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Eradication of H. Pylori during COVID pandemic based on treatment regimens

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ABSTRACT

Introduction: During the Coronavirus Disease 2019 (COVID-19) pandemic, widespread vaccination efforts played a critical role in controlling the global health crisis, yet the long-term effects of these vaccines remain unclear. Helicobacter pylori (HP) infections, which can worsen under altered gastric mucosal defenses, pose significant challenges during this period. This study aims to explore the impact of COVID-19 vaccination history on HP eradication success, comparing outcomes between standard triple therapy (TT) and quadruple therapy (QT) with bismuth supplementation.

Materials and Methods: 116 patients diagnosed with Helicobacter pylori via gastroscopic biopsies between January 2020 and December 2021 included. Patients were divided into two groups based on eradication therapy: standard TT and QT. Treatment regimens lasted two weeks, followed by six weeks of PPI use, and eradication was evaluated through stool antigen tests or control gastroscopy. Demographic data, comorbidities, COVID-19 history, vaccination status, and treatment side effects were recorded.

Results: The treatment success rate was 81.5% in the TT group and 96% in the QT group (p=0.017). Nonsmokers demonstrated significantly higher treatment success compared to smokers (71.4% vs. 31.3%; p=0.003). Similarly, patients with a history of COVID-19 infection had lower treatment response rates compared to those without (28.5% vs. 7.8%; p=0.017). Multivariate regression analysis identified receiving TT (OR: 5.547, p=0.033), smoking (OR: 5.226, p=0.019), and a history of COVID-19 infection (OR: 4.712, p=0.042) as independent risk factors for eradication failure.

Conclusion: It was demonstrated that the types and doses of COVID-19 vaccines didn't influence HP eradication outcomes. However, patients with a history of COVID-19 infection exhibited resistance to eradication treatments comparable to those who smoked or didn't receive bismuth-based therapy. For patients with a history of COVID-19, the selection of eradication treatment should be determined in consideration of other risk factors.

Keywords: COVID-19, helicobacter pylori, gastritis, peptic ulcus, quadriple eradication therapy

Introduction

During the Coronavirus 2019 Disease (COVID-19) pandemic, one of the most crucial steps in treatment and immunity worldwide was achieved following the widespread implementation of vaccination programs. During this period, numerous vaccines utilizing different mechanisms were developed and made available. However, these vaccines were introduced to the market without long-term outcomes being established, given the global urgency.[1]

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In the presence of diminished mucosal defense responses and increased acid levels, the gastric mucosa may develop ulcers, experience bleeding, and show an increase in Helicobacter pylori (HP) infestations. Numerous mechanisms influence this mucosal response.[2] As is well known, during inflammatory processes triggered by trauma or various stress conditions, changes in hormonal axes make the mucosal integrity of the gastrointestinal system one of the first systems to be affected. This pathophysiological pathway can occur particularly following an acute perfusion disorder (e.g., sepsis, shock) but may also result from various other mechanisms, such as chronic drug use, alterations in the microbiota spectrum, different chronic diseases, and dietary habits, which vary significantly from one another.[3,4]

When studies evaluating HP eradications during the pandemic were examined, a randomized controlled trial (RCT) revealed an increase in clarithromycin and levofloxacin resistance in eradication treatments administered to patients with a history of prior COVID-19 treatment.[5] In another recent RCT, the difference between lansoprazole and vonoprazan in standard quadruple therapy (QT) with proton pump inhibitors was assessed, and no difference was found between the groups in terms of eradication rates. Although this study was published after the pandemic, it did not specify patients' COVID-19 histories or vaccination records.[6] A recent review evaluated HP eradication strategies during the COVID-19 pandemic. Furthermore, it emphasized that HP might lead to extragastric manifestations during the progression of chronic diseases. It was highlighted that further studies are needed to assess long-term outcomes related to HP in patients who had COVID-19 or were vaccinated.[7]

During the pandemic, literature studies evaluating HP eradication following vaccination remain limited. Given the lack of knowledge about the long-term efficacy of vaccines following global vaccination efforts, this study aims to evaluate differences in eradication methods among patients with a history of COVID-19 vaccination who are undergoing HP eradication. Specifically, the study seeks to compare resistance differences between patients receiving standard triple therapy (TT) and those receiving QT where a bismuth preparation is added to the standard protocol.

