Clinical Endoscopic and Histological Characteristics of Helicobacter Pylori Positive and Negative Armenian Children with Recurrent Abdominal Pain and/or Dyspepsia

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Abstract

Background

Recurrent abdominal pain (RAP) and dyspepsia are common complaints in children. These symptoms are often associated with *Helicobacter pylori* (Hp) infection. Aim of the present study was to prospectively analyze clinical, endoscopic and histological characteristics of Hp+ and Hp- children with RAP and/or dyspepsia.

Methods

Patients aged 2-18 years with RAP and/or dyspepsia, referred for upper endoscopy to Arabkir MC from November 2015 to December 2017, were involved in the study. Histology was assessed according to the updated Sydney system. Gastric and duodenal specimens were stained by modified Giemsa staining for Hp infection. One antral biopsy was cultured in Hp selective media.

Results

150 patients were included into the study: 70.7% Hp+, 29.3% Hp-. Nausea and vomiting were significantly more common in Hp+ patients ($p < 0.05$). Gastric nodularity ($p = 0.02$), erosions in the stomach ($p = 0.056$), and duodenal erosions ($p = 0.019$) were more common in Hp+. Chronic active ($p = 0.027$) and non-active gastritis ($p = 0.002$), cumulative findings of metaplasia/dysplasia/atrophy in the stomach ($p = 0.014$) and chronic non-active duodenitis ($p = 0.016$), were significantly more common in Hp+ patients.

Conclusion

Hp infection prevalence is high in Armenian children with dyspepsia and/or RAP. Clinical symptoms, endoscopic findings and histopathological findings were significantly different in Hp+ patients as compared to Hp- patients.

Introduction

Currently *Helicobacter pylori* (Hp) infection is a leading cause of inflammatory and malignant diseases of the upper gastrointestinal tract [1, 2, 3, 4].

Prevalence of Hp infection differs and depends on age, geographical, socio-economical, ethnical and other factors [1, 5]. In developing countries it reaches 70%, and younger ages are more commonly affected [2, 3].

Hp infection is usually acquired during the first years of life in both developing and developed countries. In children it is mainly manifests as gastritis and duodenitis (up to 90–95%). Peptic ulcer disease (PUD) is observed approximately in 5% of children younger than 12 years and in 10% older than 12 years. Gastric malignancies associated with Hp are very rare in the paediatric age group [4, 6, 7, 8].

Armenia is a country with high incidence of peptic ulcer of stomach and duodenum in patients older than 15 years (100.3/100.000 and 468.2/100.000 respectively in 2018). Penetrating ulcers make 4.08–4.1/100.000. There is also high prevalence of stomach cancer in the adult population (57.7%) [9]. Although there is no data on prevalence of Hp infection among children, and limited data in adults in Armenia [10], high level of Hp infection prevalence is assumed in Armenian children.

Hp eradication therapy aims to prevent complications such as bleeding and penetrating ulcers as well as gastric malignancies. A limiting factor for the treatment success is antibiotic resistance, which differs in developed and developing countries and depends on the spectrum of antibiotic use [11].

Aim Of The Study

Aim of the present study is to prospectively analyze clinical, endoscopic and histological characteristics of Hp positive and negative Armenian children with recurrent abdominal pain and/or dyspeptic symptoms.

Methods

230 patients referred to Arabkir MC from November 2015 to December 2017 for upper endoscopy because of recurrent abdominal pain and/or dyspeptic symptoms were involved in the study.

Inclusion criteria were: children and adolescents aged 2–18 years with RAP and/or dyspeptic symptoms, undergoing upper endoscopy.

Exclusion criteria were: Familial Mediterranean fever, coeliac disease, use of non-steroidal anti-inflammatory drugs or proton pump inhibitors up to 2 weeks and antibiotics up to 4 weeks prior to investigation.

A questionnaire was developed for structured collection of the patients history and clinical data. Patients signed a consent form for study which was approved by the Ethics Committee of Yerevan State Medical University (2016). History included information about personal details, family members suffering from GDD, gastric malignancies in the family as well as data on, main complaints, disease onset and eradication treatment before. We included data of 1st and 2nd line relatives suffering from GDD and/or gastric cancer taking into consideration peculiarities of Armenian society - common living with them

All patients underwent esophagogastroduodenoscopy (EGD) under general anesthesia with 4 biopsies by Olympus GIF-XP170N and Olympus GIF-H170 endoscopes. Two biopsies were taken from the antrum (one for rapid urease test and histology, one for Hp culture), one from the duodenal bulb and one from the distal esophagus. We used the rapid urease test Helpyl (Association of Medicine and Analytics, Russian Federation, <http://www.amamed.ru/index.php?i=7>). Histology was assessed according to the updated Sydney system (20). Gastric and duodenal specimens were stained by modified Giemsa staining for Hp infection. One of the antral biopsies was cultured in Hp selective media (ChromID, Biomerieux, France) and Columbia agar with 5% sheep blood (Biomerieux, France).

