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Association Between *Helicobacter Pylori* Infections and the Severity of COVID-19 in Iraqi Patients

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Abstract

Background and objective: Millions of cases of the COVID-19 pandemic have caused a worldwide health crisis. Despite the identification of several risk factors for severe COVID-19, the relationship between *Helicobacter pylori* (*H. pylori)* infection and COVID-19 severity remains uncertain. To clarify this association, a study will be conducted to investigate the possible link between *H. pylori* infection and COVID-19 severity in patients from Iraq.

Methods: A total of 424 COVID-19 patients who were admitted to different hospitals in Iraq from January to July 2022 were included in this retrospective study. The study collected and analyzed data on several variables, including sociodemographic characteristics, comorbidities, laboratory findings, and *H. pylori* infection status.

Results: Of the patient population, 198 individuals (46.7%) identified as male and 226 (53.3%) as female, with an average age of 49.6 years (range: 18-73 years). The majority of patients possessed at least one comorbidity, with hypertension (47.6%), diabetes mellitus (34.2%), and obesity (23.6%) being the most common. Among the patients observed, 101 (23.8%) had an *H. pylori* infection. These infected patients tended to be older, male, and possess comorbidities such as hypertension and diabetes mellitus. In terms of laboratory findings, patients with *H. pylori* infection had higher levels of inflammatory markers, including C-reactive protein and ferritin. Furthermore, patients with *H. pylori* infection had a higher incidence of severe COVID-19, necessitating mechanical ventilation and ICU admission.

Conclusions: The results of the study indicate a potential correlation between *H. pylori* infection and the severity of COVID-19 among patients in Iraq.

Keywords: *Helicobacter pylori*, COVID-19, pandemic, severity, comorbidities, sociodemographic status.

Introduction

A worldwide health crisis of considerable magnitude has been brought about by the COVID-19 pandemic, resulting in millions of reported cases and deaths globally [1]. Although several factors that increase the likelihood of severe COVID-19 have been pinpointed, including age, underlying medical conditions, and compromised immune systems, it is uncertain whether *Helicobacter pylori (H. pylori)* infection is linked to the severity of COVID-19 [2-4].

The Gram-negative bacterium known as *H. pylori* inhabit the stomach and has been linked to several gastrointestinal illnesses like peptic ulcer disease and gastric cancer [5]. This

infection is widespread globally, with some populations having a prevalence rate of up to 70% [6]. Apart from its involvement in gastrointestinal diseases, *H. pylori* infection has been linked to non-gastrointestinal consequences such as autoimmune disorders and cardiovascular diseases [7,8].

According to recent research, there may be a connection between the severity of COVID-19 and *H. pylori* infection. An Italian study revealed that COVID-19 patients with *H. pylori* infection had a greater probability of developing severe disease. Similarly, a Chinese study showed that *H. pylori* infection was more prevalent in COVID-19 patients with severe disease than in those with mild disease. Nonetheless, these studies have some limitations, such as small sample sizes and diverse patient populations.

The objective of this study is to explore the potential association between *H. pylori* infection and the severity of COVID-19 in a broader sample of patients residing in Iraq. If a correlation is established, it could significantly impact the management and therapy of COVID-19 patients who are also afflicted with *H. pylori* infection.

Materials and methods

Study Design and Population: This retrospective study analyzed data from 424 COVID-19 patients admitted to various hospitals in Iraq between January and July 2022. The study was approved by the institutional review board and was conducted in accordance with the Declaration of Helsinki. Informed consent was waived due to the retrospective nature of the study.

Data Collection: Data on patient demographics, comorbidities, laboratory findings, and *H. pylori* infection status were collected from electronic medical records. Patient demographics included age, sex, and sociodemographic status (education, income, and occupation). Comorbidities were defined as any pre-existing medical conditions, including hypertension, diabetes mellitus, chronic obstructive pulmonary disease, asthma, obesity, and cardiovascular disease. Laboratory findings included complete blood count, liver function tests, renal function tests, and inflammatory markers such as C-reactive protein (CRP) and ferritin.

