Helicobacter pylori gastritis in Jordanian children: persistence versus resolution

Eyad Altamimi[1], Lma Salameh[2], Hanin AlNsour[2], Naif Rawabdeh[3]

[1]Paediatric Department, Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan
[2]Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan
[3]Pediatric Department, King Abdullah University Hospital, Irbid, Jordan

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Address for correspondence: Eyad Altamimi MD, Paediatric Department, Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan, e-mail: eyadtamimi@gmail.com

Abstract:

Introduction: *Helicobacter pylori* (*H. pylori*) is the most common cause of infectious gastritis. *Helicobacter pylori* is an infection that is typically acquired during childhood.

Aim: This study aims to describe children with *H. pylori* infection and compare the clinicopathological features of children with resolved and persistent infection.

Material and methods: This is a retrospective review of all children with biopsy-proven *H. pylori* infection over a 6-year period. Hospital electronic files, endoscopic database, and histopathology database were reviewed. Patients who underwent follow-up endoscopy were identified, and their data was compared.

Results: A total of 176 patients were identified, of whom 100 (56.2%) were females. The average age at presentation was 10.2 years (range: 2.5–17 years). Children older than 10 years were the most affected age group. The most commonly presenting symptom was recurrent abdominal pain (92 (51.69%)), followed by epigastric pain/dyspepsia and vomiting (44 (24.72%) and 18 (10.11%), respectively). The most common macroscopic feature was antral nodularity (76 (42.70%)). The most prevalent microscopic findings were moderate inflammation of moderate chronicity. None of the patients developed gastric atrophy. Forty-four (23.5%) patients had comorbid diseases. On follow-up, upper endoscopy was available for 42 (23.59%) patients. The resolution of *H. pylori* based on histological examination was observed in only 10 (23.81%) patients. Children whose infections resolved were older.

Conclusions: A significant number of children with biopsy-proven *H. pylori* infection presented with abdominal pain. Female gender, older age, and less severe macroscopic and microscopic findings may be associated with a higher chance of infection resolution.

Introduction

Helicobacter pylori is a gram-negative, microaerophilic, spiral bacterium linked to chronic gastritis and peptic ulcer disease, which can result in more serious sequelae, such as gastric cancer and mucosa-associated lymphoid tissue (MALT) lymphoma [1–3]. Most *H. pylori* infections are acquired during childhood, and many remain asymptomatic. The colonization of the gastric mucosa persists in cases in which no eradication therapy is administered [4]. *Helicobacter pylori* infections can be non-specific and may be related to the development of complications. The most specific symptom associated with *H. pylori* infection was found to be nausea [5]. Epigastric pain was reported more frequently in *H. pylori*-infected children [6].

Helicobacter pylori infection is associated even with non-gastrointestinal manifestations, such as unexplained iron-deficiency anaemia and chronic immune thrombocytopaenia, and it has an inverse relationship with the development of bronchial asthma and Crohn's disease [7–9]. *Helicobacter pylori* infection is transmitted in a household setting between family members, most importantly mother-child transmission. *Helicobacter pylori* is transmitted through faecal-oral, oral-oral, and even gastro-oral routes [10]. Numerous factors,

such as socioeconomic status, overcrowding, number of family members, lack of clean water, family size, schooling, and childhood sanitation practices, affect the risk of transmitting the bacterium to children [11]. The worldwide prevalence of *H. pylori* among children varies significantly between regions and cities, as well as between age groups in each country. High-income countries have lower rates of *H. pylori* infections as compared to low-income countries [12].

Despite the scarce data regarding *H. pylori* in Middle Eastern children, a cohort study conducted in Oman in 2014 showed an overall prevalence of biopsy-diagnosed *H. pylori* infection of about 25% [13]. Additionally, data collected in Egypt and Saudi Arabia showed prevalence levels of 65% and 62%, respectively [14, 15]. As for local evidence, a study of dyspeptic children conducted in Northern Jordan revealed an 82% prevalence based on histologic evidence [16]. Another study from central Jordan reported a rate of 25% for *H. pylori* gastritis in children who underwent upper endoscopy regardless to the indication [17].

