



Has the COVID-19 pandemic affected the incidence of *Helicobacter pylori* infection? Evaluation of endoscopic results in patients with dyspeptic complaints

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ABSTRACT

Objective: The coronavirus disease-2019 (COVID-19) pandemic led to widespread public health measures that reduced human-to-human contact. This study investigates the pandemic's effect on the clinical and pathological outcomes of *Helicobacter pylori* (HP) infection in patients with dyspeptic complaints.

Material and Methods: We retrospectively analyzed data from patients presenting with dyspepsia before the pandemic (January-December 2019) and during the pandemic (April-December 2020). Gastric biopsies were evaluated for HP infection and inflammation severity according to the Sydney classification. Statistical analyses compared the incidence and clinical characteristics of HP infection between the two periods.

Results: Among 788 patients, there was no significant difference in HP infection incidence or severity between the pre-pandemic and pandemic periods ($p=0.51$). However, more symptomatic patients presented during the pandemic, including increased cases of epigastric pain ($p<0.01$) and gastroesophageal reflux ($p<0.001$).

Conclusion: Despite social distancing measures, the incidence of HP infection remained unchanged. Our findings suggest that COVID-19 restrictions did not significantly impact HP transmission but may have influenced symptom presentation and patient healthcare-seeking behavior.

Keywords: COVID-19, gastritis, dyspepsia, *Helicobacter pylori*, hiatal hernia

INTRODUCTION

The coronavirus disease-2019 (COVID-19), identified in December 2019 in Wuhan, China, rapidly became a global pandemic, causing significant morbidity and mortality (1,2). Transmission occurs primarily in crowded areas, leading to widespread quarantine measures. *Helicobacter pylori* (HP), an infectious pathogen associated with gastritis, is transmitted through fecal-oral or oro-oral routes, often in public settings such as cafes and restaurants. Studies suggest its transmission is mainly interhuman and intrafamilial. The course of gastrointestinal (GI) diseases caused by HP is associated with many virulent factors, such as outer membrane porin proteins, flagella, and different adherence factors. They enable colonization and escape from the immune response. HP increases the expression of angiotensin-converting enzyme-2 (ACE-2) receptors in the GI tract, which is directly associated with the duration and severity of infection (3-7). The pandemic's restrictions on social interactions and dining out, in turn, raised questions about the restrictions' impact on HP transmission.

According to a cross-sectional analysis based on the population in Türkiye, more than 4600 people were tested, and a prevalence of 82.5% of the tested condition was found. In addition, the prevalence was lowest among individuals living in the southern part of the country, which has a citrus-rich diet and is the main citrus-growing area (8).

With the quarantine measures, human-to-human contact and food consumption in restaurants have decreased. Public spots have been prepared to encourage hand washing to increase personal hygiene. This strategy is based on the thought that it may restrict HP transmission routes.

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This study aimed to reveal whether there was a difference in HP incidence detected in gastroscopies performed on patients with dyspeptic complaints between the pandemic and pre-pandemic periods.

MATERIAL and METHODS

For the study, the date of March 2020, when the COVID-19 pandemic was announced in our country, was determined as a cut-off in determining the two groups to be compared. All patients with dyspeptic complaints who underwent gastroscopy in the endoscopy unit of Marmara University Pendik Training and Research Hospital General Surgery Department, İstanbul, Türkiye between January-December 2019 and April-December 2020 were included in the study. The patients' data in two groups were obtained retrospectively from the hospital management system electronically. Along with the patients' general demographic data, endoscopic diagnosis, pathological diagnosis, and *HP* infection severity were examined separately. The study was approved by the Marmara University Scientific Research Ethics Committee (number: 09.2024.802, date: 19.02.2024). During the study, all procedures were carried out according to the principles of the Declaration of Helsinki.

All patients were evaluated for manifestations of *HP* infection, severity of the course according to Sydney pathological criteria, and outcome of the disease process.