Materials and Methods

Study Plan and Ethical Approval

The study was initiated by planning to include patients who were diagnosed with Helicobacter pylori through biopsies obtained via gastroscopy at the Endoscopy Unit of Besni State Hospital between January 2020 and December 2021 and subsequently started on eradication therapy. Monocentric data collection began after obtaining ethical approval from the Zonguldak Bülent Ecevit University Faculty of Medicine Ethics Committee on December 16, 2024, with decision number 2024/22/9. As this was a retrospective study, the requirement for informed consent was waived by the ethics committee.

Evaluations and Recorded Data

The records of patients diagnosed with HP through gastroscopic biopsies were reviewed. Among these records, patients who had received eradication therapy were identified. Patients were divided into two groups based on the type of eradication therapy they received. The first group consisted of patients who received standard triple therapy (proton pump inhibitor [PPI], clarithromycin, and amoxicillin)[8], while the second group included those who received quadruple therapy, which involved the addition of bismuth preparations to the standard protocol.[9] In both groups, the treatment regimen consisted of a two-week course of twice-daily PPI and antibiotic therapy (with bismuth therapy added in the QT group), followed by continuous PPI use for the remaining six weeks, as described in other studies.[10,11]

To evaluate eradication, serological stool antigen tests or histological confirmation through control gastroscopy were performed within two months after the completion of treatment, and no later than one year.[12] Patients' demographic data, comorbidities, habits (if any), family or personal history of gastric cancer, history of COVID-19 infection[13], COVID vaccination status and doses[14], and the severity of any side effects experienced[9-11] were assessed using outpatient clinic or preparation records prior to gastroscopy.

Inclusion and Exclusion Criterias

The study included patients over 18 years of age who either participated in the gastroscopy screening program for individuals over 45 years old or presented with dyspeptic complaints that persisted despite two months of

medical treatment and lifestyle modifications. Among these patients, only those diagnosed with HP and who underwent serological or histopathological follow-up after eradication therapy were included in the study.

Patients under 18 years of age, those who did not complete their treatments, those who provided samples earlier than the designated follow-up period, those with incomplete clinicopathological data, those who declined treatment, and those requiring alternative antibiotic regimens due to penicillin allergy, which precluded the use of standard TT or QT protocols, were excluded from the study.

Statistics

Statistical analyses were performed using SPSS software version 27.0 (SPSS Inc., Chicago, IL). The normality of continuous variables was evaluated using the Kolmogorov-Smirnov test. For comparisons of normally distributed variables between independent groups, independent samples t-tests were applied, whereas the Mann-Whitney U test was utilized for variables that did not follow a normal distribution. Associations between categorical variables were analyzed using the chi-square test. Descriptive statistics for continuous variables with a normal distribution were reported as mean±standard deviation, while non-normally distributed variables were summarized as median (interquartile range, 25^{th}–75^{th} percentile). Categorical variables were described as frequencies and percentages. A p-value of less than 0.05 was considered indicative of statistical significance.

Results

A total of 116 patients with complete data who received either standard TT or QT were included in the study. Of these, 65 patients received TT, while 51 received QT. When evaluated based on the eradication regimen, the success rate of treatment was 81.5% in the TT group, compared to 96% in the QT group (p=0.017). Other variables were similarly distributed between the two groups when comparing the treatments (p>0.05) (Table 1).

