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CO-EXISTENCE OF HELICOBACTER PYLORI IN GASTRIC AND GALLBLADDER MUCOSA IN CHOLECYSTITIS PATIENTS: A CROSS-SECTIONAL STUDY

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Abstract

Background: Helicobacter pylori (H. pylori) is a gram-negative bacterium often linked to gastric conditions, such as gastritis, peptic ulcers, and gastric cancer. Recently, its potential role in biliary diseases, including cholecystitis and cholelithiasis, has been explored. Cholecystectomy remains the standard treatment for cholecystitis, yet the involvement of *H. pylori* in gallbladder pathology is not well understood.

Objective: This study aims to determine the prevalence of *H. pylori* in both gastric and gallbladder mucosa in cholecystitis patients and assess any associations between *H. pylori* infection and demographic factors such as age, gender, smoking status, and body mass index (BMI).

Methods: We conducted a cross-sectional study over one year at King Edward Medical University/ Mayo Hospital, Pakistan in the duration from November, 2023 to April, 2024. A total of 141 patients with diagnosed cholecystitis were enrolled using consecutive sampling. During cholecystectomy, biopsy samples from both gastric and gallbladder mucosa were collected and examined for H. pylori presence using histological and immunohistochemical methods. Patient demographics and clinical history were also collected, and statistical analyses were conducted to evaluate associations between *H. pylori* infection and patient characteristics.

Results: *H. pylori* was found in the gastric mucosa of 53.2% of patients and in the gallbladder mucosa of 17.7%. Co-existence in both sites occurred in 12.1% of patients. Significant associations were noted between *H. pylori* presence in the gastric mucosa and factors like smoking status ($p = 0.04$) and BMI ($p = 0.03$). No significant link was observed between *H. pylori* presence and hypertension or diabetes.

Conclusion: The study shows distinct patterns of *H. pylori* localization in gastric and gallbladder mucosa among cholecystitis patients, with notable demographic associations. These results suggest a limited role for *H. pylori* in gallbladder diseases, emphasizing the need for targeted screening and treatment strategies in areas with high *H. pylori* prevalence.

Keywords: *Helicobacter pylori*, cholecystitis, gastric mucosa, gallbladder mucosa, cross-sectional study, Pakistan.

Introduction

Helicobacter pylori (H. pylori) is a gram-negative bacterium predominantly found in the gastric mucosa and has been associated with a range of gastrointestinal conditions, including gastritis, peptic ulcers, and gastric cancer (1). Recent studies indicate a potential link between *H. pylori* and biliary diseases, such as cholecystitis and cholelithiasis, suggesting its possible involvement in their pathogenesis (2). Cholecystitis, which involves inflammation of the gallbladder and is frequently related to the presence of gallstones, represents a significant global health challenge. The standard treatment for symptomatic cholecystitis is surgical removal of the gallbladder, known as cholecystectomy. Nevertheless, the specific mechanisms underlying gallbladder inflammation and the potential role of infectious agents like *H. pylori* are not yet fully understood (3).

Research exploring the presence of *H. pylori* in the gallbladder mucosa and its potential co-occurrence with gastric infection has yielded inconsistent results. Some studies report a high incidence of *H. pylori* in gallbladder tissues of patients with cholelithiasis, implying a possible association with gallstone formation and gallbladder inflammation (4). In contrast, other studies have detected little to no presence of *H. pylori* in the gallbladder, highlighting the need for further investigation (5). The dual presence of *H. pylori* in both gastric and gallbladder mucosa in cholecystitis patients remains a topic of debate, with its clinical significance still not fully defined (6).

This study seeks to fill this gap by investigating the prevalence of *H. pylori* in both the gastric and gallbladder mucosa of cholecystitis patients in Pakistan. By examining the co-existence of *H. pylori* in these two distinct mucosal environments, the research aims to clarify its potential role in gallbladder inflammation and evaluate its viability as a therapeutic target.

The primary objective is to determine the prevalence of *H. pylori* in the gastric and gallbladder mucosa of cholecystitis patients and to analyze any associations between the presence of the bacterium and demographic factors such as age, gender, body mass index (BMI), smoking status, and comorbidities like hypertension and diabetes.

The outcomes of this study could have significant clinical implications, particularly in regions such as Pakistan where both *H. pylori* infection and cholecystitis are common. By clarifying the relationship between *H. pylori* infections in the stomach and gallbladder, this research could inform screening and treatment strategies for cholecystitis patients, potentially improving patient outcomes and reducing healthcare costs. Furthermore, identifying demographic and clinical predictors of *H. pylori* co-infection could enable clinicians to better tailor interventions, thereby enhancing patient care.

