The prevalence of Helicobacter Pylori and related conditions in Van province and its region

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Abstract
Aim: The prevalence of Helicobacter Pylori (HP) is up to 90% in developing countries, whereas it is less than 40% in developed countries. This study aims to determine the prevalence of HP in Van city and its region and to investigate the relationship between the presence of HP and the clinical, endoscopic appearance

Material and Methods: A total of 367 cases that presented with the dyspeptic complaints to the Gastroenterology outpatient-clinic and underwent upper-gastrointestinal endoscopy and gastric biopsies between July/2017-March/2019 were included in the study. The patients included in the study were divided into three age-groups (1-5 years, 6-10 years, 11-18 years). The clinical complaints, endoscopic findings were recorded in all patients. The relationship between HP positivity and clinical complaints, the endoscopic appearance was analyzed.

Results: The presence of HP was found in 234(63.8%) patients. However, the incidence of HP was 63.8% in all patients; it was found 34.6% between 1-5 years, 61.8% between 6-10 years, and 71.2% between 11-18 years, respectively. The duodenal ulcer was found in 8.5%(20/234) of HP positive cases, and 3.5%(5/133) of HP negative cases. In predicting the presence of HP, the ulcer specificity was determined 96%, the sensitivity was 8.5%, the positive predictive value was 80%, and the negative predictive value was found 37.4%

Conclusion: HP should be considered in patients with recurrent and chronic abdominal pain. Endoscopic appearance of nodular antral gastritis and the ulcer should suggest HP infection. The high rate of activity and chronicity in HP positive cases indicates the importance of HP eradication therapy.

Keywords: Clinical complaint; endoscopy; helicobacter pylori; prevalence.

INTRODUCTION
Helicobacter Pylori (HP) is a spiral-shaped gram-negative bacterium which colonizes the gastric mucosa. HP is the most common cause of resistant bacterial infection in the world (1). HP is located in the gastric mucosa and causes diseases such as peptic ulcer, B cell lymphoma and gastric cancer in addition to gastritis (2). HP disrupts the mucosal barrier, initiates inflammation and paves the way for the ulcer. In this context, it has been reported that HP is responsible for 95% of the etiology of duodenal ulcer and 70-85% of gastric ulcers (3,4). It has been shown that the gastric mucosa improves histologically after eradication and the possibility of ulcer recurrence decreases (3,4). Also, the antral nodularity and gastric-duodenal ulcers have been reported to be the most sensitive in detecting the presence of HP among endoscopic mucosal appearances in the adult group studies (2-4).

While the prevalence of HP infection in developed countries is around 5-20%, it reaches up to 70-90% in developing countries. Concordantly, HP infection rates are higher in developing countries in the childhood age group while infection rates are lower in developed countries and prevalence increases with age (4-6). Less prevalence of infection in developed countries has been associated with hygiene measures and socioeconomic status. Crowded family, sharing the same room and environment, improper drinking water, poor hygiene, and low-income level increase the risk of infection (7). Different seroprevalence values were found in studies conducted in some provinces or regions of our country. These rates vary according to age, region and diagnostic method; however, rates ranging from 23-78% have been reported (8,9).

Most of the current studies have been performed by searching for HP antigen in serum and feces or by a urea breath test. There are few studies performed with histopathological examination using the endoscopic method in order to determine the prevalence of HP in the
child age group. Since the histopathological examination of the biopsy specimen obtained by endoscopy provides valuable information both for the examination of gastric mucosa and the presence of HP, it is considered as the gold standard in the diagnosis. In this study, we aimed to determine the prevalence of HP from endoscopic tissue samples taken from Van province and its region histopathologically, to investigate the relationship between the presence of HP and clinical findings and to determine the sensitivity between the presence of HP and endoscopic findings.

MATERIAL and METHODS

Study design
A total of 367 patients who presented with recurrent abdominal pain and dyspeptic complaints to the Pediatric Gastroenterology outpatient clinic of Health Sciences University Van Training and Research Hospital between July 2017 and March 2019 and who underwent upper gastrointestinal system (GIS) endoscopy were included in the study. The study included patients aged 1-18 years who had granted permission for upper GIS endoscopy, had not previously received eradication therapy for HP and volunteered to participate in the study. Patients with a history of gastroduodenal surgery, a history of antibiotic and/or proton pump inhibitor (PPI) use up to one month before the study, those with the chronic disease and non-volunteers were not included in the study.