When patients were evaluated based on treatment success, it was found that non-smokers responded better to treatment compared to smokers (71.4% vs. 31.3%; p=0.003). Additionally, patients with a history of COVID-19 infection had lower treatment response rates (28.5% vs. 7.8%; p=0.017). Other variables related to treatment success were similarly distributed between the groups (p>0.05) (Table 2).

Parameters that showed significant results in the evaluation of treatment regimens and treatment success were included in the regression analysis. It was observed that eradication rates were lower in patients receiving TT compared to those who did not (OR: 5.547, p=0.03). Similarly, treatment failure was more frequent among patients who smoked (OR: 5.469, p=0.007). Additionally, eradication success was found to be significantly lower in patients with a history of COVID-19 (OR: 4.7, p=0.026). A multivariate regression analysis was performed as all three parameters were found to be significant. The analysis demonstrated that receiving TT (OR: 5.547, p=0.033), smoking (OR: 5.226, p=0.019), and a history of COVID-19 infection (OR: 4.712, p=0.042) were independent risk factors for eradication failure (Table 3).

Discussion

This study was conducted to evaluate the impact of a history of COVID-19 infection and the treatment process on the effectiveness of HP eradication during the COVID-19 pandemic. It was found that having had COVID-19 was associated with increased resistance to eradication treatment. In contrast, vaccination history and the number of vaccine doses did not affect HP eradication outcomes. Furthermore, the choice of eradication regimen did not influence treatment effectiveness in patients with a history of COVID-19 infection.

The COVID-19 pandemic has left lasting impacts not only in the field of healthcare but also across various global sectors.[15] Beyond the multisystemic long-term effects of the disease, research continues to investigate the clinical outcomes that have emerged or are expected to emerge following the administration of COVID-19 vaccines.[16,17] Among post-COVID gastrointestinal symptoms, nausea, vomiting, and diarrhea are the most frequently reported. However, the impact of a history of COVID-19 infection or COVID-19 vaccinations on gastrointestinal conditions remains an active area of investigation. In this context, studies linking global issues such as Helicobacter pylori eradication with COVID-19 are limited.[18]

A limited number of studies in the literature have addressed this topic. In a retrospective cohort study by Saeedi et al.[19], COVID-19 patients with and without gastrointestinal symptoms were evaluated. The study demonstrated a higher prevalence of HP in patients with gastrointestinal symptoms. Furthermore, this incidence was reported to be even higher among patients requiring hospitalization.

Table 1. Patients evaluated based on eradication regime

	TTR (n=65) (n, %)	QTR (n=51) (n, %)	p†
Gender			
Female	41 (63.0)	27 (52.9)	0.271
Male	24 (36.9)	24 (47.0)	
DM			
No	56 (86.1)	47 (92.1)	0.309
Yes	9 (13.8)	4 (7.8)	
Hypertension			
No	45 (69.2)	30 (58.8)	0.244
Yes	20 (30.7)	21 (41.1)	
COPD / Asthma			
No	60 (92.3)	47 (92.1)	0.976
Yes	5 (7.6)	4 (7.8)	
Previous HP History			
No	58 (89.2)	41 (80.3)	0.182
Yes	7 (10.7)	10 (16.9)	
Smoking			
No	39 (60.0)	35 (68.6)	0.337
Yes	26 (40.0)	16 (31.3)	
Alcohol			
No	58 (89.2)	45 (88.2)	0.866
Yes	7 (10.7)	6 (11.7)	
COVID Vaccination			
mRNA	19 (29.2)	18 (35.2)	0.230
Inactive	27 (41.5)	25 (49.0)	
Both	19 (29.2)	8 (15.6)	
Vaccination Dosage			
1	44 (67.6)	35 (68.6)	0.715
2	19 (29.2)	13 (25.4)	
3	2 (3.0)	3 (5.8)	
Gastroscopic Diagnosis			
Gastritis With Athrophy	5 (7.6)	5 (9.8)	0.692
Gastritis Without Athrophy	57 (87.6)	42 (82.3)	
Peptic Ulcer	3 (4.6)	4 (7.8)	
Intestinal Metaplasia			
No	50 (76.9)	45 (88.2)	0.116
Yes	15 (23.0)	6 (11.7)	
Alkaline Reflux			
No	58 (89.2)	47 (92.1)	0.593
Yes	7 (10.7)	4 (7.8)	
Polyp			
No	60 (92.3)	49 (96.0)	0.397
Yes	5 (7.6)	2 (3.9)	
Family History for Gastric Cancer			
No	60 (92.3)	46 (90.1)	0.688
Yes	5 (7.6)	5 (9.8)	

