

# Gastroesophageal Reflux Disease and *Helicobacter pylori* in Children

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**Introduction:** The role of *Helicobacter pylori* in gastroesophageal reflux disease remains controversial, particularly in children, since there are limited published data. More than half of the world's population carries this infection. Infection rates vary among the developed and developing countries of the world.

The **aim** of our study was to determine the role of *Helicobacter pylori* infection in the development of gastroesophageal reflux disease in a pediatric population.

**Material and method:** We retrospectively reviewed medical records of patients hospitalized in the Two Pediatric Clinic Târgu-Mureș, Gastroenterology Department, from 2009 to 2010. We included in the study 376 children between 1 and 18 years with clinical symptoms (epigastric pain, vomiting, nausea, anorexia, loss weight) and the outcome of endoscopy confirmed the *Helicobacter pylori* gastritis and gastroesophageal reflux disease.

**Results:** Among the 376 patients, 55.05% were positive for *Helicobacter pylori* and 12.5% were found to have gastroesophageal reflux disease. The prevalence of gastroesophageal reflux disease in the *Helicobacter pylori* positive population was 11.6 % compared to 13.61 % in the *Helicobacter pylori* negative population ( $p > 0.05$ ). The biggest prevalence of this infection was in the 10–14 yrs age group (63.05%).

**Conclusions:** We found no significant difference in gastroesophageal reflux disease between children with and without *Helicobacter pylori* infection. Antral predominant nonatrophic gastritis is common in children.

**Keywords:** gastroesophageal reflux disease, *Helicobacter pylori*, children

## Introduction

Gastro-esophageal reflux disease (GERD) is defined as the involuntary passage of gastric contents into the esophagus. From a clinical point of view, the term “GERD” means a non-specific symptomatic complex, with a high variability between individuals.

Pathologic gastro-esophageal reflux is the consequence of several pathological digestive or extradigestive processes that disturb gastrointestinal motility. It is about a disease with a complex clinical presentation - there are patients with reflux esophagitis, with no symptoms, the disease is being proved endoscopically and/or histologically – but, there are also patients with clinical manifestations (digestive and/or extradigestive) with no reflux esophagitis. In order to better understand this disease with its multifactorial pathogenesis, the terminology to describe it, has undergone many changes. In pediatrics the term “GERD” is used [1].

According to a recent definition, we talk about the presence of GERD when gastro-esophageal reflux is symptomatic and there are complications related to tissue damages [2].

In newborns the following signs and symptoms occur: regurgitations, growth failure, reflux esophagitis, extradigestive manifestations: acute or chronic bouts of cough, aspiration pneumonia, stridor, dysphonia, recurrent wheezing. In older ages or in teenagers there are signs such

as: reflux esophagitis, broncho-obstructive crisis, chronic cough [1].

It seems that infection with *Helicobacter pylori* (*H. pylori*) would decrease the rate of GERD by reducing the gastric acid. On one hand the infection could foster the occurrence of severe gastric diseases, but on the other hand it could have a protective role against GERD [3]. In this way appeared the idea of *H. pylori*'s protective role against causing GERD or its aggravation.

The aim of this study was to assess potential relationships between *H. pylori* infection and GERD in pediatric patients.

## Material and method

A retrospective analysis of 376 patients (M : F = 147 : 229) who presented to the Gastroenterology Department of the Two Pediatric Clinic Târgu-Mureș between January 2009 and December 2010 was performed.

The including criteria were: a) patients with age between 0–18; b) clinical symptoms (epigastric pain, vomiting, nausea, anorexia, loss weight); c) the outcome of endoscopy that confirms the *H. pylori* gastritis and GERD.

The excluding criteria were: a) patients whose biopsies were unavailable for review by the pathologist; b) patients who refused endoscopy.

The selected subjects underwent physical examinations, their case histories were taken and personal ques-

Table I. General characteristics of the study population

Characteristics	Number of patients
Study population	N = 376 (%)
Age	
1–4 yrs	33 (8.8%)
5–9 yrs	117 (31.11%)
10–14 yrs	92 (24.46%)
> 14 yrs	134 (35.63%)
Gender	
Female	229 (61%)
Male	147 (39%)
Place of living	
Urban	188 (50%)
Rural	188 (50%)
H. pylori	
Positive	207 (55.05%)
Negative	169 (44.95%)
Clinical symptoms	
Epigastric pain	221 (58.77%)
Diffuse pain	100 (26.6%)
Persistent vomiting	62 (16.49%)
Nausea and vomiting	114 (30.32%)
Weight loss	57 (15.16%)
Pirois	34 (9.04%)
GERD	47 (12.5%)

tionnaires completed. The questionnaire data were sorted, systematized, processed using professional computer programmes.

The clinical indications for esophagogastroduodenoscopy (EGD) were as follows: abdominal pain- especially epigastric pain, persistent vomiting, nausea + vomiting, weight loss. Patient demographics, clinical indications for EGD and the prevalence of GERD, in two groups, H. pylori positive and H. pylori negative, were reviewed. Biopsy specimens were taken from the gastric antrum and distal esophagus during the procedure. A diagnosis of chronic gastritis was made on the basis of a neutrophilic infiltration of the glandular epithelium.

