Iran J Pediatr. 2024 June; 34(3):e144497. https://doi.org/10.5812/ijp-144497.

Published online 2024 April 27. **Research Article**

Effects of *Helicobacter pylori* Infection Before and After Eradication Treatment on Physical Development and Nutritional Indicators of Children

Xiao Liu [1, 2], Yuanda Zhang [3, 2], Li-Po Han [4, 4], Meiying Wang [5] and Jing Bi [6, 7, *]

[1] Baoding Hospital, Beijing Children's Hospital Affiliated to Capital Medical University, Baoding, Hebei, China
[2] Key Laboratory of Clinical Research on Respiratory Digestive Disease, Baoding, Hebei, China
[3] Department of Nutriology, Baoding Hospital, Beijing Children's Hospital Affiliated to Capital Medical University, Baoding, Hebei, China
[4] Department of Ophthalmology, Baoding Hospital, Beijing Children's Hospital Affiliated to Capital Medical University, Baoding, Hebei, China
[5] Department of Clinical Laboratory, Baoding Traditional Chinese Medicine Hospital, Baoding, Hebei, China
[6] Department of Infectious Diseases, Baoding Hospital, Beijing Children's Hospital Affiliated to Capital Medical University, Baoding, Hebei, China
[7] Baoding Accurate Diagnosis and Treatment Laboratory of Children's Infectious Diseases, Baoding, Hebei, China

[*] *Corresponding author*: Department of Infectious Diseases, Baoding Hospital, Beijing Children's Hospital Affiliated to Capital Medical University, P. O. Box: 071000, Baoding, Hebei, China. Email: xinxian7968577@163.com

Received 2023 December 30; **Revised** 2024 March 16; **Accepted** 2024 April 02.

Abstract

Background: *Helicobacter pylori* (Hp) infection causes digestive disorders in children.
Objectives: To investigate whether Hp infection affects the physical development and nutritional indicators of children.
Methods: This retrospective study included 100 healthy children and 112 children with Hp infection who received eradication treatment. A retrospective statistical analysis was conducted on the height, weight, hemoglobin (Hb), serum ferritin (SF), serum iron (SI), albumin (ALB), and 25-(OH)D3 levels of all selected children.
Results: Of the 112 children with Hp infection, 23 (20.5%) showed a positive 13C-urea breath test after a 1-year follow-up, and they were classified into the recurrence group. Following a 1-year follow-up, 89 (79.5%) children demonstrated negative results in the 13C-urea breath test and were selected for the non-recurrence group. Analysis of physical development and nutritional indices revealed lower Hb, SI, SF, and 25-(OH)D3 levels in the study group than in the control group before eradication treatment ($P < 0.05$). However, no significant difference was observed between the control and study groups regarding body height, body weight, and ALB levels ($P > 0.05$). Following 1 year of eradication treatment, Hb, SI, SF, 25-(OH)D3, and ALB levels showed no significant difference between the study and control groups ($P > 0.05$). However, a relevant contrast was noted in 25-(OH)D3 levels between the non-recurrence and recurrence groups after 1 year of eradication treatment ($P < 0.05$), with the former group having lower levels than the latter.
Conclusions: *Helicobacter pylori* infection may impact Hb, SI, SF, and 25-(OH)D3 levels in children. Decreased 25-(OH)D3 may be a hazard for the recurrence of Hp infection.

Keywords: *Helicobacter pylori*, Children, Eradication Treatment, Physical Development, Nutritional Indicators

1. Background

Helicobacter pylori (Hp) infection is a major cause of digestive disorders in children (1). Patients with Hp infection may develop indigestion, gastric and duodenal ulcers, etc. (2). Hp infection can damage the gastric mucosa and affect inflammatory factor levels, resulting in gastrointestinal symptoms such as vomiting, abdominal pain, and loss of appetite, thus leading to malnutrition and stunted development (3), which may affect the normal growth and nutritional status of children. Hp infection has been reported to significantly participate in the development of dyspepsia, which can cause malnutrition in children (4).