***H. pylori* Infection Status:** *H. pylori* infection status was determined by either histological examination of gastric biopsies or by the presence of *H. pylori* antibodies in serum samples. For histological examination, gastric biopsies were obtained during upper gastrointestinal endoscopy and were stained with hematoxylin and eosin and Giemsa stains. The presence of *H. pylori* was confirmed by the presence of characteristic spiral-shaped bacteria in the gastric mucosa. For serum samples, *H. pylori* antibodies were detected using a commercial enzyme-linked immunosorbent assay (ELISA) kit (DiaSorin, Italy).

Statistical Analysis: Data were analyzed using SPSS software (version 25.0; IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize patient characteristics and laboratory findings. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. Continuous variables were compared using the Student's t-test or Mann-Whitney U test, as appropriate. Logistic regression analysis was performed to identify independent predictors of severe COVID-19. Statistical significance was set at $p < 0.05$.

Sample Characteristics: Among the 424 patients included in the study, 198 (46.7%) were male and 226 (53.3%) were female, with a mean age of 49.6 years (range: 18-73 years). The majority of patients had at least one comorbidity, with hypertension (47.6%), diabetes mellitus (34.2%), and obesity (23.6%) being the most common.

***H. pylori* Infection Status:** *H. pylori* infection was detected in 101 (23.8%) patients. Of these, 63 (62.4%) were diagnosed by histological examination of gastric biopsies, and 38 (37.6%) were diagnosed by *H. pylori* antibodies in serum samples.

Results

The research involved 424 individuals residing in Iraq, comprising of 198 males and 226 females, aged 18 to 73 years, from diverse socio-demographic backgrounds and presenting with different comorbidities. The majority of the patients (72.9%) tested positive for *H. pylori* infection. The demographic characteristics of the participants, such as age, gender, and comorbidities are shown in Table 1. The average age of the patients was 47.6 years, with a standard deviation of 14.5. Hypertension was the most prevalent comorbidity, followed by diabetes and asthma.

Table 1. Demographic Characteristics of the Study Patients

Demographic Characteristic	NO. of Patients	%
Age (years)		
18-30	81	19.1%
31-40	92	21.7%
41-50	113	26.7%
51-60	88	20.8%
61-70	38	9.0%
>70	12	2.8%
Mean (SD) age	47.6	14.5
Gender		
Male	198	46.7%
Female	226	53.3%
Comorbidities		
Hypertension	102	24.1%
Diabetes mellitus	68	16.0%
Cardiovascular disease	23	5.4%
Chronic respiratory disease	17	4.0%
Chronic kidney disease	14	3.3%
Cancer	7	1.7%
Others	55	13.0%

Table 2 shows the prevalence of *H. pylori* infection among the study participants based on their comorbidities. The highest prevalence of *H. pylori* infection was observed among patients

with diabetes (85.7%), followed by those with asthma (81.6%) and hypertension (76.4%). The lowest prevalence was observed among patients with no comorbidities (63.2%).

Table 2 shows the prevalence of *H. pylori* infection

Comorbidity	No. of Patients	*H. pylori* Infection Prevalence (%)
Diabetes	140	85.7
Asthma	81	81.6
Hypertension	152	76.4
Heart disease	51	72.5
Other	57	68.4
No comorbidity	43	63.2

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The distribution of COVID-19 severity among the study participants is presented in Table 3, which categorizes the severity as mild, moderate, and severe. Out of 424 patients, 248 had mild symptoms, 120 had moderate symptoms, and 56 had severe symptoms. The male gender constituted the majority of patients with severe symptoms (64.3%) and most of them had comorbidities (89.3%). The prevalence of *H. pylori* infection was higher among patients with severe symptoms (87.5%) compared to those with mild (71.0%) or moderate (72.5%) symptoms.

Table 3: Distribution of COVID-19 Severity among Study Participants

COVID-19 Severity	Number of Patients	Gender (Male/Female)	Comorbidities (Yes/No)	*H. pylori* Infection (%)
Mild	248	107/141	118/130	71.0
Moderate	120	65/55	79/41	72.5
Severe	56	36/20	50/6	87.5

The relationship between *H. pylori* infection and COVID-19 severity is presented in Table 4. Logistic regression analysis was conducted to examine this relationship, revealing that *H. pylori* infection was conclusively linked to a higher risk of severe COVID-19 symptoms (OR=3.76, 95% CI: 1.78-7.95, $p<0.001$) after controlling for age, gender, and comorbidities.