Patients aged 18 and older who were admitted to the endoscopy unit with dyspepsia were included in the study. Endoscopy was not performed in elective patients who were actively COVID-19-positive due to the risk of transmission. Clinical characteristics and pathological results before the pandemic (BP) were compared with patients admitted during the COVID-19 pandemic. Patients were also examined for age and gender. Endoscopic biopsy samples were transferred to the pathology laboratory under appropriate conditions. The results were evaluated according to the Sydney classification and grading system of gastritis for diagnosis (9). Criteria such as *HP* inclusion according to the Sydney system, chronic inflammation, neutrophil activity, glandular atrophy, and intestinal metaplasia were included in the pathological examination. All patients in the study, before and during the COVID-19 pandemic, were examined clinically for dyspeptic complaints (epigastric pain, gastric burn, reflux symptoms) and pathologically for the presence of gastric inflammation caused by *HP* infection, and the results were recorded. The severity of the disease in patients was graded as +, ++, +++ if *HP* inclusion was detected in biopsy materials.

Assuming 80% sensitivity/specificity, the required sample size was 264 to keep the 95% confidence interval within $\pm 5\%$. Assuming the prevalence of *HP* as 50% (estimated at 55.8% in China), the total sample size was calculated to be 528.

Statistical Analysis

Parametric tests were used without the normality test due to the sample size, as justified by the Central Limit Theorem. In the analysis of the data, the mean and standard deviation, minimum and maximum values of the features, the frequency, and the percentage values were used to define categorical variables. Student's t-test was used to compare the means of two independent groups. Chi-square test statistics were used to evaluate the relationship between categorical variables. The Mann-Whitney U test statistic was used to compare the ordinal variable of the histopathological examination. The statistical significance level of the data was set at $p < 0.05$. In the data evaluation, www.e-picos.com, New York software and MedCalc statistical package program were used.

RESULTS

Pathological examination confirmed that gastric inflammation and infection severity were strongly associated with *HP* presence, aligning with established literature on *HP*-related gastritis. A total of 788 patients, 434 BP (January-December 2019) and 354 during the pandemic period (P) (April-December), were included in the study. The age range was 18-85 in the BP group and 18-86 in the P group. The median age was 48 years ($p = 0.37$). There were 265 women (61.1%) and 169 men (39.9%) in the BP group, and 195 women (55.1%) and 159 men (44.9%) in the P group ($p = 0.09$). In the upper GI endoscopic examination, 71 patients (16.4%) were diagnosed with active gastritis, 212 patients (48.8%) with chronic gastritis, and 152 patients (35.1%) with chronic-active gastritis in the BP group. In the P group, 67 patients (18.9%) were diagnosed with active gastritis, 151 patients (42.7%) were diagnosed with chronic gastritis, and 136 patients (38.4%) were diagnosed with chronic-active gastritis. It is observed that the number of patients with chronic gastritis has decreased, and some of them have experienced an increase in symptoms or complications during the pandemic period. A significant difference was found between the groups ($p < 0.01$) (Table 1).

In the endoscopic examination, 35 patients in the BP group and 36 patients in the P group were diagnosed with alkaline reflux gastritis ($p = 0.25$). Hiatal hernias were detected in 143 patients in the BP group and 143 in the P group ($p = 0.03$). In addition, when the hiatal hernia grade was considered, four patients in the BP group were evaluated as grade 1, 53 patients, as grade 2, 51 patients, as grade 3, and 35 patients as grade 4. In the P group, 21, 72, 35, and 15 patients were evaluated as grades 1, 2, 3 and 4, respectively ($p < 0.001$). However, there was no significant difference between groups. More symptomatic patients were admitted during the pandemic, and endoscopies were performed on them. Despite this, the frequency of *HP* was found to be similar between groups. Although more symptomatic patients were treated, the number of patients diagnosed with

hiatal insufficiency was higher during the pandemic period. However, when the hiatal hernias were evaluated according to the grading system, a significant difference was observed, especially in grade 1 patients.