2. Objectives

This study aimed to test and clarify whether Hp infection affects the physical development and nutritional indicators of children with Hp infection before and after eradication treatment.

3. Methods

3.1. General Information

This study included 112 children diagnosed with Hp infection from the outpatient and inpatient departments of our hospital between January 2020 and June 2021. The study group consisted of 63 boys and 49 girls, with an average age of 9.7 ± 2.0 years. Additionally, the control group consisted of 100 healthy children who had undergone a physical examination in the outpatient department of our hospital during the same period. The control group included 44 girls and 56 boys, with a mean age of 9.6 ± 1.9 years. No significant difference was found in age and sex between the two groups ($P > 0.05$).

3.1.1. Inclusion Criteria

(1) Children who fulfilled the diagnostic criteria for Hp infection, which included testing positive for endoscopic pathological staining, rapid urease test, and/or 13C-urea breath test (5)

(2) Children aged 7 - 14 years.

3.1.2. Exclusion Criteria

(1) Children diagnosed with serious organic illnesses

(2) Children diagnosed with acute infectious diseases in the last month

(3) Children who had received Hp eradication treatment

(4) Children who had used vitamin preparations or trace element supplements within half a year

(5) Children with a positive 13C-urea breath test after eradication treatment

(6) Children who failed to complete follow-up due to poor compliance.

3.2. Method

Treatment involved administering omeprazole orally twice a day at a dose of 0.6 - 1.0 mg/kg.d, with a maximum dose of 20 mg per time. Amoxicillin was given orally twice a day at a dose of 50 mg/kg.d, with a maximum dose of 1 g per time. Clarithromycin was administered orally twice a day at a dose of 20 mg/kg.d, with a maximum dose of 0.5 g per time, and colloidal bismuth subcitrate at a dose of 6 - 8 mg/kg.d (twice a day orally) for 2 weeks. The children with Hp infection enrolled in this study underwent a 13C-urea breath test 4 weeks after treatment and were followed up for 1 year. Furthermore, this study recorded the physical development and nutritional indicators of the enrolled children before and 1 year after eradication treatment. Data were obtained from the hospital information and management system. Various patient information, including main clinical features, and laboratory tests, were collected.

3.3. Sampling and Detection

Before and 1 year after treatment, 5 mL of peripheral venous blood was extracted from each child with Hp infection, and 5 ml of peripheral venous blood was drawn from healthy children during their physical examinations.

3.4. Measurement of Physical Development Indicators

The body height and weight of these children were measured in the same environment after defecation and urination in the morning and on an empty stomach.

3.5. Detection of Nutritional Indicators

Baoding Key Laboratory of Clinical Research on Children's Respiratory and Digestive Diseases assessed nutritional indicators. Haemoglobin (Hb) was measured using a Mindray BC-5300 Auto Hematology Analyzer. Serum ferritin (SF) and serum iron (SI) were detected using a Beckman Coulter-AU5800 biochemical analyzer using test kits provided by Beckman Coulter and Abbott Laboratories, respectively. The level of 25-(OH)D3 was detected by chemiluminescence using an i2000 chemiluminescence instrument (Abbott Laboratories) with the test kit provided by Abbott Laboratories. Additionally, the albumin (ALB) level was tested using the bromocresol green method using the AU5800 biochemical analyzer with the test kit purchased from Beckman Coulter.

3.6. Statistical Analysis

SPSS 25.0 was utilized for conducting data analysis. The measurement data were represented using ($\bar{X}$), and an independent samples *t*-test was used for analysis. Enumeration data were expressed as the rate (%) and were analyzed using the chi-square test. A P-value of < 0.05 denotes statistical difference.

