Journal of Clinical and Nursing Research, 2025, Volume 9, Issue 9
http://ojs.bbwpublisher.com/index.php/JCNR
Online ISSN: 2208-3693
Print ISSN: 2208-3685

Research Progress on the Mechanism of Helicobacter pylori Infection in Extra-gastrointestinal Diseases in Children

Liuchun Mo[1], Yunfeng Huang[2] *, Yueyan Huang[2]

[1]Youjiang Medical University for Nationalities, Baise 533000, Guangxi, China
[2]Department of Pediatrics, Affiliated Hospital of Youjiang Medical University for Nationalities, Baise 533000, Guangxi, China

**Author to whom correspondence should be addressed.*

Abstract: Helicobacter pylori (Hp) is a bacterium present in the pyloric region of the human stomach, which can cause gastrointestinal diseases such as gastritis and peptic ulcers. In addition, studies have found that it may be related to some extra-gastrointestinal diseases. This article will review the research progress on the mechanism of Helicobacter pylori in extra-gastrointestinal diseases in children.

Keywords: Helicobacter pylori; Infection; Children; Extra-gastrointestinal diseases; Mechanism

Online publication: Oct 16, 2025

1. Introduction

Helicobacter pylori is a small, spiral-shaped Gram-negative bacterium, whose main pathogenic toxin components include cytotoxin-associated gene A (CagA) and vacuolating cytotoxin A (VacA). The global Hp infection rate is approximately 50%, and the infection rate in Chinese children is 30.31% [1]. Childhood is a high-risk stage for infection, and it usually persists unless eradicated, ultimately affecting health in adulthood. Hp infection can not only cause gastrointestinal diseases but also is closely related to the occurrence of some extra-gastrointestinal diseases [2]. Hp infection may promote or hinder the occurrence and development of extra-gastrointestinal diseases through immune responses, chronic infections, and interactions between various pro-inflammatory cytokines and the body.

2. Hp infection and iron deficiency anemia (IDA)

IDA is essentially a disease of hemoglobin synthesis disorder caused by imbalance of iron metabolism

homeostasis in the body. Studies have shown that persistent Hp infection of the gastric mucosa can lead to iron deficiency or IDA, especially in some children and adolescents. However, the pathogenesis and risk factors for such clinical outcomes in children with Hp remain incompletely clear. Li Jing explored the clinical effect of iron supplementation combined with anti-Hp therapy in children with iron deficiency anemia and positive Hp infection [3]. The results showed that after Hp combined with iron supplementation therapy, serum iron and ferritin levels in Hp-infected children increased significantly, hemoglobin content also showed an upward trend, and in terms of improving anemia, the effect of eradicating Hp combined with iron supplementation therapy was significantly better than that of simple iron supplementation therapy. It can be seen that Hp infection affects the synthesis of red blood cells and hemoglobin, the absorption of serum iron, and the binding capacity of serum ferritin to a certain extent. Hp infection can interfere with iron metabolism homeostasis through multiple pathways, and the specific mechanisms was mentioned below.

2.1. Impaired iron absorption and transport

Long-term Hp infection can damage gastric mucosal parietal cells, reduce gastric acid secretion, affect the conversion of ferric iron to ferrous iron, and hinder transmembrane iron transport. At the same time, damage to gastric mucosal cells affects the normal expression and function of iron transporters in the duodenum and upper jejunum, and also leads to a decrease in Vitamin C, aggravating iron absorption disorders.

2.2. Excessive iron loss

Hp infection can cause dysfunction of gastric and duodenal mucosal epithelium, resulting in increased epithelial cell permeability, which in turn causes the loss of iron and ferritin from the gastric and duodenal mucosa [4].

2.3. Excessive iron consumption and utilization

The growth and reproduction of Hp require the consumption of iron in the body, increasing the body's demand for iron. Hp can uptake and utilize iron in the host by expressing proteins related to iron metabolism, such as iron-binding proteins, lactoferrin, and iron uptake regulatory factors, all of which play key roles in iron uptake and utilization [4].

2.4. Impact on iron metabolism

The body's immune response to Hp infection releases a variety of inflammatory cytokines, which promote the synthesis of hepcidin in the liver. Serum hepcidin binds to ferroprotein on the surface of intestinal cells and macrophages, promoting its internalization and degradation. This process causes iron to be retained in macrophages, making it impossible to transport iron to tissues, resulting in functional iron deficiency.

