

## Reinfection Rate after Successful *Helicobacter pylori* Eradication in Children

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### Abstract

**Objective:** Reinfection rate of *Helicobacter pylori* after successful eradication is low in developed countries. This study was performed to determine the reinfection rate of *H. pylori* during a follow up period of 12 months in Iranian children.

**Methods:** In this prospective study, children with *H. pylori* infection were treated with triple omeprazole based regimen. Patients with negative <sup>13</sup>C urea breath test (UBT) performed after 8 weeks of therapy, were followed up by the same test after 1 year.

**Findings:** Thirty seven patients, aged 5 to 17 years, were studied. Among them 25 (67.5 %) were boys. After eradication therapy of *H. pylori*, 34 patients had negative <sup>13</sup>C UBT. Reinfection occurred in 5 (14.7 %) patients. Reappearance or continuing symptoms after treatment were associated with higher rate of recurrence ( $P=0.042$ ).

**Conclusion:** Recurrence rate of *H. pylori* was high in our children. Successful eradication significantly decreased complaints and further symptoms. Follow up and reevaluation of patients is necessary especially when there are symptoms after eradication.

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**Key Words:** *Helicobacter Pylori*; Gastritis; Peptic Ulcer; Breath Test; Furazolidone; Omeprazole

### Introduction

*Helicobacter Pylori* (*H. pylori*) is the most important etiology of gastritis and peptic ulcer disease. The infection occurs more frequently in adults than in children<sup>[1]</sup>. Successful eradication of *H. pylori* reverses gastritis and significantly

reduces recurrence of peptic ulcer<sup>[2-5]</sup>. So in all patients with *H. pylori* peptic ulcer disease eradication therapy has been recommended.

*H. pylori* is the most common bacterial infection in the world. In developing countries acquisition of primary infection occurs

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predominantly in childhood<sup>[6,7]</sup>. However it can occurs in adults, as estimated 0.5-1% of the susceptible population become infected each year. Low socioeconomic level, poor hygienic conditions, sharing a bed, overcrowding, and having infected parents or siblings are risk factors for primary *H. pylori* infection<sup>[1,7-9]</sup>.

In adults reacquisition of bacteria is low especially in developed countries<sup>[10,11]</sup>. It has been hypothesized that the reinfection rates may be higher in children, in developing countries, and in those from low socioeconomic status<sup>[12,13]</sup>.

There are only a few reports on reinfection rate in children all over the world<sup>[13,17]</sup>. The purpose of this study was to determine the rate of *H. pylori* reinfection after successful eradication in children by <sup>13</sup>C UBT. Also to determine possible symptoms suggestive of reinfection, and the role of family and environment as risk factors of reinfection.

## Subjects and Methods

A total of 45 consecutive patients with *H. pylori* positive peptic disease, were treated between October 2006 and June 2007, of whom 37 patients took part in our study.

Upper gastrointestinal endoscopy was carried out after midazolam sedation in all patients. Gastric antral biopsy specimens were taken for histological examination, and urease test performed.

In accordance with other studies the presence of *H. pylori* in histology was accepted as diagnostic for infection<sup>[14]</sup>. *H. pylori* positive children were treated with a two-week course of amoxicillin (50 mg/kg/day) and furazolidone (6 mg/kg/day) divided into two doses per day plus omeprazole 1-2 mg/kg/day once daily. This medication continued eight to ten weeks and was discontinued after negative <sup>13</sup>C-UBT.

Children were included if they had negative <sup>13</sup>C-UBT result after 8 weeks of eradication therapy, indicating clearance of infection. Children with positive <sup>13</sup>C-UBT received a further course of two weeks with quadruple regimen, but were excluded from the study. Also

patients who had consumed antacids or antibiotics during 4 weeks prior to testing were excluded from study. The <sup>13</sup>C-UBT was performed after a fasting period of at least 6 hours. Children swallowed capsules containing urea labeled with <sup>13</sup>C and 20 minutes later, <sup>13</sup>C was measured in the expired air using infrared spectrophotometer (IRIS, Dr. Wagner, Bremen, Germany).

The difference between the values obtained at baseline and after 20 minutes was expressed as delta over baseline (DOB‰). The cut-off value for negative UBT was less than 2.5 and for positive UBT more than 4.0  $\delta$  units (delta over base)<sup>[14]</sup>.

Successfully treated children were reevaluated about 6 months and one year later for reinfection by UBT, and during this period all patients were observed for any appearing problem. The parents had been requested to call the responsible physician if children had any problem.

All children and family members were investigated for symptoms of peptic disease. These symptoms including epigastric pain or burning, nausea, vomiting, postprandial fullness, overflow, recurrent abdominal pain, and halitosis were recorded. To evaluate effectiveness of familial and environmental factors in reinfection we completed an epidemiologic questionnaire at the time of admission. The recorded demographic data included age, sex, age and number of siblings, parents' level of education, parents' occupation and crowding index.

Infection rates were calculated per patient year of follow up. Chi-square test or Fisher's exact test was used for qualitative variables and the Student t-test for quantitative variables. The influence of age and gender as risk factors was evaluated by using logistical regression models. Odds ratios with 95% confidence interval were computed by simple logistical regression analysis for each risk factor. SPSS software for Windows version 11 was used for processing of data. A *P*-value of less than 0.05 was considered significant.

In our center repeat <sup>13</sup>C-UBT is always recommended for children after eradication of *H. pylori*. Informed consent was obtained from

parents. The study was approved by the Ethics Committee of the Tehran University of Medical Sciences.