Patients were divided into 2 groups:

The first group were patients Hp + by 2 invasive tests. This group was divided in 2 subgroups: subgroup 1 were patients with ulcers, and/or erosions, and/or nodularity in the stomach or duodenum; subgroup 2 were patients with normal appearing mucosa of stomach and duodenum or only superficial changes.

The second group were Hp- patients by 2 invasive tests.

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

150 patients were included into the study: 106 patients were positive for Hp testing by two invasive tests: 50 males, 56 females, aged 2–18 years (mean age 9.67 ± 0.37 years). 44 patients were Hp negative: 20 males, 24 females, aged 2-18y, mean age 8.13 ± 0.58).

Preschool children aged 2-5y made 15 (14.2%) of the Hp + group, 6-10y old children 48 (45.2%), 11-14y old children 31 (29.2%), and 15-17y old adolescents 12 (11.3%).

Distribution of gender in the groups was: Hp + male/female 50/56 and Hp- 56/24, shown in the Fig. 2, there was no statistically significant difference between gender concerning Hp presence ($p > 0.05$)

Comparative analysis of number of Hp + patients from urban area (capital Yerevan and regional towns) and country side did not show any statistical difference in distribution of Hp (Fig. 3).

Clinical Data Comparison

Gastric cancer was not significantly more common in families of Hp + patients ($F = 1$), however most of the family members of Hp + group had dyspeptic symptoms and/or abdominal pain, but were not investigated ($F = 0.001$) (Table 1).

The most common symptoms in both groups were recurrent epigastric pain, nausea and vomiting. Distribution of symptoms in the two groups is shown in Table 2. Nausea and vomiting were significantly more common in Hp + patients ($p < 0.05$).

When we have compared 2 subgroups in the Hp + group divided by the severity of endoscopic changes, Regurgitation and night time pain were significantly more common in Hp + patients with stomach and duodenal ulcerative and aphthous erosive lesions (Table 3).

Analysis of endoscopic data has shown that gastric nodularity, erosions in the stomach, erosive lesions in the duodenum are significantly more common in Hp + compared to Hp- patients (Table 4). Besides of 7 Hp+ (15.9%) patients, 2 (4.5%) of Hp- patients had ulcers in the stomach and duodenum.

Histological data comparison showed that chronic active 10 (9.4%) and non-active gastritis 85 (80.2%), chronic non-active duodenitis 49 (46.2%) and cumulative findings of metaplasia/ dysplasia/atrophy in the stomach 10 (9.4%) are statistically more common histologic signs of Hp infection in Armenian children (Table 5).

The comparison of significant histologic changes in Hp + patients with superficial and ulcerative/erosive lesions did not show any statistical difference (Table 6) ($p > 0.05$).

Discussion

This is the first study assessing clinical, endoscopic and histological characteristics of Hp + and Hp- Armenian children with recurrent abdominal pain and/or dyspepsia.

Prevalence of Hp in symptomatic children differs from country to country: 34.6% in Ethiopia (15), 25% in Hong Kong (14), 24.5% in Bulgaria (13), 64.6% in Egypt (16). The prevalence is mainly depending on socio-economic status and number of family members. There is only one study assessing seroprevalence of Hp infection in symptomatic adults with dyspeptic symptoms in Armenia showing of 49% being positive [10]. In our cohort of patients with recurrent abdominal pain and/or dyspepsia *Helicobacter pylori* was diagnosed in 70.6%. This high prevalence might be explained by the fact of acquiring infection in the childhood, developing status of Armenia and intrafamilial distribution of infection (high number of family members with gastritis, PUD and dyspeptic symptoms).

There are different concepts on decision of making endoscopy in pediatric patients with repeated or chronic abdominal pain and dyspepsia. Hyams JS et al. found that duration of vomiting and other dyspeptic symptoms more than 1 year were risk factors for mucosal inflammation of upper GI tract [12]. Other study suggested importance of EGD in patients with symptom duration more than 6 months, severe symptoms affecting sleep and family history of peptic ulcer disease or Hp infection [22].

Our patients were referred to medical attention with symptoms persisting median more than a year in both groups. According to the current literature data, there is no significant difference in symptoms of Hp positive vs Hp negative children shown in symptomatic pediatric population [13, 14, 15, 16]. In contrast to published studies from other countries our study showed that night time abdominal pain and regurgitation were statistically more common in Hp + children with PUD and/or aphthous lesions in the upper GI tract.