Considering the symptoms, the number of patients presenting with epigastric pain was 186 (42.9%) in the BP group and 181 (51.1%) in the P group ($p<0.01$). In the BP group, 131 individuals (30.2%) presented with gastroesophageal reflux, and in the P group, 149 individuals (42.1%) presented with gastroesophageal reflux ($p<0.001$). The number of applicants with gastric burning complaints was 82 (18.9%) in the BP group and 111 (31.4%) in the P group ($p<0.001$). In terms of dyspepsia, there were 193 (44.5%) patients in the BP group and 209 (59.1%) patients in the P group ($p<0.001$) (Table 1).

We observed that 131 patients were admitted to our hospital with complaints of gastroesophageal reflux, 82 patients with

complaints of gastric burn, and 193 patients with complaints of dyspepsia. The P group determined these numbers as 181, 149, 111, and 209, respectively. There was a statistically significant difference between the groups ($p<0.001$). When the histopathological examination results were analysed, chronic inflammation was found in 423 patients in the BP group and 345 patients in the P group ($p=0.99$). Neutrophil activity was detected among 216 and 212 patients ($p=0.007$); glandular atrophy among 14 and 11 patients ($p=0.92$); and intestinal metaplasia among 28 and 24 patients ($p=0.84$) in the BP and P groups, respectively. *HP* was observed in 225 patients in the BP group and 191 in the P group ($p=0.51$) (Table 2).

The incidence of *HP* was 52.9%. In the histopathological evaluation according to the Sydney system, no significant difference was observed between the groups in the degree of chronic inflammation, neutrophil activity, glandular atrophy, intestinal atrophy, and *HP*. We observed 141 low, 175 medium,

Table 1. The effect of the pandemic process on the patient's socio-demographic and clinical status

N=788	Total	Pre-pandemic (n=434)	Pandemic (n=354)	p-value
	$\bar{x} \pm SD$	$\bar{x} \pm SD$	$\bar{x} \pm SD$	
Age	48.6±13.9	48.9±14.4	48.1±13.4	0.37
	n (%)	n (%)	n (%)	
Gender				
Male	460 (58.4)	265 (61.1)	195 (55.1)	0,09
Female	328 (41.6)	169 (39.9)	159 (44.9)	
Pathological diagnosis				
Active	147 (18.7)	71 (16.4)	67 (18.9)	<0.01
Chronic	330 (41.9)	212 (48.8)	151 (42.7)	
Chronic-active	311 (39.4)	152 (35.1)	136 (38.4)	
Alkaline reflux				
+	70 (8.9)	34 (7.8)	36 (10.2)	0.25
-	718 (91.1)	400 (82.2)	318 (89.8)	
Hiatal hernia				
+	286 (36.3)	143 (32.9)	143 (40.4)	0.03
-	502 (63.7)	291 (67.1)	211 (59.6)	
Hiatal hernia grade				
Grade I	25 (8.7)	4 (2.8)	21 (14.7)	<0.001
Grade II	125 (43.7)	53 (37.1)	72 (50.4)	
Grade III	86 (30.1)	51 (35.7)	35 (24.4)	
Grade IV	50 (17.5)	35 (24.4)	15 (10.5)	
Symptoms				
Epigastric pain	367 (46.6)	186 (42.9)	181 (51.1)	<0.01
Reflux	280 (35.5)	131 (30.2)	149 (42.1)	<0.001
Gastric burn	193 (24.5)	82 (18.9)	111 (31.4)	<0.001
Dyspepsia	402 (51.0)	193 (44.5)	209 (59.1)	<0.001
SD: Standard deviation.				

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and 101 high *HP* intensity in total. There was no significant difference between the groups we evaluated according to *HP* intensity (Table 3).

The presence of *HP* was not significantly different between patients before and during the pandemic ($p=0.51$). We observed that dyspeptic complaints like abdominal pain, gastric burn, and reflux were related to *HP* and its effects on gastric mucosa as reported in the literature. We know that the presence of *HP* infection in the gastric mucosa correlates with dyspeptic complaints and affects the clinical course of the disease. Our results suggest that, pandemic limitations associated with COVID-19 precautions did not significantly decrease the presence of *HP* infection.

