

Reflux Esophagitis in *Helicobacter pylori* Positive and Negative Armenian Children with Recurrent Abdominal Pain and Dyspepsia

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Introduction

Gastroesophageal reflux disease (GERD) is defined as gastroesophageal reflux (GER) which leads to generation of troublesome symptoms and/or complications, such as esophagitis or stricturing. Reported symptoms of GERD vary and for older children may include typical adult symptoms such as heartburn and regurgitation. Other common symptoms are abdominal and/or chest pain, vomiting, respiratory manifestations such as chronic cough, sore throat, hoarseness and/or laryngitis [11].

The role of *Helicobacter pylori* (Hp) in development of reflux esophagitis is disputable. The protective influence of Hp infection for GERD was first reported by Labenz in 1997 [7], when an increased risk of development of GERD after *H. pylori* eradication was found. The suggested protective mechanism was reduced gastric secretion in Hp associated atrophic gastritis [6,8]. Other publications did not support these finding and any association between Hp and GERD [12].

In pediatric population there are limited data on the relationship between *H. pylori* infection and GERD. The available studies mainly indicate that Hp may aggravate GERD symptoms in children and eradication of HP does not play a major role in GERD symptoms [9].

The aim of our study was to evaluate clinical, endoscopic and histological findings of reflux esophagitis in Hp positive (Hp+) and negative (Hp-) Armenian children with recurrent abdominal pain (RAP) and /or dyspepsia.

Material and Methods

230 patients referred to the “Arabkir” Medical Complex - Institute of Child and Adolescent Health (“Arabkir” MC-ICAH), for recurrent abdominal pain and /or dyspepsia were involved in the study. Inclusion criteria were: children and adolescents aged 2-18 years with recurrent abdominal pain and/or dyspeptic symptoms, underwent upper endoscopy. Exclusion criteria were: Familial Mediterranean fever, Coeliac disease, the use of non-steroidal anti-inflammatory and proton pump inhibitors up to 2 weeks and the use of antibiotics up to 4 weeks prior to investigation.

One hundred fifty patients aged 2-18 years (70 males and 80 females, mean age 9.2 ± 3.9 years) were selected for the study. Thirty-six patients with endoscopic and/or histological signs of reflux esophagitis were involved in the study.

Specially developed questionnaire was used for structured collection of anamnestic and clinical data. Patients signed consent form for study enrolment approved by the Ethics Committee of Yerevan State Medical University (2016).

All patients underwent esophagogastroduodenoscopy (EGDS) with biopsies under general anesthesia with 4 biopsies by video-endoscopes Olympus GIF-XP170N and Olympus GIF-H170: two from the antrum, one from the duodenal bulb and one from the distal esophagus. Endoscopic grading of reflux esophagitis was done according to the Los Angeles classification of GERD. Rapid urease test (Hepyl test, Association of Medicine and Analytics, Russian Federation, <http://www.amamed.ru/index.php?i=7>) was done in one of antral biopsy specimen. One of the antral biopsies was cultured in Hp selective media (Chrom ID, Biomerieux, France) and Columbia agar with 5% sheep blood (Biomerieux, France).

Histological examination of all biopsy specimens was performed by one histologist; tissues were stained by hematoxylin-eosin and assessed according to updated Sydney system [5]. Gastric and duodenal biopsy specimens were stained by modified Giemsa staining for *Helicobacter pylori* infection. Histologically reflux esophagitis was defined as basal cell hyperplasia, papillary elongation, dilation of intercellular spaces, and inflammatory infiltration [13].

The Statistical Package for Social Science (SPSS version 20) program was used for data analysis. Bivariate analysis was carried out by using the chi-square for comparing categorical variables. A p value ≤ 0.05 and two tailed Fisher exact coefficient value ≤ 0.05 were considered significant.

Results and Discussion

150 patients with RAP and/or dyspepsia were involved in the study: Hp was positive in 106 (70.7%) and negative in 44 (29.3%) of them. Reflux esophagitis was diagnosed in 36 (24%) of patients from 150 patients: in 28

(26.4%) Hp positive and 8 (18.2%) Hp negative patients, $RR=1.12$, $p=0.11$ (Fig. 1).

We have noticed that esophagitis was more frequent in Hp negative children aged 2-10 years, and Hp positive children aged 11-17y, although this observation was not statistically significant (Fig. 2, Table 1).

Table 1

Esophagitis distribution by age groups and Hp status

Age	Hp+	%	Hp-	%	Total	F
02-05 y	7	25	4	50	11	$F>0.05$
06-10 y	6	21.4	1	12.5	7	$F>0.05$
11-14 y	8	28.6	2	25	10	$F>0.05$
15-17 y	7	25	1	12.5	8	$F>0.05$
Total	28	100	8	100	36	

Symptoms

Nausea was statistically significant more common symptom for Hp+ group ($F=0.03$). Other symptoms such as vomiting ($F=0.53$), regurgitation ($F=0.53$), abdominal pain ($F=0.66$), night time pain ($F=0.7$), and even dysphagia ($F=0.7$) were not statistically significant in our cohort of patients (Table 2, Fig. 3).