Methods

Study Design:

This research employed a cross-sectional design to investigate the co-existence of *Helicobacter pylori* (*H. pylori*) in the gastric and gallbladder mucosa of patients with cholecystitis. A cross-sectional approach was chosen due to its ability to assess the prevalence of *H. pylori* in both gastric and gallbladder tissues at a single point in time, which is useful for identifying associations and generating hypotheses about potential risk factors within a specified population.

Setting and Centers:

The study was conducted at King Edward Medical University/ Mayo Hospital, Pakistan in the duration from November, 2023 to April, 2024, a prominent tertiary care center that serves a diverse

patient population from various regions. This facility was selected because it treats patients from both urban and rural areas, encompassing different socioeconomic backgrounds. This diversity enhances the generalizability of the study results to the broader population of Pakistan.

Participant Selection:
Patients were recruited using consecutive sampling from those admitted to the General Surgery Department, King Edward Medical University/ Mayo Hospital, Pakistan with a diagnosis of cholecystitis. Inclusion criteria were: (1) adults aged 18 years or older, (2) a confirmed diagnosis of cholecystitis based on clinical symptoms, ultrasonographic findings, and laboratory tests, and (3) willingness to participate with informed consent. Exclusion criteria included: (1) a history of gastric surgery, (2) current use of antibiotics or proton pump inhibitors, (3) known malignancies, and (4) severe comorbid conditions. Consecutive sampling was used to select every eligible patient who met the inclusion criteria until the required sample size was achieved, minimizing selection bias and enhancing the representativeness of the sample.

Intervention Details:
During cholecystectomy, biopsy samples were obtained from both the gastric and gallbladder mucosa of each patient. Gastric biopsies were taken from the antrum, a common site for *H. pylori* colonization, while gallbladder biopsies were collected from the mucosal lining. All procedures were performed under sterile conditions to prevent cross-contamination, with samples preserved in sterile containers with saline and sent to the pathology laboratory for analysis. No additional interventions, such as specific stents or surgical techniques, were utilized beyond the standard cholecystectomy procedures.

Outcomes:
The primary outcome was the detection of *H. pylori* in the gastric and gallbladder mucosa, determined through histological examination and immunohistochemistry. Secondary outcomes included exploring correlations between *H. pylori* co-infection in both sites and patient demographics, such as age, gender, and comorbidities. The study also aimed to identify associations between the presence of *H. pylori* and specific clinical features of cholecystitis.

Data Collection:
Data were collected prospectively using a standardized form to capture patient demographics, clinical history, and histopathological findings. Biopsy samples were processed in the pathology lab, where they were stained with hematoxylin and eosin (H&E) for general histological examination and immunohistochemistry for the detection of *H. pylori*. To ensure data quality and consistency, all histopathological assessments were conducted by two independent pathologists who were blinded to each other's findings. Any discrepancies were resolved by a third senior pathologist.

Sample Size Calculation:
The sample size was determined based on the prevalence of cholelithiasis in Pakistan, reported at 10.2% (7). Using this prevalence rate and the World Health Organization (WHO) sample size calculator, the required sample size was calculated to be 141 patients, with a 95% confidence level and a 5% margin of error. A power analysis confirmed that this sample size would be adequate to detect significant differences in *H. pylori* presence with 80% power, ensuring the study is sufficiently powered to identify meaningful associations.

Statistical Analysis:
Statistical analysis was performed using SPSS version 26.0. Descriptive statistics were used to summarize patient demographics, clinical characteristics, and histopathological findings. The prevalence of *H. pylori* in both gastric and gallbladder mucosa was calculated, and chi-square tests were used to evaluate associations between categorical variables. Logistic regression analysis was

conducted to identify independent predictors of *H. pylori* co-infection in both sites, adjusting for potential confounders such as age, gender, and comorbidities. A Bonferroni correction was applied to account for multiple comparisons, and a p-value of less than 0.05 was considered statistically significant.