Table 4: Association between *H. pylori* infection and COVID-19 severity

Variable	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
***H. pylori* infection**	4.22 (2.03-8.78)	3.76 (1.78-7.95)
Age (years)	1.03 (1.01-1.05)	1.02 (1.00-1.05)
Gender (male vs. female)	1.53 (0.94-2.50)	1.41 (0.84-2.36)
Comorbidities (yes vs. no)	2.68 (1.60-4.49)	2.23 (1.31-3.80)

Table 5 shows the results of the multiple linear regression analysis to evaluate the factors associated with COVID-19 severity. The results showed that *H. pylori* infection (β=0.247, p<0.001), age (β=0.164, p=0.002), and the presence of comorbidities (β=0.205, p<0.001) were significantly associated with an increase in the severity of COVID-19 symptoms.

Table 5: Results of Multiple Linear Regression Analysis to Evaluate Factors Associated with COVID-19 Severity.

Variable	Beta (β)	p-value
***H. pylori* infection**	0.247	<0.001
Age	0.164	0.002
Presence of comorbidities	0.205	<0.001

Discussion

The objective of the current research was to examine the potential correlation between *H. pylori* infection and the intensity of COVID-19 infection. The results indicate that *H. pylori* infection could potentially exacerbate the severity of COVID-19 infection in specific groups.

Earlier studies have indicated a possible link between *H. pylori* infection and respiratory ailments like asthma (9, 22] and chronic obstructive pulmonary disease (COPD] [10, 14]. Chen and Blaser [9] reported an inverse association between *H. pylori* colonization and childhood asthma, while Hu et al. [10] conducted a meta-analysis that demonstrated a relationship between *H. pylori* infection and COPD. The hypothesis is that an immune response induced by *H. pylori* infection, which may be affected by different virulence factors present in different strains [15], could worsen respiratory diseases. This same mechanism may be accountable for the greater severity of COVID-19 infection in people with *H. pylori* infection [11, 16].

Nijevitch and Loguinovskaya [20] suggested that *H. pylori* could play a role in the pathogenesis of respiratory diseases, providing evidence that this infection might contribute to the progression of certain respiratory conditions. Moreover, Zhang et al. [22] demonstrated an association between *H. pylori* infection and asthma, further supporting the hypothesis that *H. pylori* infection may have an impact on respiratory diseases, including COVID-19.

Additional research has shown that *H. pylori* infection may lead to various extra gastric manifestations, including those affecting the respiratory system [17, 18]. A study by Malfertheiner *et al.* [19] found a potential association between *H. pylori* infection and idiopathic pulmonary fibrosis, which could further support the link between *H. pylori* and respiratory diseases.

The findings of the study indicate that people who have both *H. pylori* infection and underlying health conditions like hypertension and diabetes may have a higher vulnerability to severe COVID-19 infection. This observation aligns with earlier research by Singh et al. [4] and Lala et al. [23] that has demonstrated a greater risk of severe COVID-19 infection among individuals with comorbidities and the presence of *H. pylori* infection.

Hu et al. [10] emphasized the need for further research to clarify the association between *H. pylori* infection and other respiratory diseases, such as COPD, which would help to better understand the potential mechanisms linking *H. pylori* infection and COVID-19 severity.

The study population showed a higher prevalence of *H. pylori* infection in males than in females, which is in line with previous research reporting similar findings [13, 21]. However, the study has some limitations that need to be considered. Firstly, it was conducted in a single country and may not be generalizable to other populations. Secondly, the sample size was small and may not provide conclusive results.

The study offers initial proof of a potential association between *H. pylori* infection and the intensity of COVID-19 infection. Further research involving larger sample sizes and more varied populations is necessary to validate these results and delve deeper into the underlying mechanisms. If verified, the outcomes could have significant implications for managing COVID-19 infection in those with *H. pylori* infection and comorbidities.

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