A spectrum of diagnostic tests for *H. pylori* gastritis, including invasive and non-invasive tests, are available. The choice between these tests is made by the clinician, with the aim of providing treatment given positive results and symptoms [18]. The non-invasive approach includes serology tests, urea breath test, and urine or stool *H. pylori* antigen detection. It is worth mentioning that serology testing imposes the limitation of a low specificity, as well as difficulty in diagnosing the disease as an active or a past infection [19]. On the other hand, invasive methods of diagnosis require endoscopy, along with a biopsy to examine any histological changes, a culture test, or a rapid urease test. Endoscopic findings vary among patients, with nodularity of the gastric mucosa being a prominent common finding in high-prevalence areas [20]. Description of histological specimens containing *H. pylori* is variable [20]. The Sydney classification system is widely used to describe gastritis histology, and stomach biopsies are described regarding 4 fields: the chronicity of the infection, based on presence of lymphocytes; activity, based on the presence of lymphocytes; glandular atrophy; and metaplasia [21]. Without treatment, the eradication of *H. pylori* infection is rare. Spontaneous eradication is described mainly in infants and young children; eradication decreases with age [22].

The triple-therapy protocol, consisting of a proton pump inhibitor, amoxicillin, and clarithromycin, has proven effective in eradicating *H. pylori* infection [23]. Furthermore, certain factors may come into play regarding the effectiveness of the triple-therapy regimen. One important factor to note is adherence to the course of treatment. The eradication rate drops from almost 90% to only 36.8% with non-adherence [24]. The recurrence of infection can occur via recrudescence or reinfection. Recurrence rates are higher during the 3–12 months after eradication and decrease over time, declining sharply after 1 year [22].

Aim

This study aimed to describe the prevalence of histologically proven *H. pylori* infection in Jordanian children who underwent upper endoscopy, as well as their clinical presentations, endoscopic and histological characteristics, the rate of helicobacter recurrence, and the factors associated with recurrence.

Material and methods

Retrospectively, all patients with biopsy-proven *H. pylori* gastritis were identified through reviewing the endoscopic and histopathological databases. Electronic hospital charts were retrieved for patients admitted between December 2015 and December 2020.

Demographic data, including, age, sex, and clinical data; presenting symptoms; associated symptoms; endoscopic findings; histological findings; lab results; treatment offered; and outcome were recorded. Patients with identified follow-up endoscopy with gastric biopsies were reviewed regarding clearance of the infection versus persistence. The 2 groups were compared in terms of their features.

Exclusion criteria: Patients older than 18 years at presentation. Patients with incomplete data.

Patients underwent upper endoscopy, which was performed by expert paediatric gastroenterologists using a paediatric gastroscope. Light sedation with midazolam and local lidocaine application was used in all patients. Heavier sedation was used in a case-by-case manner.

Multiple gastric biopsies were obtained from at least the antral and the body of the stomacH. Biopsies were preserved in formalin and transferred to the pathology section immediately for fixation and processing. Other biopsies (oesophageal and duodenal) were obtained if the endoscopist found an abnormality, or to rule out other conditions.

The biopsies were reviewed by senior pathologist or gastrointestinal pathologist. The histological reporting graded the gastric biopsies according to Sydney classification (inflammation degree, chronicity, and presence of atrophy or metaplasia).

Definitions

Epigastric pain/dyspepsia: pain or discomfort in the central upper abdomen right below the costal margin. Abdominal pain: pain or discomfort poorly localized or occupying the whole abdomen. Co-morbid disease/

chronic illness: any medical condition co-existed with the *H. pylori* infection.

Statistics analysis

Descriptive statistics were used to describe the demographic data. For categorical variables, frequencies and percentages were reported. Comparisons of categorical variables were carried out using Pearson's χ^2 test. *P*-value < 0.05 was considered significant to reject the null hypothesis.

