




# Analysis of Risk Factors for the Recurrence of *Helicobacter Pylori* Infection in Baoding Children Aged 4 - 16 Years

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Received 2023 August 6; Revised 2024 March 10; Accepted 2024 April 1.

## Abstract

**Background:** *Helicobacter pylori* (*H. pylori*) infection affects over 50% of the world's population and is the primary cause of duodenal and gastric ulcers, as well as gastric cancer.

**Objectives:** To investigate the risk factors for recurrence following successful eradication of *H. pylori* infection in children aged 4 - 16 years in the Baoding area.

**Methods:** The study included 328 children diagnosed with *H. pylori* infection at our hospital from January 2021 to June 2022, who had successfully undergone eradication treatment. A questionnaire covering personal history, family history, health status, and family socioeconomic status was administered to the children, coupled with a 1-year follow-up. Recurrence within this period was monitored, along with an analysis of the risk factors for recurrence post-eradication.

**Results:** Out of 328 children with *H. pylori* infection, 295 (89.9%) were successfully followed up. Among these, 55 (18.6%) tested positive on the 13C-urea breath test and were considered to have recurrent infection (recurrence group), while 240 (81.4%) tested negative and were considered to have no recurrence (non-recurrence group). Univariate chi-square analysis of the questionnaire results indicated that age ( $P < 0.05$ ), number of eradication treatments ( $P < 0.05$ ), mother's education level ( $P < 0.05$ ), place of residence ( $P < 0.05$ ), family income ( $P < 0.05$ ), family history of *H. pylori* infection ( $P < 0.05$ ), separate meals ( $P < 0.05$ ), and lunch location ( $P < 0.05$ ) significantly influenced *H. pylori* recurrence. Multivariate analysis, which included factors showing significant differences in univariate analysis, was performed using a logistic regression model. This analysis identified multiple treatments (> 2 eradication attempts), residing in rural areas, and low family income as combined risk factors for *H. pylori* recurrence in children. Conversely, being older than 10 years, eating separate meals, and higher maternal education level emerged as protective factors against recurrence.

**Conclusions:** There is a relatively high rate of *H. pylori* recurrence among children aged 4 - 16 years in this region, which may be linked to age, number of eradication treatments, dietary and hygiene habits, educational levels of family members, and economic status.

**Keywords:** *Helicobacter pylori*, Children, Recurrence, Questionnaire Survey

## 1. Background

*Helicobacter pylori* (*H. pylori*) infection affects more than 50% of the world's population and is the primary cause of duodenal and gastric ulcers, as well as gastric cancer (1). Children are particularly susceptible to *H. pylori* infection (2), with approximately one-third of children worldwide being infected (3). Moreover, about

two-thirds of adult patients acquired their *H. pylori* infection before the age of 10 (4, 5), underscoring the importance of controlling *H. pylori* infection during childhood. Currently, "triple therapy" is commonly used clinically to eradicate *H. pylori* infection (6). However, some patients may experience a recurrence of the infection after receiving treatment, which represents a significant challenge in the management of *H. pylori*

infection (2), with approximately one-third of children worldwide being infected (3). Moreover, about two-thirds of adult patients acquired their *H. pylori* infection before the age of 10 (4, 5), underscoring the importance of controlling *H. pylori* infection during childhood. Currently, "triple therapy" is commonly used clinically to eradicate *H. pylori* infection (6). However, some patients may experience a recurrence of the infection after receiving treatment, which represents a significant challenge in the management of *H. pylori* infection (7). Recurrence rates are notably higher among younger patients.

## 2. Objectives

Given the context, our research team aims to understand the recurrence of *H. pylori* infection in children in the local region and the risk factors associated with its recurrence. We utilized a standardized survey questionnaire to gather data on personal history (e.g., prior infections, history of treatment, history of drug allergy, etc.), family history (e.g., family history of *H. pylori* infection, gastric and duodenal ulcers, gastrointestinal malignancies, etc.), health status, and family socioeconomic status (e.g., family economic income, education level and occupation of the parents, etc.). This was followed by a 1-year follow-up of children in the local region who had successfully undergone eradication therapy. The findings are reported below.