4. Results

4.1. General Data

Overall, 112 children infected with Hp responded to treatment without any loss to follow-up; 23 (20.5%) children were classified into the recurrence group as they showed a positive 13C-urea breath test after 1-year follow-up. The remaining 89 (79.5%) children were included in the non-recurrence group as they showed negative results in the 13C-urea breath test after 1-year follow-up. The recurrence group included 13 boys and 10 girls, whereas the non-recurrence group consisted of 50 boys and 39 girls. The average age was 9.6 ± 2.0 and 9.7 ± 2.0 years in the recurrence and non-recurrence groups,

respectively. Table 1 shows that there was no significant difference in sex and age between the recurrence group and non-recurrence groups ($P > 0.05$).

4.2. Comparison of Physical Development and Nutritional Indicators Between the Study and Control Groups Before Eradication Treatment

Table 2 indicates that before eradication treatment, the study group had significantly lower levels of Hb, SI, SF, and 25-(OH)D3 compared to the control group ($P < 0.05$). However, there were no meaningful differences observed in body height, body weight, and ALB levels between the study and control groups ($P > 0.05$).

4.3. Comparison of Nutritional Indicators Between the Study and Control Groups After 1 Year of Eradication Treatment

Table 3 reveals that after 1 year of eradication treatment, there were no significant differences observed in the levels of Hb, SF, SI, 25-(OH)D3, and ALB between the control and study groups ($P > 0.05$).

4.4. Comparison of Nutritional Indices Between the Recurrence and Non-Recurrence Groups After 1 Year of Eradication Treatment

No significant differences were noted in the levels of Hb, SI, SF, and ALB between the recurrence and non-recurrence groups after 1 year of eradication treatment ($P > 0.05$). Table 4 demonstrates that the level of 25-(OH)D3 in the recurrence group was lower than that in the non-recurrence group after 1 year of eradication treatment ($P < 0.05$).

5. Discussion

Importantly, Hp infection is strongly linked to the development of chronic digestive system infections, which have an extremely low rate of natural remission (6). Hp infection has emerged as a disease posing a critical threat to the growth and development of children. Hp infection may recur after eradication treatment, with a high recurrence rate observed in children (7, 8). In our study, 20.5% of children with Hp infection retested positive for the 13C-urea breath test 1 year after eradication treatment, indicating a high recurrence of Hp infection in this region.

Individuals with Hp infection may experience symptoms such as anorexia, malabsorption, and dysregulation of neuroendocrine hormones (e.g., leptin and ghrelin), which are independent risk factors for short stature (9-11). After Hp infection, patients may develop iron deficiency due to gastrointestinal bleeding, increased iron absorption by bacteria, and reduced dietary iron absorption (12). Moreover, it can lead to malabsorption of vitamin D and other vitamins, significantly affecting the nutritional status of infected individuals (13-15). Ultimately, this can have a negative impact on the growth and development of children, as well as on Hb, trace elements, SF, and SI levels (13, 16, 17). Previous studies have demonstrated the relationship between iron deficiency and anemia in children (18, 19).

In this study, before eradication treatment, children with Hp infection had lower levels of SF, SI, Hb, and 25-(OH)D3 compared to healthy children. We believe that Hp infection may impact children's health in various ways, leading to appetite loss and poor nutrient absorption, resulting in anemia and vitamin D deficiency. Furthermore, this study evaluated the nutritional indicators of children with Hp infection after 1 year of successful eradication treatment. No significant differences were found in the levels of Hb, SI, SF, 25-(OH)D3, and ALB between infected and healthy children. It can be inferred that after eradication treatment for Hp infection, there is a rapid recovery of the internal environment of Hp-infected children, resulting in improvements in nutritional indicators in vivo. From another perspective, it confirms that Hp infection affects the nutritional indicators of children to some extent.

Low 25-(OH)D3 levels may be associated with the recurrence of Hp infection in children (20). In this study, the 25-(OH)D3 levels of children with Hp infection recurrence 1 year after successful eradication treatment were lower than those of children without relapse. Although there were no significant differences in Hb, SI, SF, and ALB levels, a decrease in 25-(OH)D3 levels may contribute to an increased risk of Hp infection recurrence.