Ethical approval

This study is part of the Paediatric Upper Endoscopy Project, which was approved by the institutional review board of the Jordan University of Science and Technology (Approval no. 20190077).

Results

Of 779 upper endoscopy procedures performed during the study period, 178 patients with biopsy-proven *H. pylori* gastritis were identified. The relative frequency was 22.8%. One hundred (56.2%) patients were females. The average age at presentation was 10.2 years (range: 2.5–17 years). Children older than 10 years were the most affected age group (Table I).

The most commonly presenting symptom was recurrent abdominal pain (92 (51.69%)), followed by epigastric pain/dyspepsia and vomiting (44 (24.72%) and 18 (10.11%), respectively) (Table II).

The most common macroscopic feature was antral nodularity (76, 42.70%). Sixty (33.71%) of the examinations were reported as normal (Table III). Oesophageal and duodenal examinations were normal in most of the patients. Duodenal erosions and ulcerations and oesophagitis were the most commonly reported endoscopic findings outside the stomach (20 (11.2%) and 10 (5.6%), respectively) (Tables IV and V). The most prevalent microscopic gastric findings were moderate inflammation with moderate chronicity. None of the patients developed gastric atrophy (Table VI). On the other hand, duodenitis and gastroesophageal reflux disease (GERD) were the most common histopathological findings in our cohort (Tables IV and V). Anaemia was present in 22 (12.79%) of the patients.

On follow-up, upper endoscopy was available for 42 (23.59%) cases. The resolution of *H. pylori* based on histological examination was observed in only 10 (23.81%) patients. Vomiting was more common in patients who resolved their infection as compared to the persistent infection group, which was statistically significant (p = 0.05). Children who resolved their infection were older and had less severe histological features (Table VII).

Table I. Patients' characteristics

Parameter	Count	Percentage
Gender:		
Females	100	56.18
Males	78	43.82
Age of presentation [years]:		
0–5	11	6.18
5–10	53	29.78
> 10	114	64.05

Table II. Clinical presentation: symptoms and signs of patients with *Helicobacter pylori* gastritis

Presenting complaint	Count	Percentage*
Recurrent abdominal pain	92	51.69
Epigastric pain and dyspepsia	52	24.72
Vomiting	49	10.11
Constipation	13	7.3
Nausea	7	3.9
Diarrhoea	11	2.25
Poor feeding/food refusal	13	7.3
Weight loss/poor weight gain/failure to thrive (FTT)	14	7.84
Anaemia	17	2.25
Oral ulcers	7	1.69
Weight gain	10	5.6
Heartburn	13	1.69
Gastrointestinal bleeding (melena, haematemesis)	3	1.69
Food impaction	3	0.56
Dysphagia	9	1.12
Short stature	3	1.12
Halitosis	3	0.56
Chest pain	1	0.56
Hiccups/Belching	8	0.56
Others	5	2.8

**The numbers do not add up because some patients have more than one symptom.*

Table III. Gastric endoscopic pattern reported in *Helicobacter pylori*-positive children

Gastric endoscopic pattern	Number	Percentage (%)*
Normal	60	33.7
Hyperaemia	36	20.2
Nodularity	76	42.70
Ulcer	14	7.9

**Numbers do not add up because some patients had more than one pattern.*

Table IV. Oesophageal endoscopic and histopathological findings

Oesophageal findings	Number *N* = 178	Percentage (%)
Normal	143	80.3
Hiatal hernia	18	10.1
Suggestive of GERD	10	5.6
Suggestive of EoE (furrowing, trachealization, whitish dots)	8	4.5
Stricture/Stenosis	2	1.1
Others	2	1.1
Oesophageal histopathological findings	**Number (%) *N* = 45**	**Percentage (%)**
Normal	29	64.4
GERD*	12	26.7
Eosinophilic oesophagitis	4	8.9