Antral nodularity is one of the signs of Hp associated gastritis and maybe associated with higher grade of gastritis in children [23, 25, 26]. According to our data erosive lesions in the stomach and duodenum were statistically more common endoscopic findings in Hp + patients, gastric nodularity were exclusively found in Hp + group.

Low incidence of ulcers in Hp positive children was reported in Chinese [17] 7.2% and European (6.8%) pediatric patients [4]. In contrast to it, in developing countries PUD prevalence in Hp positive children reaches 33.2% [18, 19]. Our study showed low incidence of PUD in Hp + Armenian children, which might be explained by treatment received before admission. 2 Hp - patients had ulcers, probably due to GI bleeding or false negative Hp test.

Hp infection has been reported was significantly associated with chronic (88.5%) and active (63%) gastritis [23]. Data obtained by Canan O. et al, showed that in two third of the patients with nonorganic dyspepsia had normal histological data, while one third had mild or chronic non-active inflammation of the mucosa [20]. Similarly in our cohort of patients the main histological findings in Hp + patients were chronic active and non-active gastritis and duodenitis, while in Hp- patients mainly histologically normal mucosa was seen. Nevertheless more than half of Hp- negative patients had chronic non-active inflammation in the stomach.

Our study showed that serious histologic changes were exclusively seen Hp + children, and equally observed in both patients with ulcerative/aphthous and superficial changes. This is contrast with the review analyzing atrophy and intestinal metaplasia in children, where different rates are mentioned and this changes are not always connected with Hp infection [24].

Conclusion

Hp prevalence is high in Armenian children with dyspepsia and/or recurrent abdominal pain (70.6%). Nausea and vomiting are significantly more common in Hp + patients ($p < 0.05$), while in patients having night time pain and regurgitation, ulcerative and/or erosive lesion by EGDS are observed more likely. Significant histological changes of the mucosa of the stomach such as atrophy, metaplasia or dysplasia were only observed in Hp + patients. However, histologic changes do not correlate with the severity of the endoscopic findings.

Abbreviations

GDD – gastroduodenal disease

Hp - Helicobacter pylori

Hp- - Helicobacter pylori negative

Hp+ - Helicobacter pylori positive

RAP - Recurrent abdominal pain

PUD – Peptic ulcer disease

Declarations

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Conflicts of interest/Competing interests: The authors declare that they have no conflict of interest.

Ethics approval: This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Yerevan State Medical University Named after Mkhitar Heratsi (Date 19.12.2017 /No. 4).

Consent to participate: Informed consent was obtained from the parents.

Consent for publication: N/A

Availability of data and material: All data and materials as are available in electronical database and could be shared upon request.

Code availability: N/A

Authors' contributions: All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Tatevik Shahinyan, Artashes Tadevosyan, Gayane Amaryan and Christian Braegger. The first draft of the manuscript was written by Tatevik Shahinyan and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1
Family history

Relatives	HP+	%	HP-	%	Odds Ratio	CI	p
Cancer	3	2.8	1	2.3	1.26	0.13–12.38	F = 1
PUD	20	18.7	4	9	2.32	0.75–7.25	F > 0.05
GD	23	21.7	5	11.4	2.16	0.76–6.11	p > 0.05
Symptoms	36	34	4	9	5.1	1.71–15.51	F = 0.001*
Total	82	70.7	14	29.3	7.32	3.35–15.98	F = 0.000*
*statistically significant observation							

Table 2
Symptoms

	Total	%	HP+	%	HP-	%	OR	CI	p
Nausea	78	52.0%	60	56.6%	18	40.9%	1.88	1.001–4.015	p < 0.05*
Vomiting	39	26.0%	29	27.4%	10	22.7%	1.28	0.56–2.92	p > 0.05
Dysphagia	2	1.3%	1	0.9%	1	2.3%	0.41	0.03–6.70	p > 0.05
Regurgitation	31	20.7%	22	20.8%	9	20.5%	1.02	0.43–2.43	p > 0.05
Heartburn	18	12.0%	16	15.1%	2	4.5%	3.71	0.82–16.98	p < 0.05*
Abdominal pain	123	82.0%	87	82.1%	36	81.8%	1.02	0.41–2.54	p > 0.05
Halitosis	17	11.3%	12	11.3%	5	11.4%	1	0.33–3.02	p > 0.05
Night time pain	17	11.3%	13	12.3%	4	9.1%	1.39	0.43–4.55	p > 0.05
Melena	3	2.0%	3	2.8%	0	0.0%	-1	N/A	p > 0.05
Constipation	20	13.3%	13	12.3%	7	15.9%	0.74	0.27-2.00	p > 0.05