Table 1. CONT.

	TTR (n=65) (n, %)	QTR (n=51) (n, %)	p†
Adverse Effects			
Mild	51 (78.4)	37 (72.5)	0.250
Moderate	13 (20.0)	10 (19.6)	
Severe	1 (1.5)	4 (7.8)	
COVID History			
No	59 (90.7)	45 (88.2)	0.656
Yes	6 (9.2)	6 (11.7)	
Eredication			
No	12 (18.4)	2 (3.9)	0.017
Yes	53 (81.5)	49 (96.0)	
	Median (IQR)		**p‡**
Age (years)	39 (36-46)	44 (36-50)	0.517
BMI (kg/m^2)	25 (25-27)	26 (26-27)	0.231

TTR: Triple Treatment Regime; QTR: Quadriple Treatment Regime; DM: Diabetes Mellitus; COPD: Chronic Obstructive Pulmonary Disease; HP: Helicobacter Pylori; COVID: Coronavirus; BMI: Body Mass Index; IQR: Interquartile Range; †: Chi Square Test; ‡: Mann Whitney U Test.

Regarding eradication, only one study was identified in the literature. In a randomized prospective study by Kamal et al.,[5] 270 patients were included to evaluate the efficacy of azithromycin- and levofloxacin-based triple eradication therapies in patients who had recovered from COVID-19 at least three months prior. The study found no significant differences in eradication rates, side effect profiles, treatment completion rates, or demographic characteristics among the patients. In our study, patients receiving standard triple therapy (TT), which included a single type of antibiotic, were compared with those receiving quadruple therapy (QT), where a bismuth preparation was added to the same regimen. It was observed that eradication rates were higher in patients treated with QT. Similarly, eradication therapy was found to be less successful in patients with a history of COVID-19. However, the study demonstrated that a history of COVID-19 did not result in a significant difference between the two treatment regimens.

In our study, no association was found between COVID-19 vaccinations, the number of vaccine doses, and HP eradication success. While there are no existing studies in the literature on this specific topic, it is anticipated that more comprehensive comparisons can be made as the long-term outcomes of these vaccines become available in future publications. Our study also found, consistent with the literature, that smoking was associated with lower HP eradication success compared to patients treated with bismuth-based therapies.

The primary limitation of our study is its retrospective design. The inclusion of a limited number of patients and reliance solely on medical records further constrain the study. Additionally, this approach restricted the detailed evaluation of side effects. However, to the best of our knowledge, this is the first study to evaluate eradication regimens and bismuth preparations in patients with a history of COVID-19 infection and those who received COVID-19 vaccinations.

Conclusion

This study is the first in the literature to evaluate HP eradication in patients with a history of COVID-19 infection and vaccination while comparing TT and QT methods. It was demonstrated that HP eradication was less successful in patients who had recovered from COVID-19; however, this outcome could not be attributed to either treatment regimen. No association was identified between HP eradication and the type or number of COVID-19 vaccinations. Smoking, the use of TT, and a history of COVID-19 infection were identified as risk factors for eradication failure. Future, more comprehensive studies are needed