**Basal cell hyperplasia, papillary elongation, dilatation of intracellular spaces, and inflammatory infiltration.*

Table V. Duodenal endoscopic and histopathological findings

Duodenal endoscopic findings	Number *N* = 178	Percentage (%)
Normal	138	77.5
Inflammation (duodenitis without ulcerations)	13	7.3
Duodenal ulcer/erosions	20	11.2
Suggestive of celiac disease	13	7.3
Others	5	2.8
Duodenal histopathological findings:	**Number *N* = 134**	**Percentage (%)**
Normal	117	87.3
Peptic duodenitis	6	4.5
Findings suggestive of celiac disease[$]	12*	8.9
Lymphangiectasia	1	0.7

[$]Villous atrophy, lamina propria inflammation, intraepithelial lymphocytosis.
**Two patients had duodenitis with celiac disease changes.*

Discussion

Helicobacter pylori has infected almost half the world population. Most of the infections are acquired during early infancy and persist if no eradication therapy is offered [12]. A diagnosis of gastric infection with *H. pylori* requires the demonstration of the microorganism histopathologically or culturing the microorganism [4]. Triple therapy is effective in clearing the infection given treatment compliance [4].

Table VI. Histopathological findings in the gastric biopsies of children with *Helicobacter pylori* infection

Microscopic evaluation	Count	Percentage (%)
Chronicity:		
Absent	4	2.2
Mild	48	27.0
Moderate	90	50.6
Severe	36	20.2
Activity:		
Absent	35	21.3
Mild	63	35.4
Moderate	68	38.2
Severe	12	6.74
Intestinal metaplasia:		
Absent	176	98.9
Focal	2	1.1
Atrophy:		
Absent	178	100.0
Malignancy:		
Absent	178	100.0

We demonstrated that *H. pylori* infection affected almost one-fifth of children who underwent upper endoscopy in our facility regardless of the indication for the endoscopy. In children who had repeated endoscopy, documented resolution of *H. pylori* infection was noticed in almost one-fourth of them.

Helicobacter pylori infection is considered as one of the most common infections worldwide, with a prevalence of around 50% worldwide, and the highest rates are seen in low-income countries [3]. Aguilera Matos *et al.* reported that the countries with the highest rates of *H. pylori* infection included Nigeria (89.7%), Siberia (88.3%), South Africa (86.8%), and Colombia (83.1%), whereas the countries with the lowest infection rates included Yemen (8.9%), Indonesia (10%), Belgium (11%), Ghana (14.2%), and Sweden (15%). It is believed that access to clean water, better levels of hygiene and sanitation, as well as increased awareness and educational culture in high-income countries reduce infection rates [3]. Moreover, another factor found to affect the prevalence of *H. pylori* was socioeconomic status, which was evident in the variability of prevalence rates in different regions of the same country [25]. However, a reverse pattern was also noticed, in which areas with better socioeconomic status and higher incomes reported higher infection rates, which may be related to better healthcare access and consequently higher diagnostic rates [26].

In Jordan, despite the heterogeneity of diagnostic methods, the prevalence rate of *H. pylori* infection in

Table VII. Comparison between children with biopsy-proven resolution of *Helicobacter pylori* infection and children with non-resolution

Parameter	Resolved infection 10 (100%)	Non-resolved infection 32 (100%)	*P*-value
Average age [years]	12	10.44	0.025
Gender F, *n* (%)	9 (90)	19 (59.38)	0.08
Presence of chronic illness, *n* (%)	2 (20)	13 (40.63)	0.242
Recurrent abdominal pain, *n* (%)	6 (60)	15 (46.88)	0.288
Epigastric pain/dyspepsia, *n* (%)	3 (30)	12 (37.32)	0.473
Vomiting, *n* (%)	3 (30)	3 (6.38)	0.05
Macroscopic exam, *n* (%):			
Nodularity	2 (20)	16 (50.0)	0.102
Ulcers	0	4 (12.5)	0.247
Normal	5 (50)	10 (32.26)	0.315
Microscopic exam, *n* (%):			
Inflammation:			
Moderate	7 (70)	13 (40.63)	0.112
Severe	0	4 (12.5)	0.247
Chronicity:			
Moderate	5 (50)	11 (34.38)	0.38
Severe	0	11 (34.38)	0.037
Average Hb [g/dl]	13.18	12.2	0.072
Completed triple therapy	5 (50%)	20 (62.5%)	0.482