Table 2

Symptoms in Hp+ and Hp - patients with esophagitis

Symptom	Hp+	%	Hp-	%	Total	F
Nausea	22	78.8	3	37.5	25	$F 0.03$
Heartburn	5	17.8	2	25	7	$F 0.5$
Vomiting	9	32.1	2	25	11	$F 0.53$
Regurgitation	6	21.4	4	50	10	$F 0.13$
Abdominal pain	21	75	6	75	27	$F 0.66$
Night time pain	4	14.3	1	12.5	5	$F 0.7$
Dysphagia	1	4.5	1	12.5	2	$F 0.4$

Endoscopic findings in the esophagus

In 9 patients (25%) reflux esophagitis was seen macroscopically during endoscopy: in 6 (5.6%) Hp positive and 3 (6.8%) Hp negative patients (Table 3, Fig. 4). All esophagitis recognized by EGDS were of Grade A, but 1 of Grade B

in an Hp positive patient. There was no statistically significant difference in the endoscopic grade of esophagitis in Hp positive and negative patients ($F>0.05$).

Table 3
Endoscopic findings in the esophagus in Hp+ and Hp- patients with esophagitis

EGD esophagus	Hp+	%	Hp-	%	Total	F
Normal	22	78.6	5	62.5	27	$F>0.05$
Grade A	5	17.8	3	37.5	8	$F>0.05$
Grade B	1	3.6	0	0	1	$F>0.05$
Total	28		8		36	

Endoscopic findings in the stomach

Endoscopic findings in the stomach of the HP+ and Hp- patients with esophagitis were: normal appearing mucosa in 1 (3.6%) and 1 (12.5%), superficial gastritis in 18 (64.3%) and 5 (62.5%), erosive gastritis in 7 (25%) and 2 (25%). There was no statistically significant difference in the severity of gastritis and esophagitis in Hp+ and Hp- patients (Table 4, Fig. 5).

Table 4
Endoscopic findings in the stomach in Hp+ and Hp- patients with esophagitis

EGD stomach	Hp+	%	Hp-	%	Total	F
Normal	1	3.6	1	12.5	2	$F>0.05$
Hyperemia	18	64.3	5	62.5	23	$F>0.05$
Erosions	7	25	2	25	9	$F>0.05$
Nodularity	2	7.1	0	0	2	$F>0.05$
Total	28		8		36	

Histology

In our cohort of patients with RAP and dyspepsia, reflux esophagitis was only a histological finding in the majority of the patients 27 (75%): 22 (20.7%) in Hp positive and 5 (11.3%) Hp negative (Fig. 6).

Histological spectrum of the findings in the Hp positive and negative groups were: acute esophagitis in 1 (0.9%) and 1 (2.3%), chronic esophagitis in 21 (23%) and 5 (11.4%), normal mucosa in 6 (5.6%) and 3 (6.8%). There was no statistically significant difference in grade or type of esophagitis in our Hp+ and Hp- patients. However, histologically normal mucosa of the esophagus was statistically more commonly seen ($F=0.001$) in Hp- patients (Table 5, Fig. 7).

Table 5

Histological spectrum of findings in patients with esophagitis

EGD esophagus	Hp+	%	Hp-	%	F
Normal	3	6.8	6	5.6	F=0.001
Acute esophagitis	1	0.9	1	2.3	F>0.05
Chronic esophagitis	21	23	5	11.4	F>0.05

No statistical difference (F>0.05) in development of esophagitis was found in the type of gastritis in Hp+ patients (Table 6).

Table 6

Histological type of gastritis in Hp+ patients with esophagitis

Histology	With esophagitis	%	Without esophagitis	%	Total	F
Normal mucosa	4	3.8	7	6.6	11	F>0.05
Chronic non-active gastritis	23	21.7	62	58.5	85	F>0.05
Chronic active gastritis	1	0.9	9	8.5	10	F>0.05

However, esophagitis was statistically less common (F=0.05) in Hp- patients with histologically normal gastric mucosa (Table 7).

Table 7

Esophagitis and histological type of gastritis in Hp- patients

Histology	With esophagitis	%	Without esophagitis	%	Total	F
Normal mucosa	1	2.3	18	40.9	19	F=0.05
Chronic non-active gastritis	7	15.9	18	40.9	25	F=0.05
Chronic active gastritis	0	0	0	0	0	0

Classical symptoms of reflux esophagitis in children are well known and described [11]. Our cohort of patients was mainly presented by school age children and adolescents. Interestingly that majority of the investigated patients complained of nausea 25 (69.4%, p=0.0009). The frequency of other, more specific for esophagitis, symptoms such as vomiting (F=0.53), regurgitation (F=0.53), abdominal pain (F=0.66), heartburn (F=0.5) and even dysphagia (F=0.7) was not statistically significant in our cohort of patients.

