

Does bile reflux reduce *Helicobacter pylori* gastritis?

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ABSTRACT

Background. Chronic abdominal pain is a frequent childhood complaint. This study aims to determine the relationship between bile reflux, which is increasing with the growth in packaged food consumption resulting from the changing food industry, and *Helicobacter pylori* gastritis.

Methods. In this retrospective study, 804 cases where there was an endoscopic examination for abdominal pain were included. We recorded the patients' age, sex, and macroscopic and microscopic endoscopic findings. Patients with chronic diseases were excluded.

Results. Our study included 804 cases. Of patients, 61.8% were female and 38.2% were male. The mean age was 11.56±4.14 years. The *Helicobacter pylori* gastritis rate was found to be 22.3% among all patients. Bile reflux was seen in 192 (23.9%) patients. Only 27 (14.1%) of the 192 patients had *Helicobacter pylori* positivity (p=0.002).

Conclusions. *Helicobacter pylori* gastritis is less common among patients with bile reflux. In another study conducted in our outpatient clinic before the 2000s, the frequency of *Helicobacter pylori* gastritis was found to be 40%, but after 2000 this rate decreased to 22.3% due to bile reflux caused by the changing food industry. This result may be explained by the bactericidal effects of bile acids.

Key words: bile reflux, gastritis, *Helicobacter pylori*.

Chronic abdominal pain is one of the most frequent complaints of childhood and adulthood. It is associated with poor quality of life and psychosocial deprivation.¹ Frequency ranges from 0.3-19% among school children and most of these cases have no organic pathology.^{2,3}

Helicobacter pylori (Hp) is a gram-negative bacteria colonizing the human stomach, and which can cause many gastrointestinal diseases.⁴ The prevalence of Hp varies worldwide and is affected by many factors such as age, ethnic group, and geographic and socioeconomic conditions.⁵ Most people are colonized with Hp in early childhood.⁴ Only 10-20% of these have the occurrence of gastroduodenal diseases.⁵

Although endoscopy is primarily recommended for the diagnosis of Hp infection, urea breath test, and fecal Hp antigen evaluation are non-invasive tests that can be used.⁶

Bile reflux occurs by retrograde bile movement to the stomach.⁷ Bile in the stomach causes clinical symptoms, endoscopically observed macroscopic changes, and histopathological chemical gastritis. There is no gold standard for the diagnosis of bile reflux.^{8,9} Bile reflux is divided into primary and secondary reflux. Primary bile reflux occurs without gastric surgery, while secondary bile reflux is usually seen after surgery. Bile bladder dysfunction, gastric, and duodenal dysmotility are risk factors for primary bile reflux.¹⁰ Bile is a strong alkali and causes chemical irritation to the gastric mucosa by changing the gastric pH balance. Bile acids have antibacterial action against Hp.¹¹ This study aims to determine the relationship between bile reflux and Hp gastritis

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and to show that bile reflux has increased due to the changing food industry and that this may have caused a decrease in Hp infection.

Material and Methods

Our study was retrospective, and data were taken from patients' files. Patients who applied to our pediatric gastroenterology clinic with abdominal pain and who were among the 804 cases that had undergone endoscopic examination between 2000-2019 were included. Patients with accompanying chronic diseases, alarm symptoms like diarrhea, bloody stool, growth retardation, persisting fever, elevated acute-phase reactant levels, and during follow-up, those who were diagnosed with Celiac disease and Familial Mediterranean Fever were excluded.

Diagnosis of bile reflux was made when we endoscopically observed bile in the stomach or detection retrograde bile flowed from the duodenum to the stomach. Patients with secondary bile reflux were excluded from the study.

We recorded the patients' age and sex and their macroscopic and microscopic endoscopic findings. The diagnosis of Hp infection was made by a positive rapid urease test or a positive culture result in addition to positive histopathology according to ESPGHAN guidelines.¹² At least 6 gastric biopsies (antrum and corpus) were taken for the diagnosis of Hp infection.

Statistical analysis

The statistical package for social sciences (SPSS) (Inc., Chicago, IL, USA, 22nd version) was used for data input and to analyze the demographic characteristics of the cases. Demographic characteristics were analyzed using basic definitive statistics. A Chi-square test was used to compare every 2 parameters (bile reflux and Hp infection). A p-value <0.05 was deemed statistically significant.

Clinical research ethics committee approval was received from the Ege University Ethics Committee (19-4T/44).

Results

In our study, 804 cases where all the data were included were enrolled. Of the patients 61.8% were female and 38.2% were male. The mean age was 11.56 ± 4.14 years. Microscopic and macroscopic analyses of the stomach are shown in Table I.

The number of patients where Hp was detected in the gastrointestinal system was 179 (22.3%). Among these 179 patients, 89 of them had chronic active mild gastritis, 59 of them had chronic active moderate gastritis, 13 of them had chronic active severe gastritis, 18 of them had chronic mild gastritis.