healthy schoolchildren from north Jordan range between 55% (seropositivity, in 2006) [27] to 14.6% (urea-breath test, in 2020) [28]. The positive results, however, showed no significant gender difference. This drop may reflect a worldwide phenomenon, especially given improved sanitation and access to clean water in Jordan.

These results depicted a substantial drop as compared to a previous prospective study published in 2014, which also collected data from children below the age of 14 years in northern Jordan. This study included 163 dyspeptic children, of whom 82% were found to be *H. pylori* positive [16]. Moreover, another retrospective study published in 2020 collected data from 2008 until 2016 from children who underwent oesophago-gastro-duodenoscopy at Jordan University Hospital in Amman, the capital of Jordan. In this study, of the 98 subjects studied, 54% of the children were found to be histologically positive. This study also showed a male predominance (55%) among the positive values [17]. In our study, the prevalence rate for *H. pylori* infection in scoped children was 22%, with female predominance.

Gastrointestinal symptoms, specifically abdominal pain, are very common in children. Thus, most of the children infected with *H. pylori* are asymptomatic, and the relationship between gastrointestinal symptoms and *H. pylori* infection remains controversial. Spee *et al.* concluded that only upper abdominal pain is associated with *H. pylori* infection, not recurrent abdominal pain [6]. In Russia, a study investigated 225 school children referred for chronic abdominal pain. Eighty percent of them were found to have *H. pylori* infection. It was also found that nighttime abdominal pain was more frequent in *H. pylori*-positive children as compared to *H. pylori*-negative children [29].

On the other hand, Correa *et al.* [5] reported nausea as the only dyspeptic symptom related to *H. pylori* infection in Brazilian children. Dore *et al.* [30] found that nausea and vomiting were associated with *H. pylori* infection while abdominal pain and heartburn were not. A recent Romanian endoscopy-based study reported that epigastric pain was significantly more common in *H. pylori*-infected children, reaching 56.9% [31]. A previous study from Jordan showed that there was no difference in gastrointestinal symptoms between children diagnosed with *H. pylori* infection and those who were not [17].

In our cohort, although there was no comparative (non-infected) group, gastrointestinal symptoms were

still common. Abdominal pain was present in almost half of patients, while epigastric pain was documented in 24.7%. Our numbers are in accordance with Xianohong *et al.*, who reported abdominal pain present in 47.95% of infected children [32].

On the other hand, *H. pylori* infection has been linked to extraintestinal manifestations, such as anaemia and thrombocytopaenia. In a recent meta-analysis of the association between *H. pylori* infection and iron-deficiency anaemia in children, Hamdan *et al.* concluded that a moderate level of evidence suggests that infection with *H. pylori* represents a significant risk factor for iron deficiency anaemia development [33].

In our cohort, 12.4% of our infected children had anaemia. This is relatively similar to the reported rate of Khdair *et al.* [17]. In Oman, anaemia was reported in 22% of infected children [13]. In a retrospective study of Bulgarian children, *H. pylori* was associated with anaemia in up to 76.6% of cases, which was much higher than in children with no infection (21.3%) [34]. Interestingly, other investigators found no significant difference in rates of anaemia between infected and non-infected children. Because iron-deficiency anaemia is a very common childhood disorder that is affected by socio-economic status, food intake, and eating habits, estimating the effect of *H. pylori* infection on the rate of development is difficult [35].