According to some literature data, Hp infection could contribute to reflux esophagitis through both a protective and damaging influence and depending on the type of gastritis related to Hp. Acid secretion may either increase or decrease gastritis in corpus leads to hypoacidity, while antrum gastritis leads to

hyperacidity [9]. During childhood, Hp is associated with antral predominant gastritis and duodenal ulcers [4], so it might lead to increased incidence of esophagitis. Some authors were showing twice higher rate of esophagitis in Hp+ in comparison to Hp- ones [1]. However, in our cohort of patients despite of higher frequency of esophagitis in Hp+ ones (26.4% vs 18.2%), difference was not statistically significant. No difference on type gastritis and severity of esophagitis was noticed, nevertheless, normal esophageal mucosa was most commonly seen in Hp- negative patients without gastritis ($F=0.05$).

It is well known that normal endoscopy does not necessarily rule out the possibility of GERD [11]. At the same time histologic esophagitis is generally viewed as having limited value in diagnosing GERD in children [2]. Histologic esophagitis occurs frequently in patients with abdominal pain, particularly with functional dyspepsia, however, its relationship to functional dyspepsia (FD) is not well studied. Some authors consider GERD to be a part of the FD complex [1,10].

In our cohort of patients with RAP and dyspepsia EGDS showed presence of esophagitis in minority of them (9 patients, 25%). No statistically significant difference was found in patients with erosive/ ulcerative or superficial lesions and superficial lesions of the stomach and endoscopic grade of esophagitis. In most of the patients with RAP and/or dyspepsia and reflux esophagitis it was histological finding in 27 (75%). There was no statistical difference in the grade or type of histological changes in the esophagus in Hp+ and Hp- group of our patients. Similar data was shown by other authors [1,9].

Conclusion

Reflux esophagitis was observed in 24% in all investigated Armenian children with RAP and dyspepsia. Among Hp positive patients (70.7%) reflux esophagitis made 26.4%, although this observation was not statistically significant in comparison to Hp negative patients (18.2%). Esophagitis was statistically less common ($F=0.05$) in Hp- patients with histologically normal gastric mucosa.

Main complaint in pediatric patients with RAP and dyspepsia and reflux esophagitis was nausea (69.4%). Other dyspeptic symptoms such as vomiting (30.5%), regurgitation (27.7%), heartburn (19.4%) and dysphagia (5.5%) were observed comparatively rare.

Reflux esophagitis in majority of the pediatric Armenian patients with RAP and dyspepsia (75%) was the only histological finding.

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Рефлюкс-эзофагит у *Helicobacter pylori* положительных и отрицательных детей армянской национальности с возвратными болями в животе и диспепсией

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Целью данного исследования было оценить клинические, эндоскопические и гистологические особенности рефлюкс-эзофагита у *Helicobacter pylori* положительных (Нр+) и отрицательных (Нр-) детей с возвратными болями в животе (ВБЖ) и / или диспепсией. Рефлюкс-эзофагит наблюдался у 24% исследованных пациентов с ВБЖ и диспепсией. Среди Нр+ пациентов (70.7%) рефлюкс-эзофагит составил 26.4%, хотя это наблюдение не было статистически значимым по сравнению с Нр-пациентами (18.2%). Основным симптомом у детей с рефлюкс-эзофагитом была тошнота (69,4%). Другие диспепсические симптомы, такие как рвота (30.5%), регургитация (27.7%), изжога (19.4%) и дисфагия (5.5%), наблюдались сравнительно редко. У большинства пациентов (75%) рефлюкс-эзофагит был только гистологической находкой.

Ռեֆլյուքս էզոֆագիտը կրկնվող որովայնացավերով և դիսպեպսիայով *Helicobacter pylori* դրական և բացասական հայազգի երեխաների շրջանում

Տ. Շահինյան, Գ. Ամարյան, Բ. Բրեգեր

Հետազոտության նպատակն է գնահատել ռեֆլյուքս էզոֆագիտի կլինիկական, էնդոսկոպիկ և հիստոլոգիական առանձնահատկությունները կրկնվող որովայնացավով և կամ դիսպեպսիայով *Helicobacter pylori* (Нр) դրական և բացասական երեխաների շրջանում: Ռեֆլյուքս էզոֆագիտը դիտվել է կրկնվող որովայնացավով և կամ դիսպեպսիայով հետազոտված հայազգի երեխաների 24%-ի մոտ: Нр դրական հիվանդների շրջանում (70.7%) ռեֆլյուքս էզոֆագիտը կազմել է 26.4%: Այս դիտարկումը վիճակագրորեն նշանակալի չէ *Helicobacter pylori* բացասական պացիենտների համեմատությամբ (18.2%): Ռեֆլյուքս էզոֆագիտով հիվանդ երեխաների հիմնական զանգատը սրբութառնոցն է (69.4%): Համեմատաբար հազվադեպ են դիսպեպսիկ այլ ախտանշանները՝ փսխում (30.5%), ռեգուրտացիա (27.7%), այրոց (19.4%) և դիսֆագիա (5.5%): Կրկնվող որովայնացավերով և կամ դիսպեպսիայով հիվանդ երեխաների մեծամասնության մոտ (75%)

ռեֆլյուքս էզոֆագիտը հայտնաբերվել է միայն հյուսվածքաբանական հետազոտությամբ:

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