5.1. Conclusions

The current study found no significant differences regarding body height, weight, and ALB levels between Hp-infected children and their healthy counterparts. Our study findings reveal that Hp infection alone may have no significant effect on the growth indicators of children, although Hp infection may cause symptoms of the digestive system and affect the levels of SI, 25-(OH)D3, and other nutritional indicators. This study had several limitations, such as a smaller sample size and failure to exclude and analyze the impact of family socioeconomic factors on the enrolled children.

Footnotes

Authors' Contribution: X.L and Y. Z carried out the studies, participated in collecting data, and drafted the

Table 1. General Data in the Two Groups [a]

Groups	Number of Cases	Sex		Average Age, y
		Male	Female	
Recurrence group	23	13 (56.5)	10 (43.5)	9.6 ± 2.0
Non-recurrence group	89	50 (56.2)	39 (43.8)	9.7 ± 2.0
χ^2/*t* value		0.001		0.356
P-value		0.976		0.723

[a] Values are expressed as mean ± SD or No. (%).

Table 2. A Comparison Between the Control and Study Groups Regarding Physical Development and Nutritional Indicators Prior to the Eradication Treatment [a]

Groups	Cases	Height, cm	Weight, kg	25-(OH)D3, ug/L	Serum Iron, μmoL/ L	Serum Ferritin, μg/L	Hemoglobin, g/L	Albumin, g/L
Study group	112	136.0 ± 20.4	39.7 ± 8.5	26.5 ± 5.8	12.3 ± 2.3	24.0 ± 6.6	122.3 ± 6.1	46.4 ± 6.5
Control group	100	141.8 ± 22.7	39.5 ± 9.0	33.0 ± 5.6	13.4 ± 2.4	28.3 ± 6.5	126.8 ± 9.0	47.6 ± 6.9
***t* value**		1.957	0.166	8.278	3.401	4.769	4.299	1.303
P-value [b]		0.052	0.868	0.000	0.001	0.000	0.000	0.194

[a] Values are expressed as mean ± SD.
[b] Independent samples *t*-test.

Table 3. A Comparison Between the Control and Study Groups Regarding Nutritional Indicators after 1 Year of Eradication Treatment [a]

Groups	Cases	25-(OH)D3, ug/L	Serum Iron, μmoL/L	Serum Ferritin, μg/L	Hemoglobin, g/L	Albumin, g/L
Study group	112	32.3 ± 6.2	13.1 ± 1.5	26.7 ± 6.4	125.2 ± 6.7	47.5 ± 7.0
Control group	100	33.0 ± 5.6	13.4 ± 2.4	28.3 ± 6.5	126.8 ± 9.0	47.6 ± 6.9
***t* value**		0.858	1.100	1.803	1.477	0.104
P-value [b]		0.392	0.273	0.073	0.141	0.917

[a] Values are expressed as mean ± SD.
[b] Independent samples *t*-test.

Table 4. Contrast of Nutritional Indices Between the Recurrence and Non-Recurrence Groups After 1 Year of Eradication Treatment [a]

Groups	Cases	25-(OH)D3, ug/L	Serum Iron, μmoL/L	Serum Ferritin, μg/L	Hemoglobin, g/L	Albumin, g/L
Recurrence group	23	28.8 ± 4.2	12.9 ± 1.4	25.6 ± 5.7	124.3 ± 5.6	46.6 ± 8.7
Non-recurrence group	89	33.2 ± 6.3	13.1 ± 1.6	27.0 ± 6.6	125.4 ± 7.0	47.7 ± 6.5
t value		3.121	0.680	0.934	0.717	0.675
P-value [b]		0.002	0.498	0.352	0.475	0.501

[a] Values are expressed as mean ± SD.
[b] Independent samples *t*-test.

manuscript, and are responsible and accountable for the accuracy or integrity of the work; L. H and M. W performed the statistical analysis and participated in its design; J. B participated in acquisition, analysis, or interpretation of data and drafted the manuscript. All authors read and approved the final manuscript.