The tests with which to diagnose *H. pylori* infection are variable. Non-invasive tests include the bacterial stool antigen test, urea breath test (UBT), and the detection of antibodies in the body fluids (serum, urine, or saliva). In contrast, invasive testing requires the acquisition of gastric mucosa to demonstrate the presence of the microorganisms through histopathology, tissue culture, PCR, or rapid urease test [36]. Invasive testing still represents the gold standard [4]. The prevalence rate of *H. pylori* in children who underwent endoscopy differs according to population type, age group, and the indications for endoscopy. Boyanova *et al.* reported a positivity rate of 24.5% in children who underwent upper endoscopy for gastrointestinal symptoms [34].

The rate in our study was still higher than that reported in Greece, at 13.2% [37], but still less than that reported in Romania, at 33%, [31], and Colombia, at 47% [38]. El-Mazary *et al.* investigated the presence of *H. pylori* in Egyptian children who presented with non-variceal upper gastrointestinal bleeding. They reported a prevalence rate of 65% [39]. Another study from Oman documented the overall prevalence of biopsy proven *H. pylori* infection at 25% [13]. Khdair *et al.* reported a prevalence rate of 54% in Jordanian children [17]. This represents a significant decrease as compared to the report of Shatnawi *et al.*, who reported an 82% prevalence rate in children with dyspepsia who underwent endoscopy [16].

In our study, the overall prevalence rate of *H. pylori* infection for all endoscopy causes was 22.8%. Although the difference from the results of Shatnawi *et al.* [16] may be related to the inclusion criteria, in that dyspeptic children were scoped, the lower rate as compared to that of Khdair *et al.* [17] may be related to their exclusion criteria, in that 130 of the patients who underwent endoscopy were excluded.

It has been found that the rate of infection increases with age. A recent Romanian study found that most of the diagnosed *H. pylori* infections occurred in children older than 15 years and that the infection rate increases with age [31]. The same was observed in Bulgarian children, where most of the diagnosed children were older than 8 years [40].

Dore *et al.* also found that the prevalence of *H. pylori* infection among children 13–16 years old is higher than in children 7–12 years old [30]. Khdair *et al.* found that most of the diagnosed children were older than 10 years and that the infection rate increased with age [17]. Our results are consistent with the literature; while most of the *H. pylori*-positive diagnoses were found in the age group consisting of those older than 10 years, an increasing rate of infection was noticed with age advancement.

A gender difference in *H. pylori* infection was observed and reported in a previous meta-analysis [41], with a small male predominance in children and adults. In our cohort, girls represent a higher percentage of infected children. Although this stands in contrast to the findings of Ibrahim *et al.* [41], Boyanova *et al.* reported a similar observation in Bulgarian children [40].

The endoscopic features of *H. pylori* infection in children differ from those in adults. In the paediatric population, nodularity is seen in the majority of cases, while gastric atrophy is more common in adults [42]. Domsa *et al.* reported notable nodularity, cobblestone appearance, and oedema of the gastric mucosa to be associated with *H. pylori* infection in Romanian children [43]. This was also replicated by Rosu *et al.*, who reported that nodularity and hyperaemia were the most frequent endoscopic findings [31]. In a Turkish study reporting on 102 children with *H. pylori* infection, antral nodularity was seen in 66 (64.7%) patients, while normal looking mucosa were reported in 28 (27.5%) patients [44]. Khdair *et al.* reported nodularity as the most common finding (23 (43%)), followed by normal-looking mucosa, which was seen in 22 (42%) patients [17]. In our cohort, similarly to previous reports, nodularity was the most common finding during endoscopy, being observed in 76 (42.7%) patients, followed by normal-looking muco-

sa (33.7%) and hyperaemia (20.2%). Ulcers were seen in 14 (7.9%) of the patients.

The Sydney system is widely used to describe chronic gastritis. The system describes the chronicity of inflammation; its activity; and the presence of atrophy, metaplasia, or malignancy. Children's histopathologic findings can sometimes be viewed as vague and nonconclusive compared to findings in adults [45]. In general, chronic active inflammation is commonly present in children, whereas atrophic gastritis, as well as intestinal metaplasia, are more common in adults [46].