2.5. Hp Infection enhances nitric oxide (NO) synthase activity, indirectly inhibiting hemoglobin synthesis

The activity of inducible NO synthase (iNOS) in gastric mucosal tissues infected with Hp is significantly increased, leading to increased production of NO in gastric mucosal cells. NO not only specifically hinders the differentiation of hematopoietic stem cells into the erythroid lineage by down-regulating the expression of key transcription factors such as GATA-1 but also its strong oxidative properties can induce DNA double-strand breaks in hematopoietic cells, triggering the mitochondrial apoptotic pathway and directly reducing the number of

hematopoietic cell populations.

3. Hp infection and Henoch-Schonlein purpura (HSP)

Recent studies have found that Hp infection is closely related to the pathogenesis of Henoch-Schonlein purpura. Eradication of Hp can reduce the recurrence of HSP. Hp infection is one of the main inducements or causes of aggravated gastrointestinal symptoms [5]. The research results of Wang Jing et al. showed that the infection rate of Hp in HSP patients was significantly higher than that in healthy children, especially in recurrent or refractory cases [6]. After eradicating Hp, the symptoms such as skin purpura and abdominal pain in HSP children relieved faster and the recurrence rate decreased, suggesting that Hp may be involved in disease activity. Therefore, for HSP children with repeated episodes or significant gastrointestinal symptoms, clinical Hp detection can help reduce the risk of disease recurrence and has a positive effect on improving the overall prognosis of HSP children. Therefore, Hp infection is closely related to Henoch-Schonlein purpura, and its possible mechanisms are as follows:

3.1. Molecular mimicry and immune response

Certain antigens of Hp such as CagA protein and VacA toxin may cross-react with host vascular endothelial cells or basement membrane components such as collagen through molecular mimicry, inducing the production of autoantibodies, leading to immune complex deposition in small blood vessel walls and triggering vasculitis. These immune complexes deposit in small blood vessels of the skin, joints, intestines, and kidneys, activating the complement system, such as C3 and C5a, causing local inflammation and vascular damage. In addition, Hp infection may activate Th1/Th17-type immune responses, secreting IFN-γ, IL-17, and more, further inhibit the function of regulatory T cells (Treg), break immune tolerance, and exacerbate systemic inflammatory responses, promoting the occurrence of vasculitis [7].

3.2. Intestinal barrier damage and dysbiosis

Long-term Hp infection can damage the gastric mucosal barrier, leading to intestinal dysbiosis, increased intestinal permeability, promoting bacterial toxins or antigens into the blood, and aggravating systemic inflammation and immune disorders [8,9]. Due to intestinal mucosal epithelial damage in HSP children, it not only induces abnormal immune recognition but also leads to dysregulation of the host's immune tolerance to symbiotic flora, forming a vicious cycle of intestinal dysbiosis. Hp can also change the internal environment of the digestive tract by inhibiting gastric acid secretion and releasing enzymes. This pH imbalance not only creates conditions for the colonization of opportunistic pathogens but also exacerbates the destruction of symbiotic flora structure. Therefore, combined probiotic intervention plays an important role in the anti-Hp treatment of Hp-positive HSP children [9].

3.3. Chronic inflammation and vascular endothelial damage

Chronic inflammation induced by Hp infection can release a large number of inflammatory mediators such as platelet-activating factor PAF and pro-inflammatory factors such as IL-6, IL-12, IFN-γ, and TNF-α. Inflammatory factors directly or indirectly participate in inflammatory responses through their complex interaction network, directly damaging vascular endothelial cells, promoting increased vascular permeability and leukocyte infiltration, and accelerating the formation of purpura.

4. Hp infection and asthma and other allergic diseases

Studies have shown that there is a negative correlation between Hp infection and childhood asthma. Hp infection can effectively reduce the incidence and recurrence of childhood asthma, and after eradicating Hp, the asthma symptoms of some children worsen [10]. However, persistent Hp infection in asthmatic children can aggravate their immune disorders and become the main reason for the protracted course of asthma. According to the research results of Wu Ying, Hp infection shows a protective effect on asthma [11]. Wang Zhigang and others pointed out in their research design that exposure to Hp can prevent asthma, especially in childhood [12]. The use of Hp extracts in newborns can prevent airway inflammation and goblet cell metaplasia, and injection of Hp extracts can inhibit DC processing of allergens in mediastinal lymph nodes and lungs. These results indicate that Hp extracts after sensitization can effectively prevent allergic airway diseases, and it is expected to develop an effective Hp-specific vaccine to treat allergic asthma.