Data Evaluation
The demographic data (age, gender) and clinical complaints (nausea, vomiting, retching-belching, recurrent abdominal pain, water brash, abdominal swelling, and bleeding in the mouth) of all patients were documented. The concomitant comorbid diseases and previous operations were questioned.

Endoscopic Evaluation
The endoscopies of the patients were performed in the Endoscopy Unit of Van Training and Research Hospital using Fujinon EG530WR brand endoscopy device. The verbal and written informed consent was obtained from the families before endoscopy. All patients fasted for six hours before endoscopy; after the local pharyngeal xylocaine anesthesia, the patients were sedated with midazolam at 0.1 mg/kg and ketamine at 1 mg/kg and the endoscopic procedure was performed. During the endoscopy, the esophagus, cardia, fundus, corpus and antrum regions of the stomach and duodenum were examined in detail. The endoscopic evaluations of the patients, presence of esophagitis, the appearance of the gastric mucosa (hyperemia, nodular appearance), presence of an ulcer, the appearance of bulbous and duodenal and endoscopic diagnoses were recorded.

Histopathological Evaluation
The endoscopic biopsies of corpus, antrum, and duodenum were sent to the pathology laboratory in 10% formaldehyde. After the routine tissue follow-up procedures, the paraffin-embedded tissue samples were cut to a thickness of 5 microns and stained with routine hematoxylin-eosin (H-E) and evaluated on a light microscope. HP was stained with modified Giemsa to assess its presence. The biopsies were reported according to the updated Sydney classification (inflammation, activation, dysplasia, intestinal metaplasia, atrophy, and HP intensity) (10).

Ethical approval
All participants gave written permission to participate in the study. The ethical approval to conduct the study was obtained from the Ethics Committee of our hospital (Van, Turkey). All procedures complied with the ethical standards of our institution’s human experimentation committee and the Helsinki Declaration. The written informed consent forms were obtained from all participants included in the study and evaluated by a gastroenterologist.

Data analysis
The results of our study were analyzed with the program ‘The Statistical Package for Social Sciences 19.0 (SPSS Armonk, NY: IBM Corp.). The data with continuous values were given as mean (± standard deviation) and the categorical data as frequency and percentage (n, %). The data were tested for normal distribution by Kolmogorov-Smirnov test, histogram, and ± SD. Mann-Whitney U test was used for the non-parametric data of the groups, and the Chi-square test was used for the test of categorical data. The relationship between the presence of HP and the endoscopic findings was given by calculating sensitivity, specificity, negative and positive predictive values. P < 0.05 was considered statistically significant.

RESULTS

Of the 367 patients included in the study, 132 (34%) were male, and 235 (64%) were female. HP was found in 234 (63.8%) of all cases. No significant difference was found between the two genders in terms of the presence of HP. The patients included in the study were divided into three age groups (1-5 years, 6-10 years and 11-18 years) and compared in terms of the presence of HP; HP positivity was found in 18 (34.6%) of patients aged 1-5 years, 55 (61.8%) of patients aged 6-10 years and 161 (71.2%) of patients aged 11-18 years. The presence of HP was found to be significantly higher in the 6-10 age group and the 11-18 age group than in the 1-5 age group (P = 0.001). In general, the mean age of the patients with HP positivity was determined as 12.39 ± 4.07 while the mean age of patients with HP negative was 10.21 ± 5.33. The mean age was observed as significantly higher in the presence of HP (p < 0.05) (Table 1).