This may be because the paediatric age group experienced inflammation to a lesser degree and the process of inflammation was geographically dependent, varying in intensity [45]. A study of Brazilian children concluded that, of 96 *H. pylori*-positive patients, 70.5% had moderate to severe active gastritis in the antrum, and 45.2% had such in the corpus; no intestinal metaplasia or gastric atrophy was found [45].

In a recent study of Romanian children, Domsa *et al.* reported chronic gastritis in 60.9% of the infected children, while atrophy was seen in 25% of cases [43]. Khdair *et al.* reported chronic inflammation in all infected patients, with more than half of the patients showing cell activity and 2 (4%) patients exhibiting atrophy and metaplasia [17]. Our numbers are consistent with previous reports, with a 98% rate of chronicity, no cases of gastric atrophy, and 2 (1.1%) patients manifesting metaplasia.

The relationship between reflux and *H. pylori* infection is an area of debate. The hypochlorhydria induced by *H. pylori* infection was believed to negatively affect the rate of reflux oesophagitis [47]. Grande *et al.* found no role on the part of *H. pylori* infection in the development of reflux oesophagitis [48]. Lupu *et al.* investigated children with reflux disease for the presence of *H. pylori* gastritis. They concluded that, although the presence of *H. pylori* was not an important factor in the development of gastroesophageal reflux, the presence of *H. pylori* in class A oesophagitis may suggest slowing of disease progression [49]. Yoram Elitsur *et al.* demonstrated that there was no statistical difference in the rate or severity of oesophagitis between *H. pylori*-infected and *H. pylori*-naïve children, suggesting that GERD and *H. pylori* infection can co-exist without influencing one another [50]. Bordea *et al.* studied 97 patients with *H. pylori* infection and macroscopically reported oesophagitis in 82 (84.5%) patients. After the eradication of *H. pylori*, none of the GERD patients had persistent oesophagitis, suggesting that the eradication of *H. pylori* is unlikely to induce or exacerbate reflux disease [51].

In our cohort, 12 (6.7%) patients showed histopathological evidence of oesophagitis. This is lower than the rate reported by Yoram (10%) and much lower than that reported by Adriana (84.5%), which may be related to the method of diagnosis and biopsy protocol [50, 51]. Only 2 patients underwent follow-up endoscopy, and both showed the persistence of *H. pylori* infection. In one patient, the reflux features had resolved, and the other had persistent histopathological reflux features. This makes it difficult to draw any conclusions based on such findings.

On the other hand, another type of oesophagitis was thought to interact with *H. pylori* infection. Eosinophilic oesophagitis (EoE) is an immune-mediated disease that manifests as oesophageal dysfunction with oesophageal eosinophilic infiltrate in the absence of peripheral eosinophilia [52].

Cheung *et al.* reported lower rates of *H. pylori* infection in Australian children with EoE and suggested a protective role on the part of *H. pylori* [53]. This was duplicated in an adult Swedish cohort [54]. A recent review by Doulberis *et al.* refutes the idea of *H. pylori* protection against EoE and argues that common pathogenic components are shared by both conditions [55]. Although we do not have data on the prevalence of EoE in Jordanian children, the disease is not common. In our cohort, 4 (2.2%) patients had EoE. Although it is difficult to draw any conclusions based on this finding, it may indicate that *H. pylori* infection and EoE can coexist.

Helicobacter pylori infection causes gastritis and gastric and duodenal ulcers and is classified as a definite carcinogen (linked to the development of mucosa-associated lymphoid tissue lymphoma and gastric cancer). Antibiotic-susceptibility choice is not readily available, especially in low-income countries, leaving physicians to make treatment decisions based on clinical experience and the local/regional antibiotic susceptibility profile. Triple therapy is still the recommended first-line therapy [4, 56, 57].

