



“A PROSPECTIVE STUDY TO IDENTIFY THE ASSOCIATION OF HELICOBACTER PYLORI INFECTION WITH SYMPTOMATIC CHOLELITHIASIS”

General Surgery

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ABSTRACT

Introduction: Cholelithiasis, or gallstone disease, is a prevalent gastrointestinal disorder with a multifactorial etiology involving genetic, metabolic, and environmental factors. Recent studies suggest that *Helicobacter pylori* infection may play a role in gallstone formation by altering bile composition, impairing gallbladder motility, and inducing chronic inflammation. This study aimed to assess the association between *H. pylori* infection and symptomatic cholelithiasis by evaluating its presence in gastric mucosa, gallbladder mucosa, and bile specimens of patients undergoing cholecystectomy. **Materials And Methods:** This prospective analytical study was conducted at Kanti Devi Medical College, Hospital & Research Centre, Mathura, over two years. A total of 86 patients diagnosed with symptomatic cholelithiasis undergoing laparoscopic or open cholecystectomy were included. Gastric and gallbladder mucosal biopsies were obtained intraoperatively and tested using the rapid urease test (RUT). Bile samples were subjected to culture studies. Statistical analysis was performed using SPSS version 25, with a p-value < 0.05 considered significant. **Results:** The mean age of patients was 45.95 ± 17.94 years, with 55.81 percent males and 44.18 percent females. *H. pylori* infection was detected in 48.83 percent of gastric mucosa, 43.03 percent of gallbladder mucosa ($p = 0.02$), and 36.05 percent of bile cultures ($p = 0.01$). A significant association was observed between *H. pylori* infection and symptoms like bloating, fullness, and early satiety. **Conclusion:** This study supports the association between *H. pylori* infection and symptomatic cholelithiasis. The presence of *H. pylori* in the gastric mucosa, gallbladder, and bile suggests its potential role in gallstone formation. Screening and eradication strategies for *H. pylori* may be considered for gallstone patients, warranting further research to evaluate causality and therapeutic implications.

KEYWORDS

Helicobacter pylori, Cholelithiasis, Cholecystectomy and Rapid Urease Test (RUT).

INTRODUCTION

Cholelithiasis, commonly known as gallstone disease, is a prevalent gastrointestinal condition that significantly impacts global healthcare systems. The etiology of cholelithiasis is multifactorial, involving a combination of genetic, metabolic, and environmental factors^[1]. Gallstone disease is among the most prevalent disorders affecting the digestive system worldwide. Gallstones are composed of cholesterol, black pigment, brown pigment, or mixed constituents, underscoring that cholelithiasis is a multifaceted condition influenced by diverse risk factors.^[2] However, recent studies have suggested that infections, particularly those involving *Helicobacter pylori* (*H. pylori*), may play a contributory role in gallstone formation.^[3] However, the exact mechanism by which *H. pylori* influences gallstone formation remains unclear. Some researchers have hypothesized that *H. pylori* reaches the gallbladder via the ascending duodenal route or the portal venous system^[4]. *H. pylori*, a gram-negative microaerophilic bacterium, is primarily known for its association with peptic ulcer disease and gastric malignancies^[6]. Gallstones are categorized based on cholesterol content into cholesterol stones ($\geq 70\%$ cholesterol), pigment stones ($\leq 30\%$ cholesterol), and mixed stones (30-70% cholesterol)^[5]. Chronic cholecystitis is characterized by prolonged mechanical or functional gallbladder disturbances and is a significant complication of gallstones. Symptoms can range from nonspecific discomfort to severe upper abdominal pain, with recurrent acute biliary colic being a common presentation^[6]. This study seeks to explore the association between *Helicobacter pylori* (*H. pylori*) infection and gallstone formation, with a particular focus on the Asian population, where data on this relationship remain limited.

MATERIALS AND METHODS

“A Prospective Study was conducted in the Department of General Surgery, Kanti Devi Medical College, Hospital & Research Centre, Mathura, to evaluate the effect of *H. Pylori* infection on cholelithiasis over a period of two years. Data were collected after obtaining ethical clearance from the institute and written informed consent from each participant. The study included a total of 86 patients.

Inclusion Criteria

- Age between 18 and 75 years.
- Cases of cholelithiasis presenting with upper abdominal pain, burning sensation, regurgitation, dyspepsia, or right hypochondrium pain.
- Symptomatic cases opting for surgery (laparoscopic or open cholecystectomy).
- Patients who provided written informed consent.

Exclusion Criteria

- Those presenting with an acute abdomen.
- Known cases of peptic ulcer disease.
- Patients who had received *H. Pylori* eradication therapy within the last six months.
- Alcoholic patients.
- Patients taking NSAIDs.
- Immunocompromised individuals.
- Pregnant women up to the first trimester.
- Patients unwilling to provide consent.

Methodology

Following endoscopy and necessary investigations, patients were scheduled for either open or laparoscopic cholecystectomy. After gallbladder excision, a biopsy sample was collected from the gallbladder mucosa and subjected to RUT, following the same procedure used for gastric biopsies. A color change from yellow to pink confirmed *H. pylori* infection. The excised gallbladder tissue and bile samples were immediately placed in 10% buffered formaldehyde solution and sent to the pathology laboratory for histopathological assessment. Hematoxylin-eosin staining was used for histological analysis.

Statistical Analysis

Data were entered into **SPSS Version 25** and **MS Excel** for generating reports and distribution statistics. Quantitative data were analyzed using descriptive epidemiological methods, including rates, ratios, proportions, and measures of central tendency. Continuous variables were analyzed using means and standard deviation, while categorical variables were analyzed using the chi-square test. A **p-value of less than 0.05** was considered statistically significant.