<table>
<thead>
<tr>
<th>Age groups</th>
<th>HP positive N(%)</th>
<th>HP negative N(%)</th>
<th>TotalN(%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-5</td>
<td>18 (34.6%)</td>
<td>34 (65.4%)</td>
<td>52 (100%)</td>
<td>0.346</td>
</tr>
<tr>
<td>6-10</td>
<td>55 (61.8%)</td>
<td>29 (38.2%)</td>
<td>84 (100%)</td>
<td>0.001</td>
</tr>
<tr>
<td>11-18</td>
<td>161 (71.2%)</td>
<td>65 (28.8%)</td>
<td>226 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gender</th>
<th>HP positive N(%)</th>
<th>HP negative N(%)</th>
<th>TotalN(%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>80 (34.2%)</td>
<td>52 (39.1%)</td>
<td>132 (35.9%)</td>
<td>0.346</td>
</tr>
<tr>
<td>Female</td>
<td>154 (65.8%)</td>
<td>81 (60.9%)</td>
<td>235 (64.1%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age(Meant±SD)</th>
<th>HP positive N(%)</th>
<th>HP negative N(%)</th>
<th>TotalN(%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.39 ± 4.07</td>
<td>10.21 ± 5.33</td>
<td>11.59 ± 4.39</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Presence of HP by age groups
When the relationship between clinical symptoms and presence of HP was analyzed; recurrent abdominal pain, which was the most common presenting complaint, was significantly more frequent in the HP positive group than the HP negative group. No significant relationship was found between HP positivity and nausea, vomiting, retching-belching, water brash, abdominal swelling, and bleeding in the mouth (p > 0.05) (Table 2).

<table>
<thead>
<tr>
<th>Presence of Helicobacter Pylori</th>
<th>HP positive (N=234) N (%)</th>
<th>HP negative (N=133) N (%)</th>
<th>Pvalue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>123 (52.6)</td>
<td>60 (45.1)</td>
<td>0.170</td>
</tr>
<tr>
<td>Vomiting</td>
<td>56 (23.9)</td>
<td>27 (20.3)</td>
<td>0.424</td>
</tr>
<tr>
<td>Retching and belching</td>
<td>79 (33.8)</td>
<td>43 (32.3)</td>
<td>0.780</td>
</tr>
<tr>
<td>Recurrent abdominal pain</td>
<td>108 (46.2)</td>
<td>31 (23.3)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Water brash</td>
<td>73 (31.2)</td>
<td>37 (27.8)</td>
<td>0.497</td>
</tr>
<tr>
<td>Abdominal swelling</td>
<td>8 (3.4)</td>
<td>2 (1.5)</td>
<td>0.279</td>
</tr>
<tr>
<td>Bleeding in the mouth</td>
<td>11 (4.7)</td>
<td>7 (5.3)</td>
<td>0.811</td>
</tr>
</tbody>
</table>

*Significant at <0.05 level.

In the endoscopic examination; gastritis was detected in 95% (349/367) of the patients. Also, duodenitis was detected in 4.8% (17/349) and duodenogastric biliary reflux in 8.3% (29/349) of patients with endoscopic gastritis. Furthermore, 221 (60.2%) patients were found to have antral nodularity, and 25 (6.8%) patients were found to have a duodenal ulcer. When the relationship between the presence of HP and endoscopic appearance was analyzed histopathologically; 90% (210/234) of the HP positive cases were found to have an antral nodular appearance, and 8.5% (20/234) were found to have a duodenal ulcer. Antral nodularity was detected in 11% (19/133) and duodenal ulcer in 3.5% (5/133) of HP negative cases. HP positivity was present in 80% (20/25) of the cases with duodenal ulcer. Although the incidence of the ulcer was higher in the HP positive group, no statistically significant difference was found (p = 0.087). In predicting the presence of HP, antral nodularity was found to have specificity of 85.5%, the sensitivity of 89.7%, the positive predictive value of 91.7%, and the negative predictive value of 82%. In predicting the presence of HP, the ulcer was found to have specificity 96%, the sensitivity of 8.5%, the positive predictive value of 80% and the negative predictive value of 37.4% (Table 3).

<table>
<thead>
<tr>
<th>HP positivity and endoscopic appearance</th>
<th>Specificity</th>
<th>Sensitivity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antral nodularity</td>
<td>85.5%</td>
<td>89.7%</td>
<td>91.7%</td>
<td>82%</td>
</tr>
<tr>
<td>Ulcer</td>
<td>96%</td>
<td>8.5%</td>
<td>80%</td>
<td>37.4%</td>
</tr>
</tbody>
</table>

DISCUSSION

In the literature, studies investigating the incidence of HP histopathologically in the pediatric age group appear to be relatively low compared to the adult age group. It is known that studies using invasive tests and histopathological methods are very rare, especially in the pediatric age group (11,12). The results appear to be contradictory although Turkey shows similar appearance as developing countries in terms of the HP frequency.