## Findings

Thirty-seven children (67.5% boys) were enrolled in the study. Two children were under 6 years, 27 children between 6-12 years, and 5 children more than 12 years old with a mean age of 10.2 years.

The endoscopic findings of the patients is shown in Table 1. In the first follow up 6 months after eradication therapy, <sup>13</sup>C-UBT was negative in 34 patients. Out of 34 patients, 5 cases (14.7%) had positive result in the second UBT test 12 months after eradication therapy. A reinfection rate of 14.7% per patient per year was calculated (Table 2).

In histology of all patients *H. pylori* was found in gastric antrum. The presence of bacterium was associated with chronic gastritis with variable degrees of activity. The mean age at treatment of baseline infection in reinfected children and not reinfected was 9 and 10.3 respectively ( $t=0.326$ ). Young age ( $P=0.6$ ) and male gender ( $P=0.73$ ) were not found to be a risk factor for reinfection.

In the group with re-infection 80% of patients complained of continuing of abdominal symptoms. None of these patients had duodenal ulcer at the initial diagnostic work up, so a second endoscopy was not necessary.

In the group without reinfection, occurrence of abdominal symptoms was 27.6 % ( $P=0.042$ ).

**Table 1:** Endoscopic findings in 37 patients with *H. pylori*

Endoscopic finding	No (%)
Normal	7 (18.9)
Nodularity	22 (73.3)
Gastric erythma	16 (53.3)
Duodenal ulcer	7 (23.3)
Gastric ulcer	0

**Table 2:** Response to therapy and reinfection rate in 37 patients)

Variable	No	Total percent	Variable percent
Without re-infection	29	78.4	85.3
Re-infection	5	13.5	14.7
Patient under study	34	91.9	100
No response to treatment	3	8.1	
All	37	100	

Sustained abdominal pain predicted probability of recurrence.

An epidemiologic questionnaire was completed for all children. The origin of the index child, number of siblings, or socioeconomic status were not associated with reinfection.

Bed sharing was seen in 60% of children with reinfection, and only in 27.7% of patients without reinfection, but because of the small population of patients with reinfection, it was not meaningful ( $P>0.05$ ). In all children with reinfection and in 44.8 % of children without reinfection ( $P=0.046$ ) a positive family history for *H. pylori* could be found.

Of 5 reinfected patients, parents of three (60%) gave consent for a second treatment. Eight weeks after completing treatment UBT was negative in all patients. Eradication was accompanied by resolution of symptoms. None of the reinfected children had endoscopic evidence of ulcer in their first endoscopy, so a second endoscopy was deemed not necessary.

## Discussion

Reinfection needs to be distinguished from eradication after failed therapy (recrudescence) with temporary suppression of the bacteria. By definition, reinfection means a new infection after the patient has been treated and infection successfully eradicated<sup>[5,13,15]</sup>.

The range of reinfection in adults is between 2.4-20% in different studies<sup>[10,11]</sup>. In developed countries the rate of reinfection is lower. Current reports indicate that reinfection rate is higher in children than in adults<sup>[12,13]</sup>. The reinfection rate reported in pediatric studies varies from 2% to 12.8% per patient year<sup>[13-17]</sup>.

Magista et al<sup>[13]</sup> clearly showed that living in an area of high prevalence for *H. pylori* increases the yearly risk of reinfection at least four times over areas in which the prevalence of *H. pylori* is low. In adults, studies from developing countries, where the base line prevalence rate is high, the recurrence rate is also high<sup>[18-21]</sup>. In a study from China<sup>[22]</sup> which also has a high prevalence of *H. pylori*, the reinfection rate was 1.08%.

In our study the rate of reinfection was 14.7% per patient per year. Iran is among the countries with high prevalence rate. There is only one report on reinfection rate in Iranian adults<sup>[23]</sup>. In this report the reinfection rate three years after successful eradication has been 20.5%.

Risk of reinfection is higher in younger children, especially in children younger than 7 years of age<sup>[13,16]</sup>. However two studies have shown that children can become reinfected later during childhood (age 10 years) and adolescence (age 14-16)<sup>[14,15]</sup>. In our study one of five reinfected children was less than 7 years old. There was no evidence that the reinfection rate depends on the age or sex. Increased prevalence rate of *H. pylori* within the families of reinfected children has been found ( $P=0.042$ ), suggesting that person to person spread from other family members is an important source of infection.

Numerous studies have shown that the risk of ulcer recurrence is markedly reduced after successful eradication of *H. pylori*<sup>[24,25]</sup>. In our study, 80% of patients with re-infection complained from persisting abdominal problems. None of these patients had duodenal ulcer at the initial diagnostic work up, so a second endoscopy was not necessary.

In the group without reinfection, occurrence of abdominal symptoms was 27.6 % ( $P=0.042$ ). So persisting abdominal symptoms predicted probability of recurrence.

In the study by Magista et al<sup>[13]</sup>, reinfected children had significantly more frequent digestive symptoms than non reinfected

children. The small number of children that were treated does not allow drawing conclusion, or the efficacy of re-treatment.

Eradication regimen used in our study consisted of omeprazole, with amoxicillin and furazolidone for two weeks. Success rate of eradication was about 91.9%. With respect to no report of serious side effects during treatment, we can suggest this protocol as an effective therapy for *H. pylori*. Since efficacy of treatment can efficiently decrease the rate of reinfection<sup>[20,26]</sup>, so the results have special consideration.

## Conclusion

The rate of reinfection is higher in developing countries and it is higher in children than in adults. Our results emphasize that only children with endoscopic proved *H. pylori* need to be treated. Reevaluating of the *H. pylori* status even after a successful eradication must be considered.

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**Conflict of Interest:** None

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