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Original Research Article

Helicobacter pylori in Gastric and Gallbladder Mucosa among patients with Gallstone disease – A Prospective Cohort study

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Abstract:

Background: Gallstone disease, including cholelithiasis and chronic cholecystitis, is a global health concern with multifactorial etiologies. The role of Helicobacter pylori (H. pylori) in gallstone disease has been debated, but emerging studies suggest its presence in extra gastric sites, including the gallbladder. This study aims to evaluate the prevalence of H. pylori in gastric and gallbladder mucosa and investigate its potential association with gallstone disease.

Aim: To determine the prevalence of H. pylori in the gastric and gallbladder mucosa and assess its association with gallstone disease.

Methods: A prospective cohort study was conducted at PSG Hospitals, Coimbatore, India, over one year. Seventy-two patients diagnosed with symptomatic cholelithiasis or chronic cholecystitis scheduled for laparoscopic cholecystectomy were included. Biopsy samples from both gastric and gallbladder mucosa were analyzed using the Rapid Urease Test (RUT) and Giemsa staining. Statistical analysis was performed using SPSS software.

Results: Among the 72 patients, 58.3% tested positive for H. pylori in gastric mucosa, and 43.1% in gallbladder mucosa via RUT. Giemsa staining confirmed H. pylori in 36.1% of gallbladder samples. Statistically significant associations were found between younger age and H. pylori positivity in both gastric and gallbladder mucosa ($p = 0.049$ and $p = 0.041$, respectively). Dual positivity for H. pylori in both gastric and gallbladder mucosa was observed in 43.1% of patients, with strong correlations to triple positivity across all testing methods ($p < 0.001$).

Conclusion: This study supports the hypothesis that H. pylori may contribute to the pathogenesis of gallstone disease. The findings advocate for the potential clinical benefit of screening for and eradicating H. pylori in patients with gallstone disease, especially younger individuals. Further research is needed to elucidate the molecular mechanisms linking H. pylori to gallstone formation and to validate its role as a preventive target.

Keywords: Gallstone Disease, Helicobacter Pylori, Cholecystitis, Cholelithiasis, Cholecystectomy, Rapid Urease Test (RUT).

Introduction

Gallstone disease, encompassing both cholelithiasis and chronic cholecystitis, remains a prevalent concern globally, with multifactorial etiologies involving metabolic, genetic, and infectious factors. The association between H. pylori and gallstone disease has been a subject of debate, with studies yielding varying results. Recent meta-analyses have provided compelling evidence linking H. pylori infection in the gallbladder to an increased risk of chronic cholecystitis and cholelithiasis.[1] Traditionally, its presence has been confined to the gastric environment; however, emerging studies have identified H. pylori DNA in extra gastric sites, including the gallbladder mucosa, suggesting a potential role in biliary tract diseases.[2] Despite these study findings, the exact mechanism by which H. pylori may influence gallstone formation remain unclear. Proposed mechanisms include chronic inflammation leading to altered bile composition, impaired gallbladder motility, and increased cholesterol saturation.[3]

This study is undertaken to assess the prevalence of H. pylori in both gastric and gallbladder mucosa and to explore its potential association with gallstone disease in our institute. Understanding this relationship could provide insights into the pathophysiology of gallstones and inform preventive or therapeutic strategies.

Aim: This study primarily aims to determine the prevalence of Helicobacter pylori in gallbladder and gastric mucosa and its association with gallstone disease.

Materials and Methods

Study Design and Setting: This prospective cohort study was conducted over a period of one year in the Department of General and GI Surgery at PSG Hospitals, Coimbatore, India. The study aimed to evaluate the prevalence of Helicobacter pylori in gastric and gallbladder mucosa and its association with gallstone disease.

Study Population: A total of 72 patients diagnosed with symptomatic cholelithiasis and chronic cholecystitis, and scheduled for elective laparoscopic cholecystectomy, were included. Diagnosis was based on clinical presentation and confirmation via abdominal imaging.

Inclusion Criteria

- Adult patients aged 18 years or older with symptomatic gallstone disease (cholelithiasis) or chronic cholecystitis who were being scheduled for elective laparoscopic cholecystectomy

Exclusion Criteria

- Acute cholecystitis
- History of H. pylori eradication therapy
- Presence of cholangitis, biliary or hepatic tumors, Crohn's disease
- History of previous gastric surgery
- Patients undergoing Endoscopic Retrograde Cholangiopancreatography (ERCP)

Methodology: After confirmation of gallstone disease and preoperative evaluation, all eligible patients underwent upper gastrointestinal (GI) endoscopy. During endoscopy, a biopsy was taken from the antral region of the gastric mucosa. The sample was subjected to the Rapid Urease Test (RUT) for the detection of H. pylori.