## 3. Methods

### 3.1. General Information

This study is a retrospective clinical investigation. The sample size was calculated based on the eradication rate of *H. pylori* in China, which ranges from 70% to 85%. The sample size formula used for counting data (rate) is  $n = z^2 \times p \times (1 - p) / d^2$ , employing a 95% confidence interval where  $z = 1.96$ ,  $p = 77.5\%$ , and the acceptable margin of error ( $d$ ) = 0.05. The minimum sample size calculated was 268 individuals. Due to potential data incompleteness and other factors, the final sample comprised 328 participants.

The study subjects were 328 children aged 4 - 16 years, diagnosed with *H. pylori* infection and successfully treated in a hospital from January 2020 to June 2021. Among the enrolled children, there were 177 boys and 151

girls, with an average age of  $8.9 \pm 2.8$  years. The children were assessed through a questionnaire survey covering personal history, family history, health status, and family socioeconomic status, followed by a 1-year follow-up. The study received approval from the Institutional Ethics Committee of the Hospital, and written informed consent was obtained from all participants.

Diagnostic criteria for *H. pylori* infection included children exhibiting positive results from any of the following tests: rapid urease test, endoscopic pathological staining, or the 13C-urea breath test, conducted due to digestive system symptoms or a strong demand for an *H. pylori* test (8).

### 3.2. Inclusion Criteria

- (1) Children aged 4 - 16 years;
- (2) Positive 13C-urea breath test, gastric mucosal rapid urease test, or tissue section staining, followed by a negative 13C-urea breath test after 4 weeks of eradication treatment;
- (3) Children capable of completing a 1-year follow-up and returning to the hospital every 6 months for a repeat 13C-urea breath test.

### 3.3. Exclusion Criteria

- (1) Children with major organ or mental diseases;
- (2) Children with poor compliance who cannot complete follow-up on time;
- (3) Children who had an acute infectious disease in the past month.

### 3.4. Research and Investigation Methods

Our unified survey questionnaire was based on the national *H. pylori* infection research questionnaire, adapted to reflect local economic levels and dietary habits. The questionnaire covered various topics, including sociodemographic characteristics (gender, age, parental education level, income status, etc.), dietary habits (shared meals, meal structure, etc.), lifestyle (living in rural or urban areas, cohabitation with parents, campus residency, etc.), and *H. pylori*-related diseases (treatment history, treatment plans, frequency, and presence of digestive tract diseases). All enrolled children were surveyed on personal history, family history, health status, and family socioeconomic status by medical staff with intermediate or higher

professional titles and systematic training. The authenticity and reliability of the questionnaire were maintained during the survey, with care taken to avoid leading questions. Additionally, the 13C-urea breath test was re-administered at 6 and 12 months post-enrollment. Children testing positive on these subsequent tests were considered to have a recurrence of *H. pylori* infection. The study process flowchart is shown in Figure 1.

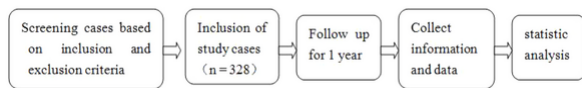


Figure 1. The flowchart of study process.

### 3.5. Statistical Analysis

Statistical analysis was conducted using SPSS 25.0 software. Enumerated data were expressed as n(%), and measurement data were presented as means ( $\pm$  standard deviation). The chi-square test was used for inter-group comparisons of categorical data, such as gender and recurrence rate, while the *t*-test was used for inter-group comparisons of continuous data, such as age. The results of the questionnaire survey were statistically analyzed using a binary logistic regression equation, with the recurrence rate as the dependent variable. A *P*-value of  $< 0.05$  was considered statistically significant.

## 4. Results

Out of the 328 children enrolled with *H. pylori* infection, 295 (89.9%) were successfully followed up, while 33 cases were lost to follow-up, resulting in a loss rate of 10.1%. Among the children who were successfully followed up, 55 (18.6%) tested positive on the 13C-urea breath test and were considered as having a recurrence (the recurrence group), while 240 (81.4%) tested negative and were considered as not having a recurrence (non-recurrence group). The recurrence group comprised 31 boys and 24 girls, while the non-recurrence group included 132 boys and 108 girls, with average ages of  $8.3 \pm 2.1$  years and  $9.0 \pm 2.8$  years, respectively. No statistically significant differences were found in the comparison of gender and age between the two groups ( $P > 0.05$ ), as presented in Table 1.

Table 1. Comparison of General Data between the Recurrence Group and the Non-Recurrence Group

Groups	Cases	Number of Boys	Age, y
Recurrence group	55	31	$8.3 \pm 2.2$
Non-recurrence group	240	132	$9.0 \pm 2.8$
$\chi^2/t$ value		0.034	1.652
<i>P</i> -value		$> 0.05^a$	$> 0.05^b$

<sup>a</sup>  $\chi^2$  test.