The prevalence of GERD in the H. pylori positive and H. pylori negative groups was further analyzed based on gender and age (1–4 yrs, 5–9 yrs, 10–14 yrs, ≥ 14yrs).

Table III. Comparison of study population GERD negative versus positive

Characteristics	GERD negative	GERD positive
	329	47
Age		
1–4 yrs	29 (87.87%)	4 (8.51%)
5–9 yrs	110 (94%)	7 (14.90%)
10–14 yrs	82 (89.13%)	10 (21.28%)
> 14 yrs	108 (80.6%)	26 (55.31%)
Gender		
Female	199 (86.9%)	30 (63.83%)
Male	130 (88.43%)	17 (36.17%)
Clinical symptoms		
Epigastric pain	189 (57.44%)	32 (68.08%)
Diffuse pain	89 (27.05%)	11 (23.40%)
Persistent vomiting	58 (17.63%)	4 (8.51%)
Nausea and vomiting	94 (28.57%)	20 (42.55%)
Weight loss	47 (14.28%)	10 (21.27%)

Table II. Comparison of study population H. pylori negative versus positive

Characteristics	H. pylori negative	H. pylori positive
	169 (44.95%)	207 (55.05%)
Age		
1–4 yrs	20 (11.83%)	13 (6.28%)
5–9 yrs	58 (34.32%)	59 (28.51%)
10–14 yrs	34 (20.12%)	58 (28.02%)
> 14 yrs	57 (33.73%)	77 (37.19%)
Gender		
Female	99 (58.58%)	130 (62.80%)
Male	70 (41.42%)	77 (37.20%)
Clinical symptoms		
Epigastric pain	92 (54.43%)	129 (62.32%)
Diffuse pain	58 (34.31%)	42 (20.29%)
Persistent vomiting	35 (20.71%)	27 (13.04%)
Nausea and vomiting	61 (36.09%)	53 (25.60%)
Weight loss	24 (14.20%)	33 (15.95%)

The Chi-square test and Fisher's exact test were used to evaluate the association between patients' demographic characteristics, H. pylori status, and GERD status. All statistical tests were two-sided and  $p < 0.05$  was considered statistically significant.

## Results

Using the above criteria for admission into the study, we analyzed medical records of 327 patients. Of all patients, 207 (55.05%) were positive for H. pylori and 47 (12.5%) were found to have GERD. In the studied group, females were predominant 229 (61%). The most frequent symptoms were: abdominal pain- especially epigastric pain (58.77%), diffuse pain (26.6%), nausea + vomiting (30.32%) (Table I).

The prevalence of H. pylori was lower in the 1–4 yrs age group (6.28%) and in the 5–14 yrs age group the prevalence of H. pylori was 28%. The biggest prevalence of this infection was in the oldest age (37.19%). Females were predominant 62.80%. There were no patients with H. pylori in the youngest age group (< 1 yr) (Table II).

The lower prevalence of GERD was in the youngest age group 8.51%, compared to the highest prevalence of 55.31% in the oldest age group (Table III).

Epigastric pain was the most common symptom, occurring in 58.77% of all the patients. Among 221 patients

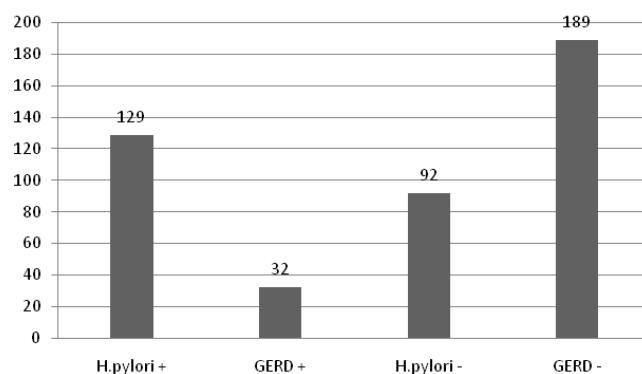


Fig. 1. Incidence of epigastric pain

**Table IV.** *H. pylori* and gastroesophageal reflux disease by age and gender

	GERD		p	OR
	positive	negative		
Age (1–10 yrs)	11	139	0.3544	1.992
H. pylori +	7 (4.66%)	65 (43.33%)		
H. pylori –	4 (2.66%)	74 (49.33%)		
Age (> 10 yrs)	36	190	0.09	0.5459
H. pylori +	17 (7.52%)	118 (52.21%)		
H. pylori –	19 (8.40%)	72 (31.85%)		
Male	17	130	0.6150	13.43
H. pylori +	10 (6.81%)	67 (45.57%)		
H. pylori –	7 (4.76%)	63 (42.85%)		
Female	30	199	0.2423	0.6261
H. pylori +	14 (6.11%)	116 (50.66%)		
H. pylori –	16 (6.99%)	83 (36.24%)		
H. pylori	47	329	0.6387	0.83
Positive	24 (6.38%)	183 (48.67%)		
Negative	23 (6.11%)	146 (38.82%)		

with epigastric pain, 129 (58.38%) of patients had *H. pylori* while 32 (14.48%) had GERD (Figure 1).