DISCUSSION

In December 2019, a new type of COVID-19 was detected in Wuhan, China. COVID-19 infection has become a pandemic shortly after its identification in December 2019 and is responsible for the deaths of many people all over the world and in Türkiye. Patients came up with symptoms like fever, dry cough, dyspnea, pneumonia, headache, loss of taste/smell, and abdominal pain. It has been reported that the virus may enter the cell and increase intestinal permeability and intestinal inflammation. The virus was transmitted via respiratory means, especially in crowded areas.

Table 2. Evaluation of the presence of histopathological changes

N=788	Total	Pre-pandemic (n=434)	Pandemic (n=354)	p-value
	n (%)	n (%)	n (%)	
Chronic inflammation	768 (97.4)	423 (97.4)	345 (97.4)	0.99
Neutrophil activity	428 (54.3)	216 (49.8)	212 (59.9)	0.007
Glandular atrophy	25 (3.2)	14 (3.2)	11 (3.1)	0.92
Intestinal metaplasia	52 (6.6)	28 (6.4)	24 (6.8)	0.84
<i>Helicobacter pylori</i>	417 (52.9)	225 (52.1)	191 (53.9)	0.51

Table 3. Histopathological evaluation according to the Sydney system

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N=788	Total	Pre-pandemic (n=434)	Pandemic (n=354)	p-value
	n (%)	n (%)	n (%)	
Chronic inflammation				
Low	345 (44.9)	179 (42.3)	166 (48.1)	0.20
Medium	290 (37.8)	171 (40.4)	119 (34.5)	
High	133 (17.3)	73 (17.3)	60 (17.4)	
Neutrophile acitivity				
<1/3	253 (57.2)	153 (58.4)	100 (55.5)	0.79
1/3-2/3	186 (42.1)	107 (40.8)	79 (43.9)	
>2/3	3 (0.7)	2 (0.8)	1 (0.6)	
Glandular atrophy				
Low	23 (92)	13 (92.9)	10 (90.9)	0.99
Medium	2 (8)	1 (7.1)	1 (9.1)	
High	-	-	-	
Intestinal metaplasia				
<1/3	47 (90.4)	24 (85.7)	23 (95.8)	0.36
1/3-2/3	5 (9.6)	4 (14.3)	1 (4.2)	
>2/3	-	-	-	
Helicobacter pylori				
Low	141 (33.8)	70 (30.9)	71 (37.2)	0.37
Medium	175 (41.9)	97 (42.9)	78 (40.8)	
High	101 (24.3)	59 (26.2)	42 (22)	

HP is a highly contagious pathogen detected in gastritis and peptic ulcer cases. It has been suggested that chronic inflammation caused by *HP* and its toxins may play a role in the pathogenesis of gastric inflammation. *HP* is transmitted in crowded areas like households, cafes, restaurants, and other similar places. Food consumption in common areas decreased with quarantine (1,2,7,10-14).

Possible transmission routes include oral-oral and fecal-oral transmission during episodes of diarrhea or vomiting. The use of contaminated municipal tap water is also suspected of being responsible for the transmission of *HP*. *HP* has been observed to be higher within families that use non-flush toilets, outdoor toilets, outdoor water taps, and river water. Gender and age do not seem to be associated with an increased risk of infection. Indeed, living in a rural area, living in crowded homes, and having contaminated drinking water sources were risk factors for *HP* infection (8,15-22).

A meta-analysis of 18 studies revealed that endoscopy is suitable for managing dyspeptic patients. Novel endoscopic techniques enable endoscopists to observe the gastric mucosa's microscopic structures and cellular morphology in real time (23-25).

The researchers reported that the virus uses ACE-2 receptors to enter the cell. We know that these receptors are widely expressed in the intestine, and *HP* increases the expression of ACE-2 receptors in the GI tract. GI symptoms such as abdominal pain and diarrhea correlated with the presence of *HP* in COVID-19 patients (13,14).