Table 3
Symptoms: comparison of endoscopic Hp + group subgroups

Complaint	All patients		Endoscopic ulcer/ aphthous erosions/nodular		Superficial changes / normal mucosa		
Total	(106)	100%	(59)	100%	(47)	100%	
Nausea	60	56.6%	35	59.3%	25	53.2%	p > 0.05
Vomiting	29	27.4%	18	30.5%	11	23.4%	p > 0.05
Bloody vomit	2	1.9%	1	1.7%	1	2.1%	F > 0.05
Dysphagia	1	0.9%	0	0.0%	1	2.1%	F > 0.05
Regurgitation	22	20.8%	16	27.1%	6	12.8%	p < 0.05*
Heartburn	16	15.1%	10	16.9%	6	12.8%	p > 0.05
Rec. epigastric pain	87	82.1%	49	83.1%	38	80.9%	p > 0.05
Halitosis	12	11.3%	7	11.9%	5	10.6%	p > 0.05
Night time pain	13	12.3%	10	16.9%	3	6.4%	F = 0.054*
Melena	3	2.8%	3	5.1%	0	0.0%	F > 0.05
Constipation	13	12.3%	7	11.9%	6	12.8%	p > 0.05
*statistically significant observation							

Table 4
Endoscopic data

	EGDS	Total	%	HP+	%	HP-	%	p
Esophagus	Normal mucosa	141	94.0%	100	94.3%	41	93.2%	F > 0.05
	Hyperaemia	8	5.3%	5	4.7%	3	6.8%	p > 0.05
	Erosions	1	0.7%	1	0.9%		0.0%	p > 0.05
Stomach	Normal mucosa	9	6.0%	4	3.8%	5	11.4%	F > 0.05
	Superficial	94	62.7%	61	57.5%	33	75.0%	0.02*
	Nodular	12	8.0%	12	11.3%		0.0%	0.006*
	Erosions	33	22.0%	27	25.5%	6	13.6%	0.056*
	Ulcers	2	1.3%	2	1.9%	0	0.0%	F > 0.05
Duodenum	Normal mucosa	10	6.7%	5	4.7%	5	11.4%	p > 0.05
	Superficial	79	52.7%	50	47.2%	29	65.9%	0.019*
	Erosions	52	34.7%	44	41.5%	8	18.2%	0.029*
	Ulcers	9	6.0%	7	6.6%	2	4.5%	p > 0.05
*statistically significant observation								

Table 5
Histological data comparison in Hp + and Hp- group

	Histology	Total	%	HP+	%	HP-	%	p
Stomach	Normal	30	20.0%	11	10.4%	19	43.2%	0.000*
	Chronic non-active	110	73.3%	85	80.2%	25	56.8%	0.002*
	Chronic active	10	6.7%	10	9.4%	0	0.0%	F = 0.027*
	Metaplasia/ dysplasia/atrophy	10	6.7%	10	9.4%	0	0.0%	0.014*
	Metaplasia	2	1.3%	2	1.9%	0	0.0%	F > 0.05
	Dysplasia	3	2.0%	3	2.8%	0	0.0%	F > 0.05
	Atrophy	5	3.3%	5	4.7%	0	0.0%	F > 0.05
Duodenum	Normal	77	51.3%	46	43.4%	31	70.5%	0.001*
	Chronic non-active	61	40.7%	49	46.2%	12	27.3%	0.016*
	Chronic active	8	5.3%	7	6.6%	1	2.3%	F > 0.05
		4	2.7%	4	3.8%	0	0.0%	
	Acute							F > 0.05
	Metaplasia/dysplasia	12	8.0%	9	8.5%	3	6.8%	F > 0.05
	Metaplasia	11	7.3%	8	7.5%	3	6.8%	F > 0.05
	Dysplasia	1	0.7%	1	0.9%	0	0.0%	F > 0.05
*statistically significant observation								

Table 6
Histological data comparison in 2 subgroups of Hp + group

Atrophy/metaplasia/dysplasia	Total	Ulcerative/apthous erosions/nodularity		Superficial changes/normal mucosa		p	OR	CI
		N	%	N	%			
Stomach	10	5	8.47	5	10.64	> 0.05	0.78	0.21-86
Duodenum	11	9	15.25	2	4.26	> 0.05	4.05	0.83-19.74

Figures

Figure 1
Distribution by age groups *statistically significant observation $p<0.05$

Figure 2

Figure 3

Distribution of patients by place of inhabitation