Results

A total of 141 patients diagnosed with cholecystitis were enrolled in this cross-sectional study. The participants had a mean age of 48.2 years with a standard deviation of 12.4 years, and their ages ranged from 21 to 75 years. The majority of the study population was female, accounting for 68.8% (N = 97) of the participants, while males comprised 31.2% (N = 44). The median body mass index (BMI) among the participants was 27.4 kg/m², with an interquartile range (IQR) from 24.3 to 30.1 kg/m², suggesting that most individuals in the study were classified as overweight. Table 1 presents a comprehensive overview of the baseline characteristics of the study population, including age, gender distribution, BMI, smoking status, and the prevalence of comorbid conditions such as hypertension and diabetes.

Table 1: Baseline Characteristics of Study Participants

Variable	Total (N = 141)	Female (N = 97)	Male (N = 44)
Age, mean (SD)	48.2 (12.4)	49.1 (11.8)	46.2 (13.5)
BMI, median (IQR), kg/m²	27.4 (24.3-30.1)	27.9 (24.8-30.5)	26.5 (23.7-29.8)
Smoking Status, N (%)			
Non-smoker	105 (74.5)	78 (80.4)	27 (61.4)
Current smoker	36 (25.5)	19 (19.6)	17 (38.6)
Hypertension, N (%)	58 (41.1)	43 (44.3)	15 (34.1)
Diabetes, N (%)	39 (27.7)	30 (30.9)	9 (20.5)

Note: p-values < 0.05 are marked with an asterisk () to indicate statistical significance.

For the primary outcomes, *Helicobacter pylori* (*H. pylori*) was detected in the gastric mucosa of 53.2% of the patients (N = 75), whereas its prevalence in the gallbladder mucosa was significantly lower, found in only 17.7% of the patients (N = 25) (p < 0.001*). Additionally, the co-existence of *H. pylori* in both the gastric and gallbladder mucosa was observed in 12.1% of the patients (N = 17). These findings are visually represented in Figure 1, which shows the distribution of *H. pylori* presence across gastric and gallbladder tissues, highlighting the disparity in prevalence between the two sites.

Figure 1: Prevalence of H. pylori in Gastric and Gallbladder Mucosa

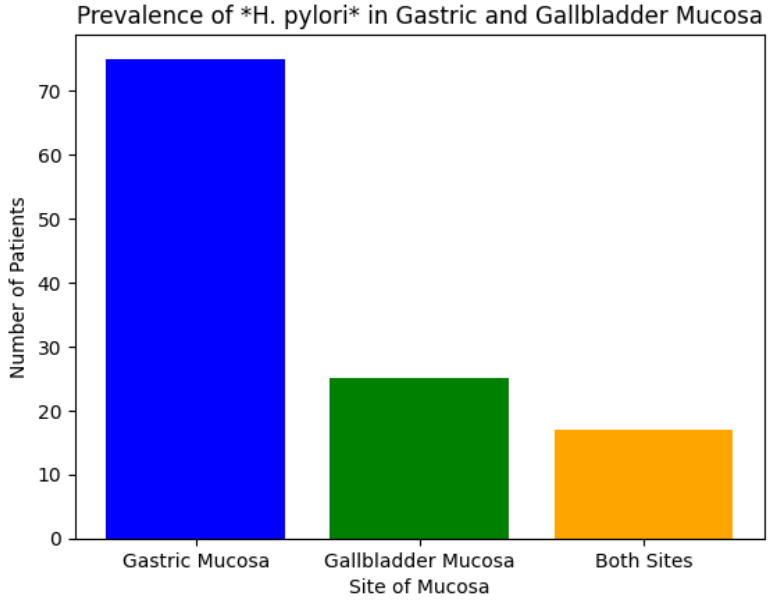

Figure 1 illustrates the prevalence of *H. pylori* in the gastric and gallbladder mucosa among patients with cholecystitis. The figure clearly shows that *H. pylori* is more frequently found in the gastric mucosa compared to the gallbladder mucosa. The relatively low co-existence of *H. pylori* in both sites suggests a distinct localization pattern for the bacterium.

Regarding secondary outcomes, the study examined the correlation between the presence of *H. pylori* and various patient demographic characteristics. A notable finding was the significant association between *H. pylori* presence in the gastric mucosa and smoking status; 66.7% of current smokers were positive for *H. pylori*, compared to 47.6% of non-smokers (p = 0.04*). Furthermore, a higher prevalence of *H. pylori* in the gastric mucosa was observed in patients with a BMI greater than 30 kg/m² (62.5%) compared to those with a BMI below 25 kg/m² (42.9%) (p = 0.03*). Table 2 provides a detailed summary of the associations between *H. pylori* presence and various demographic factors.

