There is a strong connection between *H. Pylori* and dominant B-cell lymphoma (mucosa-associated lymphoma or MALT-lymphoma) and adenocarcinoma. Therefore, *H. pylori* have been listed as group 1 carcinogenic by IARC / WHO(Pandey *et al*., 2010) Figure 3.

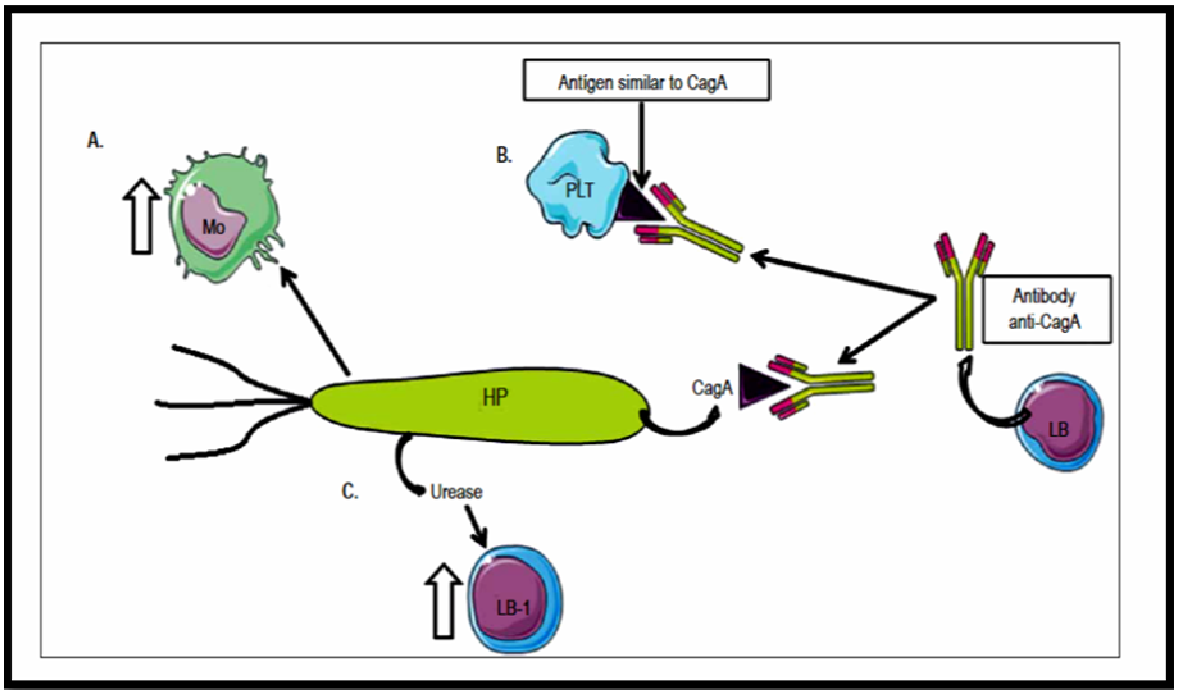

Fig. 3: Primary mechanisms involved in the association between *H. pylori* and Immune Thrombocytopenic Purpura, Cytotoxin Associated Gene A, monocytes, Platelets.

A. *Helicobacter pylori* prefer a monocytic phenotype (Mo) with decreased activation of the phagocytes.
B. CagA-protein-directed antibodies developed by *Helicobacter pylori* cross-react with proteins on the platelet surface (PLT).
C. Urease facilitates the activation of B-1 cells (BL-1), correlated with auto-antibodies development. Illustration produced from individual photographs generated in compliance with Servicer Medical Art's terms of use (Afana, 2016).

Diagnosis of *H. pylori* infection

Infection evaluation is typically achieved by looking for dyspeptic signs and tests that may suggest an infection of *Helicobacter pylori*(Marshall, Stenström, & Mendis, 2008). *Helicobacter pylori* diagnostic methods include serology, rapid urease test (RUT), urea breath check (UBT), endoscopy and biopsy/histopathology, PCR, for *Helicobacter pylori* DNA and *Helicobacter pylori* stool antigen (HpSA) (Tiwari *et al*., 2005). *Helicobacter pylori's* easiest test is serological, including the serum measurement of a higher IgG amount(Sebastian Suerbaum & Michetti, 2002).

Treatment

Treatment initiation is critical in children with an active *Helicobacter pylori* infection (identified through histopathological examination). The best care for infants, though, isn't obvious. Patient behavior, care time, and vulnerability to *Helicobacter pylori* strain management regiments play a crucial role in clinical performance (Graham *et al*., 2003; Guarner *et al*., 2010).

Acid suppressant medications include

- Inhibitors to the Proton Pump (PPIs). Such medications inhibit the development of acid in the stomach. Omeprazole (Prilosec), esomeprazole (Nexium), lansoprazole (Prevacid), and pantoprazole (Protonix) are two sources of PPIs .
- Histamine blocks (H-2) Such medicines block a substance called histamine which causes the development of acids. An example of this is cimetidine (Tagamet HB).
- Subsalicylate of bismuth. If widely known by the Pepto-Bismol brand name, this medication acts by binding the ulcer and shielding it from stomach acids.

Reports report tolerance levels of 57 percent *Helicobacter pylori* strains to metronidazole in northern Iran infants, 24 percent to tetracycline, and 16 percent to clarithromycin in infants (Maleknejad *et al*., 2015).

Your health care professional may suggest that you perform *Helicobacter pylori* testing at least four weeks after diagnosis. If the tests indicate that the therapy has failed, you can receive another round of care using a new mixture of antibiotic drugs.

Conclusion

In conclusion, we observed that *H. pylori* can be the causative agent of gastritis in children as well as in adults, the clinical symptoms leading to endoscopy and biopsy were recurrent abdominal pain with or without either vomiting, weight loss, or a family history of peptic ulcer. As described in previous reports, However, infection with *Helicobacter pylori* should be recognized in children and effective screening testing and therapies should be used. Determining the screening procedure and therapies to be utilized in each case depends on many considerations, patient's health status, illness prevalence, among others.

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