The prevalence of bile reflux was 23.9% (n=192). When evaluated according to age; bile reflux occurred in 14.2% in the 0-2 age group, 23.4% in the 3-6 age group, 19.4% in the 7-11 age group, and 27.0% in the ≥ 12 age group. Of these 192 cases with bile reflux, 108 of them had chronic mild gastritis, 69 of them had chronic active mild gastritis, 13 of them had chronic active moderate gastritis and 2 of them had chronic active severe gastritis microscopically. Only 27 (14.1%) patients had Hp positivity among the 192 patients where bile reflux was detected endoscopically (p=0.002) (Table II).

Discussion

Gastric histopathologic findings were normal in 41.7% of the patients in our study. According to another study that was carried out by Mark et al.¹³, 49.0% of 150 patients had normal histopathologic findings similar to our study. The reason for this may be the small tissue specimen taken during the endoscopic procedure, the involvement being patchy, or perhaps problems such as food allergies or psychosomatic disorders in these patients.

Table I. Microscopic and macroscopic findings of the stomach.

	Frequency (n)	Percent (%)
Macroscopic findings		
Normal	205	25.5
Bile reflux	192	23.8
Antral hyperemia	152	18.9
Antral nodularity	152	18.9
Pangastritis	94	11.7
Antral ulceration	9	1.2
Microscopic findings		
Normal	339	41.7
Chronic gastritis mild	201	24.8
Chronic active gastritis mild	181	22.4
Chronic active gastritis moderate	70	8.6
Chronic active gastritis severe	13	1.6

Table II. The relationship between bile reflux and Hp gastritis.

		Helicobacter pylori		Total	p-value
		Positive	Negative		
Bile reflux	Positive	27	165	192	0.002
	Negative	152	460	612	
Total		179	625	804	

Infections due to Hp, which has a commensal relationship with humans, are usually asymptomatic but may cause symptoms related to peptic ulcer or duodenal inflammation in some individuals.^{4,5} In developing countries, school children are at risk due to low socioeconomic conditions, poor hygienic drinking water, living in crowded conditions, low personal and environmental hygiene, and food contamination.^{14,15}

Hp infection frequency is higher in developing countries than in developed countries.⁵ In our study, Hp infection frequency was 22.3%. In Africa, this ratio is between 40-90%.¹⁶⁻¹⁹ According to Hunt et al.²⁰, while among Ethiopian children between the ages of 10-15 the Hp infection prevalence was 82%, this ratio was between 70-90% in adults.²¹ It was noted that in Canada, Hp infection had a ratio of 7.1% in children in the age range of 5-18.⁵ This variability maybe because of the different

levels of development of these countries. In a local study carried out by Gürakan et al.²¹, Hp infection frequency was found to be 52.5%. The decrease in Hp infection after the 2000s was probably a result of the adverse effects of the preservatives and unhealthy oils used in the food industry on bowel movements, and the increase in the use of macrolide group antibiotics may also explain this situation.

Bile reflux was first described in a patient with gastrocutaneous fistula in 1833 and it was perceived as an important problem.²² Bile reflux without gastric surgery is called primary bile reflux. The risk factors are gallbladder dysfunction, gastric, and duodenal dysmotility. Due to the decrement of migrating complex motor gastric exposure activity to bile, this causes chemical gastritis and clinical symptoms. The prevalence of bile reflux is unknown.¹⁰ Radev et al.²³ found bile reflux prevalence as 10% in adults. According to Slavesku et al.²⁴,

among children with atrophic gastritis, bile reflux prevalence was found to be 34%. In our study, it was found to be 23.9%. These different ratios may be because of different patient populations. Bile as a strong detergent causes gastric mucosal injury. Histopathologic antral foveolar hyperplasia, vascular congestion, edema in lamina propria, and smooth muscle leave and inflammatory cell shortage can be seen.²⁵ In our study, 108 of them had chronic mild gastritis, 69 of them had chronic active mild gastritis, 13 of them had chronic active moderate gastritis and 2 of them had chronic active severe gastritis microscopically. Gastritis was detected microscopically in all patients with bile reflux. Only 14.1% of patients had Hp positivity among patients with bile reflux ($p=0.002$). This may be since bile acids have antibacterial activity against Hp.

The changing food industry may have caused a decrease in Hp infections after the 2000s, due to an increase in bile reflux. The increase in the consumption of cheaper and easily accessible take-home foods over time may have caused a decrease in the consumption of healthy foods. Among these unhealthy products, the poor quality high-fat ratio may cause bile reflux by slowing gastric emptying and causing the release of cholecystokinin, with a negative effect on gastrointestinal system motility.^{26,27} Therefore, while Hp gastritis is investigated in the differential diagnosis of patients with abdominal pain, bile reflux should be included in the differential diagnosis and treatment should be planned accordingly.

Ethical approval

Ethics committee approval statement was received from Ege University Ethics Committee in 2019 (19-4T/44).

Author contribution

The authors contribute to the paper as follows: study conception and design: SA, EKT; data

collection: FÇ, MS; analysis and interpretation of results: BD, MK; draft manuscript preparation: EKT, MK, FÇ. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

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