Table 2: Association Between H. pylori Presence and Patient Demographics

Demographic Factor	H. pylori Present (N = 75)	H. pylori Absent (N = 66)	p-value
Gender, N (%)			
Female	55 (73.3)	42 (63.6)	0.15
Male	20 (26.7)	24 (36.4)	
Smoking Status, N (%)			
Non-smoker	50 (66.7)	55 (83.3)	0.04*
Current smoker	25 (33.3)	11 (16.7)	
BMI > 30 kg/m², N (%)	30 (62.5)	18 (37.5)	0.03*
Hypertension, N (%)	32 (42.7)	26 (39.4)	0.68
Diabetes, N (%)	20 (26.7)	19 (28.8)	0.79

Note: p-values < 0.05 are marked with an asterisk () to indicate statistical significance.

Further analysis revealed no significant difference in the prevalence of *H. pylori* in the gastric mucosa between patients with and without hypertension or diabetes (p > 0.05). However, a significant association was found between the presence of *H. pylori* in the gallbladder mucosa and increased age. Patients over the age of 50 had a higher prevalence of *H. pylori* in the gallbladder mucosa (23.4%) compared to those under 50 years of age (11.1%) (p = 0.02*). Figure 2 depicts the age distribution of *H. pylori* presence in the gallbladder mucosa, highlighting the increased prevalence among older patients.

Figure 2: Age Distribution of H. pylori Presence in Gallbladder Mucosa

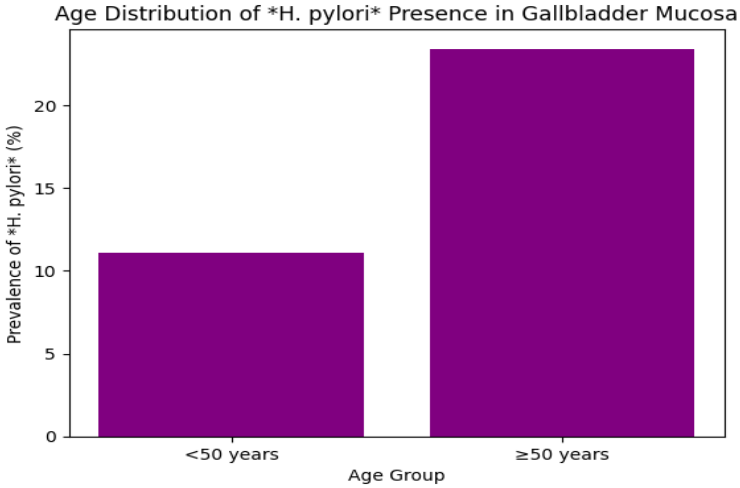

Figure 2 illustrates the prevalence of *H. pylori* in the gallbladder mucosa across different age groups. The figure demonstrates a significantly higher presence of *H. pylori* in the gallbladder mucosa among patients aged 50 years and older compared to those under 50 years, indicating that age is a crucial factor influencing the colonization of *H. pylori* in gallbladder tissues.

Overall, these findings indicate a substantial prevalence of *H. pylori* in the gastric mucosa among cholecystitis patients, with a noteworthy co-existence in the gallbladder mucosa. The observed associations between *H. pylori* presence and demographic factors such as smoking status, BMI, and age highlight the importance of considering these variables in clinical practice. Understanding these associations can aid in the management and prevention of *H. pylori*-related complications, suggesting that targeted strategies based on patient demographics could improve outcomes in cholecystitis patients.

Discussion

This study explored the co-existence of *Helicobacter pylori* (*H. pylori*) in the gastric and gallbladder mucosa of patients with cholecystitis, providing new insights into the bacterium's potential involvement in gallbladder diseases. The findings showed a significantly higher prevalence of *H. pylori* in the gastric mucosa (53.2%) compared to the gallbladder mucosa (17.7%), with a relatively low co-existence rate in both sites (12.1%). These results suggest that *H. pylori* may exhibit distinct colonization patterns in different mucosal tissues.

The prevalence of *H. pylori* in the gastric mucosa observed in this study is consistent with previous research reporting similar infection rates among patients with various gastrointestinal disorders [8]. However, the presence of *H. pylori* in the gallbladder mucosa appears to be less common. For instance, a study by Bohr et al. reported a low prevalence of *Helicobacteraceae* in patients with gallstone disease and gallbladder carcinoma in Germany, with only a small fraction of these patients harboring the bacteria [9].