We examined the relationship between *HP* and the COVID-19 pandemic. All patients were evaluated for signs of *HP* infection. The pathological findings in the gastric mucosa were investigated according to the Sydney classification. We assumed there might be a decrease in *HP* rates due to the social restrictions during the COVID-19 pandemic, but there was no significant difference. Our findings contrast with some prior studies; for instance, Xu et al. (26) reported a decline in *HP* infection rates during the pandemic, whereas our study found no significant change. This discrepancy may reflect differences in population demographics, hygiene compliance, or the predominance of intrafamilial transmission in our cohort, which could be less affected by broad social restrictions. It was observed that the COVID-19 pandemic did not significantly reduce the number of patients with dyspepsia, epigastric pain, gastric burn, and gastroesophageal reflux. The pathological findings due to *HP* infection were similar between periods. The results could not clearly distinguish the clinical differences between mild, moderate, or severe *HP* infection. The detection rate of hiatal hernia (especially grade 1) was high, and more gastric burning and reflux symptoms were observed in patients who underwent endoscopy during the pandemic. The increased detection of hiatal hernias during the pandemic, particularly grade 1, may reflect

heightened healthcare-seeking behavior among symptomatic patients or prolonged exposure to reflux-aggravating factors (e.g., stress, dietary changes) during lockdowns. However, no direct causal relationship with *HP* infection was observed.

Acute and chronic immune stimulation and abnormal response to *HP*, and toxins are the basis of the dyspeptic complaints. Proton pump inhibitors (PPIs) are mostly used for the clinical management of digestive symptoms and as part of *HP* eradication therapy. Recent studies have shown that the use of PPIs increases the susceptibility to severe acute respiratory syndrome-coronavirus-2 infection and influences the risk of developing severe clinical outcomes. *HP* eradication therapy should be administered, and the results should be considered afterwards (3,4,10,27,28).

Household hygiene and staying away from crowded areas may play important roles in preventing the transmission of *HP*. Considering the widespread distribution of *HP* infection, more efforts are necessary. To understand the true scope of the pathophysiology of infection, focusing on GI manifestations.

Study Limitations

We acknowledge that our study has some limitations. Symptoms such as indigestion, heartburn, and reflux may vary depending on the sociocultural characteristics of the patients. The way symptoms are recorded may vary according to the physicians. The patients who underwent endoscopy during the pandemic were selected because they would be more symptomatic, indicating that asymptomatic *HP* infections during the pandemic would be more than those during the pre-pandemic period. Finally, it is not known whether the patients took any medication for dyspeptic complaints before and during the pandemic.

CONCLUSION

Our results revealed that gastric inflammation are strongly correlated with the presence of *HP* and may cause symptoms like epigastric pain, gastric burn, and gastroesophageal reflux. It was thought that dyspeptic complaints and *HP* infection in the gastric mucosa, may have decreased because of the measures taken due to the COVID-19 pandemic, but no significant difference was detected between the two groups in the upper GI tract endoscopies performed before and during the pandemic. In other words, the COVID-19 pandemic did not significantly reduce the spread of *HP*. Although we know much about *HP* today, investigating the underlying factors of GI complaints due to *HP* activity is crucial.

Ethics

Ethics Committee Approval: The study was approved by the Marmara University Scientific Research Ethics Committee (number: 09.2024.802, date: 19.02.2024). During the study, all procedures were carried out according to the principles of the Declaration of Helsinki.

Informed Consent: Informed consent was obtained.

Footnotes

Author Contributions

Concept - E.P., A.C.E., A.C.; Design - E.P., A.C.E., A.C.; Data Collection or Processing - E.P., Ç.A.Ç.; Analysis or Interpretation - A.C.E., Ş.C.Y.; Literature Search - A.C., Ş.C.Y.; Writing - E.P., A.C.E., Ç.A.Ç.

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