Conflict of Interests: The authors declare no conflicts of interest.

Data Availability: The dataset presented in the study is available on request from the corresponding author during submission or after publication.

Funding/Support: This study is sponsored by Baoding Science and Technology Plan Project (2341ZF177).

Informed Consent: Written informed approval was obtained from all the children and their parents.

References

1. Sabbagh P, Javanian M, Koppolu V, Vasigala VR, Ebrahimpour S. Helicobacter pylori infection in children: an overview of diagnostic methods. *Eur J Clin Microbiol Infect Dis*. 2019;**38**(6):1035–45. [PubMed ID: 30734129]. https://doi.org/10.1007/s10096-019-03502-5.
2. Ruiter R, Wunderink HF, Veenendaal RA, Visser LG, de Boer MGJ. Helicobacter pylori resistance in the Netherlands: a growing problem? *Neth J Med*. 2017;**75**(9):394–8. [PubMed ID: 29219812].
3. Sierra D, Wood M, Kolli S, Felipez LM. Pediatric Gastritis, Gastropathy, and Peptic Ulcer Disease. *Pediatr Rev*. 2018;**39**(11):542–9. [PubMed ID: 30385583]. https://doi.org/10.1542/pir.2017-0234.
4. Hossain MS, Das S, Begum S, Rahman MM, Mazumder RN, Gazi MA, et al. Asymptomatic Duodenitis and Helicobacter pylori associated Dyspepsia in 2-Year-Old Chronic Malnourished Bangladeshi Slum-Dwelling Children: A Cross-Sectional Study. *J Trop Pediatr*. 2021;**67**(1). [PubMed ID: 33099650]. [PubMed Central ID: PMC7948384]. https://doi.org/10.1093/tropej/fmaa079.
5. Wang YK, Kuo FC, Liu CJ, Wu MC, Shih HY, Wang SS, et al. Diagnosis of Helicobacter pylori infection: Current options and developments. *World J Gastroenterol*. 2015;**21**(40):11221–35. [PubMed ID: 26523098]. [PubMed Central ID: PMC4616200]. https://doi.org/10.3748/wjg.v21.i40.11221.
6. Ruiz VE, Sachdev M, Zhang S, Wen S, Moss SF. Isolating, immunophenotyping and ex vivo stimulation of CD4+ and CD8+ gastric lymphocytes during murine Helicobacter pylori infection. *J Immunol Methods*. 2012;**384**(1-2):157–63. [PubMed ID: 22814402]. [PubMed Central ID: PMC3432732]. https://doi.org/10.1016/j.jim.2012.07.002.
7. Hu Y, Wan JH, Li XY, Zhu Y, Graham DY, Lu NH. Systematic review with meta-analysis: the global recurrence rate of Helicobacter pylori. *Aliment Pharmacol Ther*. 2017;**46**(9):773–9. [PubMed ID: 28892184]. https://doi.org/10.1111/apt.14319.
8. Sivapalasingam S, Rajasingham A, Macy JT, Friedman CR, Hoekstra RM, Ayers T, et al. Recurrence of Helicobacter pylori infection in Bolivian children and adults after a population-based "screen and treat" strategy. *Helicobacter*. 2014;**19**(5):343–8. [PubMed ID: 24830916]. https://doi.org/10.1111/hel.12137.
9. Erdemir G, Ozkan TB, Ozgur T, Altay D, Cavun S, Goral G. Helicobacter pylori Infection in Children: Nutritional Status and Associations with Serum Leptin, Ghrelin, and IGF-1 Levels. *Helicobacter*. 2016;**21**(4):317–24. [PubMed ID: 26667121]. https://doi.org/10.1111/hel.12288.
10. Franceschi F, Annalisa T, Teresa DR, Giovanna D, Ianiro G, Franco S, et al. Role of Helicobacter pylori infection on nutrition and metabolism. *World J Gastroenterol*. 2014;**20**(36):12809–17. [PubMed ID: 25278679]. [PubMed Central ID: PMC4177464]. https://doi.org/10.3748/wjg.v20.i36.12809.