Following this, all patients underwent laparoscopic cholecystectomy. During the procedure, mucosal tissue was collected from the excised gallbladder. These samples were:

1. Tested using Rapid Urease Test (RUT) to assess for H. pylori presence.
2. Fixed in formalin and sent for histopathological examination, specifically stained using Giemsa stain to microscopically identify H. pylori organisms.

Data Analysis: All collected data were systematically recorded and compiled using Microsoft Excel. Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 25. The prevalence of Helicobacter pylori in gastric and gallbladder mucosa was calculated as percentages. The association between H. pylori positivity and various demographic or clinical variables was assessed using the Chi-square test and Independent Samples t-test. A p-value of less than 0.05 was considered statistically significant.

Results

Age Distribution: Among the 72 study participants, 44.4% (n = 32) were aged 40 years or below, while 55.6%.

(n = 40) were aged above 40 years.

Table 1: Age Distribution

Age Category (in years)	Frequency (N)	Percentage (%)
40 and below	32	44.4%
More than 40	40	55.6%

Gender Distribution: Of the participants, 69.4% (n = 50) were female and 30.6% (n = 22) were male.

Table 2: Gender Distribution

Gender	Frequency (N)	Percentage (%)
Female	50	69.4%
Male	22	30.6%

H. pylori in Gastric Mucosa (Rapid Urease Test): A total of 58.3% (n = 42) of participants tested positive for H. pylori in gastric mucosa via the Rapid Urease Test.

Table 3: Gastric Mucosa – RUT Results

Gastric Mucosa	Frequency (N)	Percentage (%)
Negative	30	41.7%
Positive	42	58.3%

H. pylori in Gallbladder Mucosa (Rapid Urease Test): Positive H. pylori findings in gallbladder mucosa were observed in 43.1% (n = 31) of patients.

Table 4: Gallbladder Mucosa – RUT Results

Gallbladder Mucosa	Frequency (N)	Percentage (%)
Negative	41	56.9%
Positive	31	43.1%

Giemsa Stain (Gallbladder Mucosa Histology): Giemsa staining confirmed the presence of H. pylori in the gallbladder mucosa in 36.1% (n = 26) of cases.

Table 5: Giemsa Stain Results

Giemsa Stain	Frequency (N)	Percentage (%)
Negative	46	63.9%
Positive	26	36.1%

Stomach & Gallbladder Dual Positivity (RUT): Both gastric and gallbladder mucosa tested positive for H. pylori in 43.1% (n = 31) of patients.

Table 6: Dual Positivity – Gastric and Gallbladder (RUT)

Dual Positivity	Frequency (N)	Percentage (%)
Yes	31	43.1%
No	41	56.9%

Triple Positivity (Gastric RUT, Gallbladder RUT, Giemsa): A total of 36.1% (n = 26) of participants tested positive across all three methods: gastric RUT, gallbladder RUT, and Giemsa stain.

Table 7: Triple Positivity – All Tests

All Positive	Frequency (N)	Percentage (%)
Yes	26	36.1%
No	46	63.9%

Statistical Analysis

1. **Association Between Age and H. pylori Positivity**

- **Gastric Mucosa Positivity** was significantly associated with younger age (≤40 years): p = 0.049

Age Category	Gastric Mucosa Positive (%)	Gastric Mucosa Negative (%)
≤ 40 years	25 (71.9%)	9 (28.1%)
> 40 years	19 (47.5%)	21 (52.5%)

- **Gallbladder Mucosa Positivity** also showed significant association with younger age: p = 0.041

Age Category	Gallbladder Positive (%)	Gallbladder Negative (%)
≤ 40 years	18 (56.3%)	14 (43.8%)
> 40 years	13 (32.5%)	27 (67.5%)

- No statistically significant association was found between **age** and **Giemsa positivity** (p = 0.138), or between **gender** and any of the positivity outcomes.

2. **Association Between Gastric and Gallbladder Positivity with Giemsa staining**

- Strong statistical significance was observed for both:
  - Gastric mucosa positivity vs. All-positive group: **p < 0.001**
  - Gallbladder mucosa positivity vs. All-positive group: **p < 0.001**

Variable	All Positive	All Negative except variable	p-value
Gastric Positive	26 (61.9%)	16 (38.1%)	< 0.001
Gastric Negative	0 (0%)	30 (100%)	
GB Mucosa Positive	26 (83.9%)	5 (16.1%)	< 0.001
GB Mucosa Negative	0 (0%)	41 (100%)	

Discussion

Age and Gender Distribution: The findings of this study revealed that 55.6% of the participants were over the age of 40, while 69.4% were female. These demographic characteristics are consistent with the well-documented epidemiology of gallstone disease. Females have a higher predisposition to gallstone formation due to hormonal factors, particularly the role of estrogen, which increases bile cholesterol saturation and reduces bile acid secretion-contributing to biliary stasis and gallstone formation.