In this study, we report that the prevalence of GERD, between *H. pylori* positive patients was almost equal among *H. pylori* negative patients (6.38% vs. 6.11%). *Helicobacter pylori* positive patients had an odds ratio of 0.83 (CI = 0.4514–1.535) of developing GERD compared to *H. pylori* negative patients ( $p = 0.63$ ). In the 1–10 yrs age group, 4.66% of the *H. pylori* positive patients had GERD while 2.66% of the *H. pylori* negative patients had GERD ( $p > 0.05$ ). Both male and female patients with *H. pylori* had a lower prevalence of GERD, 6.81% and 6.11% respectively. In the >10 yrs age group, 7.52% of *H. pylori* positive patients had GERD while 8.40% of *H. pylori* negative patients presented GERD ( $p = 0.09$ ) (Table IV).

From the 207 patients with *H. Pylori*, 164 (79 %) had chronic gastritis, 37% of them being ( $n = 60$ ) in the antrum.

## Discussions

The overall incidence of GERD in pediatrics is estimated at 2–3%.

Upper digestive endoscopy represents the best method to prove the presence of GERD and its complications. In pediatrics there is not a perfect correlation between the endoscopic and histologic diagnosis of gastroesophageal reflux. This correlation can exist when obvious endoscopic lesions occur, but the existence of erythema or the pale color of the distal esophageal mucosa doesn't always show the histologic existence of esophagitis. On the other hand, a normal endoscopic aspect of the esophageal mucosa can hide the presence of gastroesophageal reflux that can be proved histologically. The lack of correlation between endoscopic and histological aspects, determined European and north-American experts to recommend the routine sampling of esophageal biopsy during the endoscopy at least when there are minimal endoscopic lesions and also

in case of a normal aspect mucosa in a symptomatic patient [2].

Labenz et al [4] who first reported in 1997 that there was an increased risk of development of GERD after *H. pylori* eradication, postulated a possible protective role of *H. pylori* infection.

However, several papers contradicted Labenz's findings showing that *H. pylori* eradication may not induce GERD symptoms in adults and in fact the infection may have no association.

*Helicobacter pylori* infection has been associated with a significantly reduced risk of developing GERD, Barrett's esophagus and esophageal adenocarcinoma in contrast to its increased risk for peptic ulcer disease and gastric cancer.

The relationship between *H. pylori* and gastroesophageal reflux disease has been controversial in published literature in the past decade. There are limited data regarding the relationship between *H. pylori* infection and GERD in the pediatric population. Levine et al [5] reported that eradication of *H. pylori* was not associated with increased symptoms of GERD in children. Pollet et al [6] found that *H. pylori* eradication did not provoke or worsen GERD in neurologically impaired children. Özçay et al [7] found no significant difference in reflux esophagitis between children with and without *H. pylori* infection while Daugule et al [8] showed a significantly higher prevalence of *H. pylori* in children with reflux esophagitis compared to children with hyperemic gastropathy.

Another study's results indicate that there is a significantly higher prevalence of reflux esophagitis in an *H. pylori* infected cohort independent of age or gender. *Helicobacter pylori* positive patients had an odds ratio of 5.79 (95% confidence interval 1.6–20.1) for having reflux esophagitis compared to *H. pylori* negative patients. Patients between 1–10 years and patients older than 10 years had odds ratios of 7.00 and 5.99 respectively of having reflux esophagitis compared to patients less than 1 year ( $p \leq 0.05$ ). Furthermore, male patients had an odds ratio of 1.84 of having reflux esophagitis compared to female patients ( $p \leq 0.05$ ). The findings suggest that *H. pylori* infection in children is positively associated with reflux esophagitis [9].

McColl et al [10] suggested that *H. pylori* infection might protect against GERD in infected patients who had atrophic gastritis and reduced gastric acid secretion.

There are studies that analyze the prevalence of GERD in children with or without chronic infection with *H. pylori* and according to these there are no significant differences concerning the existence of GERD in children with or without chronic gastritis with *H. pylori*, thus, there would not exist any support for the hypothesis of *H. pylori*'s possible protective role in GERD [11]. Longitudinal prospective studies have a valuable contribution, which show the changes in time of the clinical and paraclinical parameters; these studies do not report an increase of GERD's frequency in children after the eradication of *H. pylori* infection [1,6].

Antral predominant nonatrophic gastritis is more common in children while corpus predominant gastritis is more common in adults. Antral predominant nonatrophic gastritis causes increased acid secretion and in turn increases the risk of developing GERD and related complications including reflux esophagitis. Sixteen patients with *H. pylori* in our study had antral nonatrophic gastritis.

## Conclusions

1. The prevalence of *H. pylori* infection in children in Pediatric Department II Târgu-Mureş is 55,05%;
2. We found no significant difference in GERD between children with and without *H. pylori* infection;
3. Our data can not support the hypothesis of *H. pylori*'s protective role concerning the occurrence of GERD;
4. *Helicobacter pylori* appeared to not be a risk factor for GERD;
5. The limitations of our study include the fact that the data reflect a single clinical center.

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