11. Queiroz DM, Rocha AM, Crabtree JE. Unintended consequences of Helicobacter pylori infection in children in developing countries: iron deficiency, diarrhea, and growth retardation. *Gut Microbes*. 2013;**4**(6):494–504. [PubMed ID: 23988829]. [PubMed Central ID: PMC3928161]. https://doi.org/10.4161/gmic.26277.
12. Muhsen K, Cohen D. Helicobacter pylori infection and iron stores: a systematic review and meta-analysis. *Helicobacter*. 2008;**13**(5):323–40. [PubMed ID: 19250507]. https://doi.org/10.1111/j.1523-5378.2008.00617.x.
13. Aimasso U, D'Onofrio V, D'Eusebio C, Devecchi A, Pira C, Merlo FD, et al. Helicobacter pylori and nutrition: a bidirectional communication. *Minerva Gastroenterol Dietol*. 2019;**65**(2):116–29. [PubMed ID: 30759976]. https://doi.org/10.23736/S1121-421X.19.02568-6.
14. Mendoza E, Camorlinga-Ponce M, Perez-Perez G, Mera R, Vilchis J, Moran S, et al. Present and past Helicobacter pylori infection in Mexican school children. *Helicobacter*. 2014;**19**(1):55–64. [PubMed ID: 24165012]. https://doi.org/10.1111/hel.12098.
15. Mut Surmeli D, Surmeli ZG, Bahsi R, Turgut T, Selvi Oztorun H, Atmis V, et al. Vitamin D deficiency and risk of Helicobacter pylori infection in older adults: a cross-sectional study. *Aging Clin Exp Res*. 2019;**31**(7):985–91. [PubMed ID: 30267333]. https://doi.org/10.1007/s40520-018-1039-1.
16. Galal YS, Ghobrial CM, Labib JR, Abou-Zekri ME. Helicobacter pylori among symptomatic Egyptian children: prevalence, risk factors, and effect on growth. *J Egypt Public Health Assoc*. 2019;**94**(1):17. [PubMed ID: 32813082]. [PubMed Central ID: PMC7364677]. https://doi.org/10.1186/s42506-019-0017-6.
17. Bibi F, Alvi SA, Sawan SA, Yasir M, Sawan A, Jiman-Fatani AA, et al. Detection and Genotyping of Helicobacter pylori among Gastric ulcer and Cancer Patients from Saudi Arabia. *Pak J Med Sci*. 2017;**33**(2):320–4. [PubMed ID: 28523030]. [PubMed Central ID: PMC5432697]. https://doi.org/10.12669/pjms.332.12024.
18. Gupta PM, Perrine CG, Mei Z, Scanlon KS. Correction: Gupta, P.M.; et al. Iron, Anemia, and Iron Deficiency Anemia among Young Children in the United States Nutrients 2016, 8, 330. *Nutrients*. 2017;**9**(8). [PubMed ID: 28809788]. [PubMed Central ID: PMC5579669]. https://doi.org/10.3390/nu9080876.
19. Muhsen K, Barak M, Shifnaidel L, Nir A, Bassal R, Cohen D. Helicobacter pylori infection is associated with low serum ferritin levels in Israeli Arab children: a seroepidemiologic study. *J Pediatr Gastroenterol Nutr*. 2009;**49**(2):262–4. [PubMed ID: 19525869]. https://doi.org/10.1097/MPG.0b013e31818f0a0d.
20. Zhang Y, Bi B, Guo X, Zhang S. Analysis of Eradication, Recurrence and Levels of 25-hydroxyvitamin D(3) and Interleukin-1beta in paediatric patients with Helicobacter Pylori Infection-related Gastritis. *Pak J Med Sci*. 2020;**36**(6):1377–81. [PubMed ID: 32968412]. [PubMed Central ID: PMC7501042]. https://doi.org/10.12669/pjms.36.6.2292.