Despite the use of triple therapy, eradication rates are not satisfactory in children and remain below the recommended rate of 90% [58]. Many factors are believed to engender this pattern of increased eradication failure, mainly improper regimen, poor compliance, massive gastric loads with high gastric acidity, gene polymorphisms, biofilm generation, resistance to antibiotics, and antimicrobial washout [59, 60]. Socioeconomic class difference was considered as a potential risk factor for reinfection. For instance, in high-income communities, the annual recurrence risk was found to be 3.4%, in contrast to low-income communities, with an annual recurrence risk of 8.7% [59, 61].

Candelli *et al.* 2012 examined the recurrence risk in young diabetic patients in comparison to non-diabetics. A greater reinfection rate of 8% was found in the

diabetic group, while the non-diabetic group only had a reinfection rate of 2.33% [62]. Kim *et al.* found links between both male gender and low-income status and reinfection rates in Korea [63]. The recurrence of *H. pylori* can be caused by either reinfection or recrudescence. Recrudescence occurs when the strain causing the recurrence is genetically identical to that isolated before receiving the eradication treatment, while reinfection occurs when the strain causing recurrence is genetically different from that eradicated. Recrudescence is the most prominent cause of recurrence [25].

Although they are scarce, data regarding paediatric cases show that the recurrence rate in children varies between 2 and 10% in developing countries [25]. A wealth of studies have been carried out worldwide in various countries investigating the recurrence rate of *H. pylori*. For instance, in Brazil, the annual reinfection rate was found to be 1.8% after a 5-year follow up, which is considered consistent with values obtained from other developed countries [25]. Lithuania, a country of a high *H. pylori* prevalence, had an annual recurrence rate of 3.36% after a 9-year follow up [64], while south Korea had low recurrence rates between the years 2003 and 2010, with an annual recurrence rate of 3.51% [59]. Finally, a study carried in Alaska demonstrated an annual recurrence rate of 8.05%, and recurrence was associated with low education levels and a higher proportion of family members being infected [65].

In our centre, we use proton pump inhibitor-amoxicillin-clarithromycin for 14 days as a first-line treatment for non-penicillin-allergic children with helicobacter infection. Metronidazole is used only if the patient has a penicillin allergy. A previous study on the antibiotic resistance profile of *H. pylori* isolates from Jordanian patients showed that the prevalence of metronidazole resistance was very high (92%) while that for clarithromycin was 23% [66].

Although we do not have the facilities to document the eradication of *H. pylori* infection in our cohort, the subgroup of patients who underwent upper endoscopy later had their stomachs biopsied for *H. pylori*. Children with the documented resolution of the infection tended to be older and have less severe chronic gastritis. Although more boys failed to resolve their infection, which was consistent with data previously reported by Hu *et al*. [59], in our cohort, this was not statistically significant. Unfortunately, our cohort is a retrospective cohort, the cause of non-resolution cannot be judged with confidence, whether due to ineffectiveness of eradication, especially with the high level of drug resistance in our population [66], or due to re-infection in the families with the high prevalence rate in our population [67].

Interestingly, out of the 10 patients who had endoscopic/histological evidence of *H. pylori* eradication, 5 (50%) reported not taking the medication, pointing to spontaneous resolution of their infection (Table VII).

Although our study is the largest from our area, it still has some weaknesses. The retrospective nature of the study carries the bias of relying on the accuracy of the medical records. The unavailability of oesophageal and duodenal biopsies for all the patients also represents a weakness. The data on compliance with treatment depended solely on the patients' recall, which involves recall bias. On the other hand, the time of re-scoping the patients after treatment was not uniform, limiting the generalization of the results.

Conclusions

Helicobacter pylori is commonly encountered in our paediatric population who undergo upper endoscopy, regardless of the indication for this procedure. Patients who experience vomiting, are of the female gender, and have less severe gastritis upon histological examination are more likely to have their infections resolve with treatment as compared to other patients. Oesophagitis, whether it is peptic or eosinophilic, can co-exist with *H. pylori* infection. Assuming that the resolution of the infection after treatment may not be accurate, our data suggest the need to document the resolution of the infection rather than assuming it has been cured after treatment.

Conflict of interest

The authors declare no conflict of interest.

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