Table 2. Patients evaluated based on eradication success

	FE (n=14) (n, %)	SE (n=102) (n, %)	p†
Gender			
Female	10 (71.4)	58 (56.8)	0.299
Male	4 (28.5)	44 (43.1)	
DM			
No	12 (85.7)	91 (89.2)	0.697
Yes	2 (14.2)	11 (10.7)	
Hypertension			
No	7 (50.0)	68 (66.6)	0.221
Yes	7 (50.0)	34 (33.3)	
COPD / Asthma			
No	12 (85.7)	95 (93.1)	0.330
Yes	2 (14.2)	7 (6.8)	
Previous HP History			
No	10 (71.4)	89 (87.2)	0.116
Yes	4 (28.5)	13 (12.7)	
Smoking			
No	4 (28.5)	70 (68.6)	0.003
Yes	10 (71.4)	32 (31.3)	
Alcohol			
No	13 (92.8)	90 (88.2)	0.607
Yes	1 (7.1)	12 (11.7)	
COVID Vaccination			
mRNA	3 (21.4)	34 (33.3)	0.445
Inactive	6 (42.8)	46 (45.0)	
Both	5 (35.7)	22 (21.5)	
Vaccination Dosage			
1	9 (64.2)	70 (68.6)	0.576
2	5 (35.7)	27 (26.4)	
3	0 (0.0)	5 (4.9)	
Gastroscopic Diagnosis			
Gastritis With Athrophy	14 (100.0)	85 (83.3)	0.255
Gastritis Without Athrophy	0 (0.0)	7 (6.8)	
Peptic Ulcer	0 (0.0)	10 (9.8)	
Intestinal Metaplasia			
No	9 (64.2)	86 (84.3)	0.068
Yes	5 (35.7)	16 (15.6)	
Alkaline Reflux			
No	11 (78.5)	94 (92.1)	0.104
Yes	3 (21.4)	8 (7.8)	
Polyp			
No	13 (92.8)	96 (94.1)	0.853
Yes	1 (7.1)	6 (5.8)	
Family History for Gastric Cancer			
No	13 (92.8)	93 (91.1)	0.834
Yes	1 (7.1)	9 (8.8)	

Table 2. Cont.

	FE (n=14) (n, %)	SE (n=102) (n, %)	p†
Adverse Effects			
Mild	9 (64.2)	79 (77.4)	0.551
Moderate	4 (28.5)	19 (18.6)	
Severe	1 (7.1)	4 (3.2)	
COVID History			
No	10 (71.4)	94 (92.1)	0.017
Yes	4 (28.5)	8 (7.8)	
	Median (IQR)	**p‡**	
Age (years)	36 (34-46)	41 (37-47)	0.239
BMI (kg/m^2)	25 (25-26)	26 (26-27)	0.089

SE: Succesful Eradication; FE: Failed Eradication; DM: Diabetes Mellitus; COPD: Chronic Obstructive Pulmonary Disease; HP: Helicobacter Pylori; COVID: Coronavirus Disease 2019; BMI: Body Mass Index; IQR: Interquartile Range; †: Chi Square Test; ‡: Mann Whitney U Test.

Table 3. Regression analysis for eradication success

Variables	OR	95% CI	p	OR	95% CI	p
TTR	5.547	1.181-26.045	0.030	5.963	1.160-30.665	0.033
Smoking	5.469	1.594-18.760	0.007	5.226	1.058-25.802	0.019
COVID History	4.700	1.199-18.420	0.026	4.712	1.296-17.127	0.042

TTR: Triple Treatment Regime; COVID: Coronavirus Disease 2019; OR: Odds Ratio; CI: Confidence Interval.

to further elucidate the long-term effects of the COVID-19 pandemic, including disease progression and vaccination programs.

Disclosures

Disclosure: The authors whose names are listed immediately below certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial inter- est (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethics Committee Approval: This study was conducted in accordance with the Declaration of Helsinki, and ethical approval was obtained from the Zonguldak Bülent Ecevit University Faculty of Medicine Ethical Committee (Approval number: 2024/22/9, Date: 11/12/2024).

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