<sup>b</sup> Independent-sample *t*-test.

A questionnaire survey was conducted on the personal history, family history, health status, and family socioeconomic status of the enrolled children. Univariate chi-square analysis of the questionnaire results indicated that age ( $\chi^2 = 4.122$ ,  $P = 0.042$ ), number of eradication treatments ( $\chi^2 = 12.761$ ,  $P < 0.001$ ), the mother's education level ( $\chi^2 = 17.166$ ,  $P < 0.001$ ), place of residence ( $\chi^2 = 5.252$ ,  $P = 0.022$ ), family income ( $\chi^2 = 9.103$ ,  $P = 0.003$ ), and whether meals were separate ( $\chi^2 = 13.241$ ,  $P < 0.001$ ) were significant factors influencing *H. pylori* infection recurrence (Table 2).

Further multivariate analysis included these significant factors from the univariate analysis in a logistic regression model. The results (Table 3) revealed that undergoing fewer than two eradication treatments, living in a city, and having a high family income were combined protective factors against *H. pylori* infection recurrence in children ( $OR < 1$ ,  $P < 0.05$ ). Conversely, being younger than 10 years old, not having separate meals, and having a mother with a lower education level were combined risk factors for *H. pylori* infection recurrence in children ( $OR > 1$ ,  $P < 0.05$ ).

## 5. Discussion

*H. pylori* infection is among the most common infections in humans, typically occurring during childhood. Although most infected individuals are asymptomatic, about 30% may develop mild to severe upper gastrointestinal diseases (9). With a growing understanding of *H. pylori*, considerable research has focused on its diagnosis and treatment. In recent decades, there has also been an increasing focus on studying the recurrence of *H. pylori* infection after eradication, especially in children, where relatively fewer studies have been conducted on the risk factors

**Table 2.** Univariate Analysis of Personal History, Family History, Health Status, Family Socioeconomic Status for the Recurrence of *H. pylori* Infection in Children

Factors Related to <i>H. pylori</i> Infection Recurrence	Regression Coefficient	Standard Error	$\chi^2$	P-Value	OR	95%CI
Age	-0.833	0.410	4.122	0.042	0.435	0.195 - 0.972
Times of eradication treatment	1.339	0.375	12.761	< 0.001	3.816	1.830 - 7.956
Place of residence	0.864	0.377	5.252	0.022	2.372	1.133 - 4.967
Family economic income	1.140	0.378	9.103	0.003	3.128	1.491 - 6.562
<i>H. pylori</i> infection in the family members or not	0.670	0.386	3.007	0.083	1.953	0.916 - 4.163
Separate meals or not	-1.436	0.395	13.241	< 0.001	0.238	0.110 - 0.516
Education degree of the mother	-1.644	0.397	17.166	< 0.001	0.193	0.089 - 0.420
Lunch place	-0.670	0.396	16.126	0.091	0.512	0.235 - 1.113

**Table 3.** Multivariate Analysis of Personal History, Family History, Health Status, Family Socioeconomic Status for the Recurrence of *H. pylori* Infection in Children

Factors Related to <i>H. pylori</i> Infection Recurrence	Regression Coefficient	Standard Error	$\chi^2$	P-Value	OR	95%CI
Age of < 10 years old	0.888	0.405	4.810	0.028	2.431	1.099 - 5.377
Times of eradication treatment, < 2 times	-1.304	0.367	12.590	< 0.001	0.271	0.132 - 0.558
Living in city	-0.817	0.366	4.995	0.025	0.442	0.216 - 0.904
High economic income	-1.027	0.366	7.856	0.005	0.358	0.175 - 0.734
Non-separate meals	1.447	0.389	13.819	< 0.001	4.252	1.982 - 9.121
Lower education degree of the mother	1.614	0.392	17.001	< 0.001	5.025	2.333 - 10.823

for recurrence after eradication. This study was performed to comprehensively discuss the risk factors of recurrence of *H. pylori* infection in children in the local region.