4.1. Inducing specific immune tolerance

Virulence factors of Hp, such as γ-glutamyl transpeptidase and VacA, can inhibit the maturation of lipopolysaccharide (LPS)-induced dendritic cells (DC) and transform DC into a phenotype with immune tolerance characteristics, making DC unable to effectively stimulate T cells to exert immune effector functions [13]. IL-10 and IL-18 derived from DC are key mediators of Hp-induced immune tolerance, which can effectively induce forkhead box P3 (the main regulatory factor of regulatory T cells) and promote the differentiation of FoxP3-positive regulatory T cells (Treg) and induce specific tolerance in vitro and in vivo.

4.2. Promoting the production of IL-10 and IL-18

The VacA toxin and heat shock protein of Hp can directly target macrophages, which are induced to secrete IL-10, TGF-β, etc. TGF-β plays a key role in promoting the differentiation of peripheral Treg. The TGF-β signaling pathway can synergize with microbial signals and retinoic acid to drive Foxp3 expression in naive T cells, thereby increasing the number of Treg. In the pulmonary immune environment, Treg can effectively inhibit the helper T cell 2 (Th2) immune response to allergens, and Treg itself also has the ability to secrete IL-10 and TGF-β, further regulating the body's immune balance through autocrine and paracrine mechanisms. IL-10 acts by inhibiting antigen presentation, down-regulating the expression of effector T cell cytokines, and inhibiting mast cell degranulation. IL-18 is necessary for Treg differentiation, Hp persistence, and prevention of allergic asthma, and the urease-induced TLR2/NLRP3/CASP1/IL-18 axis is crucial for Hp-specific immune regulation.

4.3. Role of Hp neutrophil-activating protein (HP-NAP) in asthma

HP-NAP can specifically bind to and activate Toll-like receptor 2 (TLR2). Through this mechanism, HP-NAP can regulate various innate immune cells. In the immune response, HP-NAP can induce the up-regulation of Th1-type cytokines (IL-12, TNF-α, and interferon-γ), while inhibiting Th2-type cytokines (IL-4, IL-5, and IL-13), and reducing the level of IgE [14]. Based on the above mechanisms, HP-NAP has important medical value in the development of vaccine adjuvants, intervention of allergic diseases, and tumor immunotherapy.

5. Hp Infection and growth retardation in children

Long-term chronic Hp infection may have a certain impact on children's growth and development. In the study by

Wang Xiaoxian and others, it was found that it will seriously affect children's growth and development, and after radical treatment, children's growth and development gradually return to normal [15]. Therefore, effective diagnosis and treatment are particularly important for children with *Helicobacter pylori* infection. The mechanism by which Hp infection causes growth retardation in children is unclear, and its possible mechanisms are:

5.1. Affecting nutrient absorption

Hp infection impairs the gastric mucosal barrier and reduces gastric acid secretion, affecting the absorption of nutrients, especially iron and vitamin B12. Hp infection itself increases iron consumption and reduces gastric acid after infection, affecting the human body's absorption of iron, leading to or aggravating iron deficiency in the body.

5.2. Chronic Hp infection can cause intestinal dysbiosis

Hp can interfere with the composition of children's gastrointestinal flora and promote bacterial colonization. At the same time, after Hp invades the gastric mucosa, it can stimulate local inflammatory reactions, cause peptic ulcers, neutralize the acidic environment of the gastrointestinal tract, and aggravate intestinal dysbiosis [9].

5.3. Affecting the secretion and release of hormones

Ghrelin is secreted by fundic cells, directly stimulates the release of growth hormone (GH), and promotes appetite. After Hp infection, gastric mucosal inflammation and damage occur, the body's ghrelin level decreases, and serum leptin level increases.