The studies conducted have reported that it is 35% (0-18 years) in Brazil, 45% (0-10 years) in Algeria, and 69% (10-25 years) in India (7). In developed countries, it has been stated that the rate is about 13% in Germany (5-8 years), 13% in Belgium (9 months-5 years), 22% in the Netherlands (11-25 years), 24% in the United States (15-20 years) (7). In studies conducted in different geographical regions and different age groups in our country, it has been reported that the prevalence of HP varies between 19.6% and 74% (3,8,13,14). In studies conducted in Turkey, the HP seroprevalence ranges between; 19-45% under the age of 5 years, 50-60% 5-10 years of age and 54-80% over 10 years (15). In a study conducted in Germany to reveal the impact of ethnicity and environmental factors, while the HP seroprevalence among the German was found to have a low value as 13%, it was 30.4% of among the Turkish who were born and raised in Germany and 44.5% among the Turkish who were born in Turkey but live in Germany (16). In the previous studies in the province of Van, using HP antigen in the feces, it has been found; 1-5 years; 26.04%, between 6-10 years; 46%, 11-18 age range; 49.3% and 39.9% between the ages of 1-18 (3). When the patients are compared in terms of age, we have found that the prevalence of HP increases with increasing age. Significant increase in HP prevalence was observed in the 6-10 age group and 11-18 age group compared to the 1-5 age group. We think that the results are different due to different study methods and the variety of HP prevalence according to geographical regions. In epidemiological studies with HP, in parallel with our study, it has been observed that the incidence of the disease increases with age. This situation has been generally associated with low socioeconomic status, inadequate hygiene conditions and low sanitation conditions (17).

Although the majority of infected children are asymptomatic, studies are reporting a relationship between abdominal pain and HP (18,19). In the presence of HP infection, there are no symptoms or physical examination findings to diagnose the disease. In previous studies in our country, HP prevalence was reported to be between 49-61% (20,21) in patients with abdominal pain and 22.5-77% in studies conducted abroad (22,23). In our study, when the complaints of the patients were investigated, the abdominal pain was found as the most common symptom. The prevalence of HP was found to be 77.6% (108/139) in patients with recurrent chronic abdominal pain, and our rates were slightly higher than those conducted in our country but consistent with studies conducted abroad. The complaint of abdominal pain was significantly higher...
in HP positive cases than in HP negative cases. Especially in studies conducted in developing countries, eradication is recommended in children with recurrent abdominal pain and dyspeptic complaints since their symptoms improve with HP eradication treatment (24).

HP causes gastritis and peptic ulcer in children and adults. HP infection acquired in childhood is important in terms of complications in adulthood. Because HP primary infection is rare in adults, it has been claimed that the treatment of infected children may reduce HP transport to adults and the incidence of gastric cancer in adults (25). The gastroduodenal diseases caused by HP vary in children and men. The most common endoscopic pathological finding in children is the antral nodular gastritis whereas peptic ulcer is rare. Only 50% of adult patients are found to have antral nodular gastritis, and the rest are associated with gastritis and duodenal ulcer, duodenitis, mucosa-associated lymphoid tissue (MALT) lymphoma and gastric cancer (15).

In the studies conducted in the adult age group, the incidence of HP in duodenal ulcer cases has been reported at a rate of 58-74.8% (26). In studies conducted in the pediatric age group, the ulcer was found in 1-8% of HP positive cases (19,27). In our study, it was determined as 8.5%, and it was found to be low compared to adult age group studies and consistent with the literature according to pediatric age group studies. Although the presence of both antral nodular appearance and duodenal ulcer may be considered as a significant endoscopic finding in predicting the presence of HP, it is not a specific finding. In our study, the duodenal ulcer was found in 8.5% of HP positive cases and 3.5% of HP negative cases. Although the incidence of the ulcer was higher in the HP positive group, no significant difference was found. The presence of HP in 80% of cases with ulcer indicates that HP is an essential factor in the etiology of ulcer.

CONCLUSION

In conclusion, HP positivity should be considered in patients with recurrent and chronic abdominal pain. HP plays a role as the etiologic factor in 77.6% of cases with abdominal pain. The endoscopic appearance of nodular antral gastritis and ulcer should suggest HP infection. The high rate of activity and chronicity in HP positive cases indicates the importance of HP eradication therapy.

Competing interests: The authors declare that they have no competing interest.
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Ethical approval: The ethical approval to conduct the study was obtained from the Ethics Committee of our hospital (Van, Turkey).

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