It is acknowledged that the recurrence rate of *H. pylori* infection is highest in the first year post-eradication and is significantly influenced by socioeconomic conditions (10). Recurrence rates may vary significantly between different countries or even within different regions of the same country. Our study found that the recurrence rate of *H. pylori* infection in children aged 4 - 16 in the region was 18.6% after one year of follow-up. Literature suggests that recurrence rates in developing countries are much higher than those in developed countries (11, 12). For example, the annual recurrence rate in Latin America is 11.2% (13), while it is 9.3% in Mexico (14). A study in South Korea reported a recurrence rate of 10.9% following eradication (15), and in Vietnam, the reinfection rate was 23.5% after 11 months of follow-up (16). Our study's recurrence rate falls within these reported ranges, indicating significant regional differences in the recurrence of *H. pylori* infection. The annual reinfection rate among 5,193 *H. pylori*-infected patients across 15 provinces in China

after 6-84 months of follow-up is 1.5% (17), while the rate reported in Chongqing, China, is 4.75% (18). Our study has higher annual recurrence rates than those reported in China and Chongqing, which may be related to the underdeveloped local economy and the demographics of the children involved in this study. Age is another influencing factor for the recurrence of *H. pylori* infection, with a higher recurrence rate observed in children (19). Research indicates that the one-year recurrence rate of *H. pylori* infection in children under 10 years old is 20%, while it is 8% in children over 10 years old (20). Our research confirms that being under 10 years old is an independent risk factor for *H. pylori* infection recurrence, aligning with previous studies (21, 22).

The recurrence of *H. pylori* infection is a multifactorial process potentially related to personal medical history, family history, health status, and family socioeconomic status. Research has demonstrated that age and socioeconomic status are independently associated with the recurrence of *H. pylori* infection (23). Additionally, risk factors for the recurrence of *H. pylori* infection include low education levels, living in rural areas, family members not receiving simultaneous

*H. pylori* eradication treatment, contact with *H. pylori*-infected patients, and low household income (15, 17, 24-26). Our research findings suggest that living in rural areas, having low economic income, not sharing meals, and having a low maternal education level are independent risk factors for the recurrence of *H. pylori* infection, consistent with previous reports. Particularly, families with low education levels, rural residence, and low incomes often lack sufficient health knowledge, pay less attention to children's illnesses, and maintain relatively poor hygiene standards. Most of these families share tableware during meals, which are major contributors to the recurrence of *H. pylori* infection (27, 28).

Given our findings, it can be concluded that younger children may exhibit a higher recurrence rate of *H. pylori* infection. For children under 10 years old with *H. pylori* infection, the high risk of recurrence should be considered before starting eradication treatment. Additionally, patients with multiple eradication attempts may face a higher likelihood of recurrence. Therefore, it is essential to adopt regular and systematic treatment strategies to minimize the need for repeated eradication and thus reduce the recurrence rate of *H. pylori* infection. Promoting good dietary and health habits, as well as reducing the frequency of dining out, can also decrease the recurrence rate of *H. pylori* infection. This underscores the importance of actively educating the public about *H. pylori* prevention and control, encouraging meal sharing, and enhancing awareness of *H. pylori* and health prevention to reduce the recurrence of *H. pylori* infection.

It should be noted that this study has limitations, including being a single-center study with a small sample size, potential recall bias in the questionnaire survey, and the lack of strain culture and identification. Further research with a larger sample size is planned in an expanded study area to determine whether the recurrence of *H. pylori* infection is due to the recurrence of the original strain or reinfection by a new strain.

## 5. Conclusions

From January 2020 to June 2021, the recurrence rate of *H. pylori* infection in children aged 4 - 16 in the Baoding area was relatively high. The combined effect of multiple factors can lead to the recurrence of *H. pylori* infection in children. The protective factors against the recurrence of Hp infection in children include fewer

than two eradication treatments, living in cities, and higher family income. Being younger than 10 years old, not sharing meals, and low maternal education level are independent risk factors for the recurrence of *H. pylori* infection in children.

## Footnotes

**Authors' Contribution:** YN T and QW Dong carried out the studies, participated in collecting data, drafted the manuscript, and are responsible and accountable for the accuracy or integrity of the work; X L and NY Z performed the statistical analysis and participated in its design; YD Z participated in the acquisition, analysis, or interpretation of data and helped draft the manuscript. All authors read and approved the final manuscript.

**Conflict of Interests:** The authors declared 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.

**Ethical Approval:** The study was approved by the Institutional Ethics Committee of our Hospital (No.: 202035).

**Funding/Support:** This research is supported by Baoding Science and Technology Plan Project (No.: 1951ZF082).

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

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