Studies, including those by Loosen et al. (2024), have highlighted that advancing age exacerbates the risk of gallstone formation due to decreased gallbladder motility and changes in bile composition.[4] Similarly, Svanadze et al. (2024) observed that hormonal fluctuations in females, coupled with age-related factors, contribute to a higher prevalence of gallstone disease.[5]

Interestingly, this study identified a statistically significant association between younger age (≤40 years) and H. pylori positivity in both gastric and gallbladder mucosa ($p = 0.049$ and $p = 0.041$, respectively). This aligns with findings by Zhang et al. (2024), who reported that younger individuals with gallstones were more likely to harbor active H. pylori infections, potentially due to earlier colonization and prolonged exposure to bacterial virulence factors.[6] These results suggest the need for increased awareness and screening for H. pylori in younger patients presenting with gallstone disease.

Prevalence of H. pylori in Gastric and Gallbladder Mucosa: This study demonstrated a significant prevalence of H. pylori in both gastric mucosa (58.3%) and gallbladder mucosa (43.1%). This dual positivity underscores a potential role for H. pylori in gallstone pathogenesis, possibly through direct mucosal colonization or indirect mechanisms such as bile alteration and inflammation.

Ahmad et al. (2024) showed that H. pylori infection is significantly associated with gallstone disease in large cohorts, proposing that urease production by the bacterium alters bile pH and promotes cholesterol super saturation.[7] Reshi et al. (2024) provided histopathological evidence of H. pylori colonization in gallbladder tissues, linking its presence to chronic inflammation and impaired gallbladder motility.[8] The notable presence of H. pylori in gastric mucosa supports the hypothesis that the stomach serves as a primary reservoir for the bacterium, which may disseminate to the biliary tract under certain pathological conditions.

Association Between Gastric and Gallbladder Positivity: A statistically significant correlation ($p < 0.001$) was found between H. pylori positivity in gastric and gallbladder mucosa. This suggests a possible shared or sequential pathophysiological mechanism linking the two regions.

Bawali et al. (2024) have shown that H. pylori virulence factors-including cytotoxins and pro-inflammatory mediators-can disrupt epithelial integrity in the biliary tract, allowing for secondary colonization of the gallbladder.[9] Additionally, Raza et al. (2024) emphasized the role of systemic inflammation, triggered by chronic gastric H. pylori infection, in promoting gallbladder pathology.[10]

Kumar et al. (2024) proposed that simultaneous positivity in both gastric and gallbladder mucosa could result from hematogenous or lymphatic spread, further supporting the biological link between these anatomical sites.[11] These findings indicate the potential benefit of screening for and eradicating H. pylori in patients with both gastric and biliary symptoms to reduce the risk of gallstone disease.

Histopathological Analysis Using Giemsa Staining: The presence of H. pylori was confirmed in 36.1% of gallbladder mucosa samples using Giemsa staining, supporting the results of rapid urease testing. Histopathological methods such as Giemsa are particularly valuable for detecting H. pylori in tissues where the bacterial load may be lower than in the gastric environment.

Zhang et al. (2024) stressed upon the diagnostic utility of Giemsa staining in identifying H. pylori in low-density infection sites, such as the gallbladder.[6] Du et al. (2024) also demonstrated the superiority of histological staining over enzymatic tests in detecting gallbladder colonization, particularly in chronic cholecystitis.[12] These findings are synonymous with Loosen et al. (2024), who reported a strong association between H. pylori presence in gallbladder tissues and gallstone disease, thereby reinforcing its potential etiological role.[4]

Nevertheless, certain limitations must be acknowledged. The study's observational design, single-center setting, and modest sample size limit the generalization of the results. To substantiate these findings, larger, multicenter, and longitudinal

studies are warranted. These future investigations should aim to elucidate the precise molecular and physiological pathways linking H. pylori infection to biliary pathology.

Conclusion

This study underscores a potential link between Helicobacter pylori infection and gallstone disease, with findings suggesting that H. pylori may contribute to gallstone pathogenesis through mechanisms such as altered bile acid metabolism, chronic gallbladder inflammation, and impaired bile flow. The clinical implications are notable. If H. pylori is further validated as a causative factor, early detection and eradication of the bacterium could emerge as a preventive strategy, potentially reducing the incidence of gallstones and the need for surgical interventions like cholecystectomy. Such an approach may be especially beneficial for high-risk groups, including younger individuals and females, who demonstrated higher prevalence rates of H. pylori-associated gallstone pathology in this study.

In conclusion, this research shows us the possible role of H. pylori as a potential contributor to gallstone disease. Further exploration of its role in biliary disorders may open avenues for novel preventive and therapeutic strategies, ultimately helping to reduce the burden of gallstone disease and its complications.

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