6. Summary

In conclusion, Hp infection is closely and complexly related to various extra-gastrointestinal diseases in children. Although certain research results have been achieved in iron deficiency anemia, Henoch-Schonlein purpura, and asthma, many details and mechanisms need further in-depth exploration, and more high-quality, multi-center, and large-sample studies are needed. Although Hp is not the main pathogenic factor of some diseases, its synergistic effect may accelerate disease progression or become a potential inducement. HP is an eradicable bacterium, and multiple clinical trials have confirmed that eradicating Hp has a good therapeutic effect on specific diseases, which provides a new strategic direction for clinical intervention.

At the same time, studies have found that HP does not have adverse effects in all diseases, and it shows a protective effect in the pathogenesis of some diseases, which is also the focus of controversy on whether to eradicate *Helicobacter pylori* during disease treatment. The pathogenic mechanism of *Helicobacter pylori* has become a key area of future research, and related breakthroughs will help formulate more accurate clinical diagnosis and treatment plans.

Disclosure statement

The authors declare no conflict of interest.

References

[1] Li W, Li Z, Wang N, et al, 2022, Meta-Analysis of the Current Status and Influencing Factors of Helicobacter Pylori Infection in Chinese Children. Chinese General Practice, 25(28): 3569–3578.

[2] Gastroenterology Group of Pediatrics Branch of Chinese Medical Association, National Children's Medical Center Gastroenterology Alliance, Editorial Board of Chinese Journal of Pediatrics, 2023, Expert Consensus on Diagnosis and Treatment of Helicobacter Pylori Infection in Chinese Children (2022). Chinese Journal of Pediatrics, 61(7): 580–587.

[3] Li J, 2020, Clinical Observation of Iron Supplementation Combined with Anti-Helicobacter Pylori Therapy in Iron Deficiency Anemia with Positive Helicobacter Pylori Infection. China Practical Medicine, 15(26): 140–142.

[4] Ye F, 2019, Research Progress on the Correlation Between Helicobacter Pylori Infection and Hematological Diseases. Journal of Oncology, 25(6): 552–556.

[5] Pan X, Liu J, Wang Y, et al, 2023, Meta-Analysis of the Correlation Between Helicobacter Pylori Infection and Childhood Henoch-Schonlein Purpura. Medical Information, 36(2): 92–98.

[6] Wang J, Han L, Zhang Z, et al, 2021, Analysis of Risk Factors and Treatment of Helicobacter Pylori Infection in Children with Henoch-Schonlein Purpura. Systems Medicine, 6(16): 31–34.

[7] Yang X, Guo W, Luo M, et al, 2020, Study on the Imbalance of Helper T Lymphocyte/Regulatory T Lymphocyte in Children with Henoch-Schonlein Purpura Complicated with Helicobacter Pylori Infection. Chinese Journal of Applied Clinical Pediatrics, 35(22): 1703–1707.

[8] Yang L, Zhang L, Gai Z, 2021, Research Progress on the Relationship Between Helicobacter Pylori and Gastrointestinal Microecology. Chinese Journal of Microecology, 33(6): 726–731.

[9] Guan J, Ma G, Zhang X, 2021, Impact of Helicobacter Pylori Infection on Children with Henoch-Schonlein Purpura. Chinese Journal of Microecology, 33(3): 304–308.

[10] Yang M, Chen Y, 2014, Study on the Correlation Between Helicobacter Pylori Infection and the Incidence of Bronchial Asthma in Children. Chinese Journal of Gastroenterology and Hepatology, 23(6): 712–714.

[11] Wu Y, 2016, Analysis of the Correlation Between Childhood Asthma and Helicobacter Pylori Infection. Journal of Hainan Medical University, 22(13): 1429–1431.

[12] Wang Z, Shen G, Huang Y, 2023, Analysis of the Correlation Between Helicobacter Pylori Infection and the Incidence of Asthma in Children. Anhui Medical and Pharmaceutical Journal, 27(12): 2479–2482.

[13] Liu G, Li P, Li R, et al, 2017, Relationship Between Helicobacter Pylori Infection and the Incidence of Asthma in Children and Its Impact on Immune Function. Progress in Modern Biomedicine, 17(15): 2961–2964.

[14] Gao J, Xie Q, 2022, Research Progress on the Mechanism of Helicobacter Pylori Infection in Extra-gastrointestinal Diseases in Children. Shanghai Medical Journal, 45(8): 572–576.

[15] Wang X, Liu W, Chen Y, et al, 2020, Impact of Helicobacter Pylori Infection Treatment on Children's Growth and Development Status. Chongqing Medicine, 49(18): 3074.