RESULTS

The data illustrates a significant association between *H. pylori* infection across various gastrointestinal (GI) and hepatobiliary sites. The strongest association was observed between stomach RUT positivity and duodenal involvement, with 31 *H. pylori*-positive cases and a highly significant P-value of 0.0, suggesting a direct relationship between gastric and duodenal colonization by *H. pylori*. Similarly, stomach RUT positivity and gallbladder RUT positivity showed a strong correlation ($P = 0.0$), indicating that individuals with gastric *H. pylori* infection are more likely to have colonization in the gallbladder. The relationship between stomach RUT positivity and bile culture positivity was also statistically significant ($P = 0.0022$), suggesting that *H. pylori* may play a role in biliary infections. A similar trend was observed between duodenal involvement and gallbladder RUT positivity ($P = 0.0$), further emphasizing the potential migration or co-existence of *H. pylori* across these anatomical sites.

Additionally, gallbladder RUT positivity and bile culture positivity were significantly associated ($P = 0.0002$), implying that *H. pylori* presence in the gallbladder may contribute to bile culture positivity, potentially indicating bacterial cholecystitis or chronic inflammation. The association between duodenal involvement and bile culture positivity ($P = 0.0129$) further supports the theory that *H. pylori* infection may not be confined to the stomach but may also influence hepatobiliary infections.

Overall, these findings strongly suggest a systemic pattern of *H. pylori* infection, linking gastric, duodenal, and hepatobiliary sites, and emphasize the need for a broader diagnostic and treatment approach in patients with *H. pylori*-associated GI disorders. (Table 1)

Table 1: H. Pylori Infection At Different GI And Hepatobiliary Sites

Infection Site 1	Infection Site 2	H. Pylori +ve (n)	H. Pylori -ve (n)	Chi-Square	P-value
Stomach RUT Positive	Duodenum Involvement	31	4	34.659	0.0*
Stomach RUT Positive	Gallbladder RUT Positive	34	4	42.129	0.0*
Stomach RUT Positive	Bile Culture Positive	23	9	9.406	0.0022*
Duodenum Involvement	Stomach RUT Positive	31	11	34.659	0.0*
Duodenum Involvement	Gallbladder RUT Positive	26	12	19.672	0.0*
Duodenum Involvement	Bile Culture Positive	19	13	6.185	0.0129*
Gallbladder RUT Positive	Stomach RUT Positive	34	8	42.129	0.0*
Gallbladder RUT Positive	Duodenum Involvement	26	9	19.672	0.0*
Gallbladder RUT Positive	Bile Culture Positive	23	9	14.105	0.0002*
Bile Culture Positive	Stomach RUT Positive	23	19	9.406	0.0022*
Bile Culture Positive	Duodenum Involvement	19	16	6.185	0.0129*
Bile Culture Positive	Gallbladder RUT Positive	23	15	14.105	0.0002*

Test used- chi square, $p<0.05$ significant

DISCUSSION

This study explored the presence of *H. pylori* across gastrointestinal and hepatobiliary sites and its association with symptoms and clinical parameters.

A major finding of our study was the **significant associations between *H. pylori* infection in the stomach, duodenum, gallbladder, and bile**, as demonstrated by highly significant P-values ($P = 0.0$ to $P = 0.0129$). Our results suggest **systemic *H. pylori* colonization across multiple gastrointestinal and hepatobiliary sites**. Similar findings have been reported in multiple studies: Abdulall et al. (2012)^[7] found *H. pylori* DNA in **28.3% of gallbladder tissues, 26% of bile samples, and 3.3% of gallstones**, supporting our hypothesis of cross-contamination between the stomach and biliary system Memon et al. (2022)^[8] reported ***H. pylori* positivity in 70.1% of symptomatic cholelithiasis patients**, indicating a **high prevalence in biliary disorders**. Ahmad et al. (2024)^[9] using a large national dataset, found a **5.21-fold increased risk of chronic cholecystitis** in *H. pylori*-positive patients. The **strong statistical associations between *H. pylori* presence in the stomach, duodenum, gallbladder, and bile in our study** align with these findings, suggesting that ***H. pylori* may contribute to a multi-site infectious process** rather than being confined to the stomach.

Our study provides **strong evidence linking *H. pylori* infection with symptomatic cholelithiasis and bile culture positivity**, with significant associations observed across multiple gastrointestinal and hepatobiliary sites. These findings align with previous research, particularly large-scale epidemiological studies Loosen et al. 2024,^[10] Ahmad et al. 2024,^[9] While some studies (Ari et al. 2024,^[2] Bostanoglu et al. 2010)^[11] have failed to establish a direct relationship between *H. pylori* and gallstones, our data suggest that ***H. pylori***

colonization in the gallbladder and bile may be clinically relevant, potentially influencing disease progression in susceptible individuals. Further research should explore **mechanisms of bacterial translocation, the impact of eradication therapy, and long-term outcomes in *H. pylori*-infected patients with hepatobiliary disease**.

CONCLUSION

The strong association of *H. pylori* with multiple GI and hepatobiliary sites suggests that eradication therapy might offer benefits beyond gastric disorders. Screening for *H. pylori* in patients with symptomatic cholelithiasis, chronic bloating, or fullness may aid in early diagnosis and targeted treatment. This study demonstrates a strong association between *H. pylori* infection and gastrointestinal as well as hepatobiliary sites, particularly in symptomatic cholelithiasis patients. Given these findings, screening and eradication therapy for *H. pylori* could be considered in patients with persistent GI symptoms and gallbladder disorders. Future studies should explore the impact of *H. pylori* eradication on symptom resolution and hepatobiliary disease progression.

Limitations Of The Study: Small Sample Size, Single center study Reliance on RUT for *H. pylori* Detection, Lack of Advanced Imaging for Gallbladder Pathology and No Follow-Up Data

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