This contrasts with the 17.7% prevalence found in our study, suggesting that geographical or methodological differences might affect *H. pylori* detection rates in gallbladder tissues. These findings indicate that while *H. pylori* can colonize the gallbladder, its presence is less frequent than in the stomach, potentially due to differences in the tissue environment or immune responses between these sites.

Our study also identified significant associations between the presence of *H. pylori* in the gastric mucosa and demographic factors, such as smoking status and BMI. Notably, current smokers had a higher prevalence of *H. pylori* infection compared to non-smokers, supporting previous findings that smoking can impair gastric mucosal defenses and increase susceptibility to *H. pylori* colonization [10,11].

Moreover, patients with a BMI over 30 kg/m² were more likely to have *H. pylori* in the gastric mucosa, which aligns with studies suggesting a link between obesity and an increased risk of *H. pylori* infection [12,13]. These associations underscore the importance of considering lifestyle and metabolic factors in managing *H. pylori*-related conditions.

Additionally, the higher prevalence of *H. pylori* in the gallbladder mucosa among older patients, as observed in our study, is consistent with existing literature. Wang et al. found that older age is associated with a higher prevalence of *H. pylori* in the gallbladder, possibly due to age-related declines in immune function and mucosal integrity that facilitate bacterial colonization [14].

This suggests that older individuals might be more susceptible to *H. pylori* co-infection in the gallbladder, which could have important implications for managing cholecystitis in elderly populations.

Despite evidence of *H. pylori* presence in both gastric and gallbladder tissues, the clinical significance of this co-existence remains uncertain. Some studies propose that *H. pylori* may contribute to gallstone formation and gallbladder inflammation through its virulence factors and pro-inflammatory effects [15]. However, other studies have found no clear association between *H. pylori* infection and gallbladder disease, indicating that the bacterium may not play a significant role in gallbladder pathology [16]. Our study adds to this debate by showing a relatively low rate of *H. pylori* co-existence in both gastric and gallbladder tissues, suggesting that its role in cholecystitis may be limited, particularly in the gallbladder.

These findings have significant implications for clinical practice, especially in regions with high prevalence of both *H. pylori* infection and cholecystitis, such as Pakistan. Given the distinct localization pattern of *H. pylori* in the stomach versus the gallbladder, targeted screening and treatment strategies might be necessary to effectively manage *H. pylori*-related complications in these patients. Routine testing for *H. pylori* in cholecystitis patients could help identify those at risk for gastric *H. pylori* infection and guide appropriate antibiotic therapy. Additionally, demographic factors like smoking status and BMI should be considered when tailoring patient management strategies.

Future Directions

Future research should focus on understanding the mechanisms behind the differential colonization of *H. pylori* in gastric and gallbladder tissues and exploring the potential clinical benefits of targeted eradication therapy in patients with dual-site infection. Longitudinal studies are also needed to assess the long-term outcomes of *H. pylori* co-infection in gastric and gallbladder mucosa and determine whether *H. pylori* eradication can reduce the risk of recurrent cholecystitis or other biliary complications.

Limitations

This study has several limitations that must be acknowledged. The cross-sectional design limits the ability to establish causality between *H. pylori* infection and cholecystitis. The sample size, although adequate for detecting associations, may not be sufficient to generalize the findings to all cholecystitis patients. Furthermore, the study was conducted at a single center, which may limit the representativeness of the results to other populations. Additionally, potential confounding factors such as dietary habits, genetic predisposition, and other environmental exposures were not accounted for, which could have influenced the outcomes. Future research should address these limitations by employing longitudinal designs, larger sample sizes, and multicenter approaches to provide a more comprehensive understanding of the role of *H. pylori* in cholecystitis.

Conclusion

In conclusion, this study provides valuable insights into the co-existence of *H. pylori* in gastric and gallbladder mucosa among cholecystitis patients, highlighting a distinct localization pattern and significant associations with demographic factors such as smoking status, BMI, and age. These findings suggest that *H. pylori* may play a limited role in the pathogenesis of cholecystitis in the gallbladder, while its presence in the gastric mucosa is more common and potentially influenced by lifestyle and metabolic factors. The study underscores the need for targeted screening and treatment strategies for *H. pylori* in cholecystitis patients, particularly in regions with a high prevalence of infection and biliary disease. Further research is needed to explore the clinical significance of *H. pylori* co-infection in the gastric and gallbladder mucosa and to determine the potential benefits of eradication therapy in reducing biliary complications.

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