Section: Surgery

Original Research Article

THE INCIDENCE OF HELICOBACTER PYLORI IN PATIENTS WHO HAVE SYMPTOMATIC CHOLELITHIASIS NECESSITATING CHOLECYSTECTOMY

Udath[1], Kishan Rao[2], Suhas S R[3]

[1]Senior Resident, Department of General Surgery, Srinivas Institute of Medical Sciences & Research, Mangalore, India.
[2]Assistant Professor, Department of General Surgery, AJ Institute of Medical Sciences, Mangalore, India.
[3]Assistant Professor, Department of General Surgery, AJ Institute of Medical Sciences, Mangalore, India.

Received *: 12/09/2026*
Received in revised form *: 12/10/2026*
Accepted *: 25/10/2026*

Corresponding Author:
Dr. Kishan Rao,
Assistant Professor, Department of General Surgery, AJ Institute of Medical Sciences, Mangalore, India.
Email: surgeonkishan@gmail.com

DOI: 10.70034/ijmedph.2026.4.234

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (4); 1532-1538

ABSTRACT

Background: Gallstone disease (cholelithiasis) is a prevalent gastrointestinal disorder worldwide. Recent evidence suggests a possible association between *Helicobacter pylori* infection and gallbladder diseases, including cholelithiasis and chronic cholecystitis, although its pathogenic role remains unclear. **Aim:** To determine the incidence of *H. pylori* infection in the gallbladder mucosa of patients with symptomatic cholelithiasis undergoing cholecystectomy, and to evaluate its association with clinical, demographic, and histological factors.
Materials and Methods: This cross-sectional study was conducted at A.J. Medical College Hospital, Mangaluru, from April 2023 to April 2025. Seventy-one patients with symptomatic gallstone disease scheduled for cholecystectomy were enrolled. Gallbladder mucosa samples were analyzed by polymerase chain reaction (PCR) for *H. pylori* DNA. Clinical symptoms, demographic profiles, and histological findings were recorded and correlated with *H. pylori* status.
Results: *H. pylori* DNA was detected in 22.5% (16/71) of samples (95% CI: 13.8–33.8%). *H. pylori*-positive patients showed higher frequency of biliary colic (93.8%), nausea (81.3%), vomiting (68.8%; p=0.03), and fever (31.3%; p=0.04). Moderate to severe chronic inflammation (75% vs 45.5%; p=0.02) and fibrosis (62.5% vs 36.4%; p=0.04) were more common in *H. pylori*-positive gallbladders. Acute cholecystitis occurred more frequently in *H. pylori*-positive patients (37.5% vs 18.2%; p=0.03), with no significant association with pancreatitis.
Conclusion: *H. pylori* colonizes the gallbladder mucosa in a substantial proportion of patients with symptomatic cholelithiasis and correlates with greater inflammatory severity and complications. These findings support a possible pathogenic role for *H. pylori* in gallstone disease, warranting further multicentric studies to assess causality and therapeutic implications.
Keywords: Helicobacter pylori; Cholelithiasis; Cholecystectomy; Gallbladder; Cholecystitis; Polymerase Chain Reaction.

INTRODUCTION

Gallstones remain one of the most common digestive disorders encountered in clinical practice, arising from the abnormal precipitation of solid constituents within the gallbladder or biliary tree. The gallbladder, a small reservoir organ beneath the liver, concentrates and stores bile, indispensable for digesting dietary fats.[1,2] Although many individuals with gallstones remain asymptomatic for years, a meaningful subset develops recurrent biliary colic or complications involving the biliary tract, pancreas, liver, or gastrointestinal structures. Roughly one in ten asymptomatic patients develop clinically evident disease within five years of diagnosis, and this proportion approximately doubles over two decades. Risk rises with advancing age, disproportionately affecting women, with more than a quarter of those

beyond the sixth decade affected. This scale places substantial strain on healthcare systems globally.[2,3]

The pathogenesis of gallstones is multifactorial, shaped by physiological, genetic, and environmental determinants, with stone composition varying by dominant mechanism. Cholesterol supersaturation of bile, impaired gallbladder motility causing biliary stasis, and imbalance between bile acids, phospholipids, and cholesterol drive cholesterol stone formation, while pigment stones arise through distinct bilirubin-related processes. Obstruction of the cystic duct produces biliary colic, and persistent obstruction predisposes to bacterial invasion of stagnant bile and acute cholecystitis; migration into the common bile duct may precipitate jaundice, cholangitis, or pancreatitis. Chronic disease can cause irreversible gallbladder damage, and long-standing gallstones carry a nearly five-fold elevation in relative risk of gallbladder carcinoma.[4,5,6]

Epidemiologically, cholelithiasis prevalence varies by geography and ethnicity, affecting over twenty million people in the United States with roughly eighty thousand annual hospitalizations, while Asian populations show comparatively lower rates of five to twenty percent.[7] In India, cholelithiasis disproportionately affects women, particularly in northern regions, with rising detection linked to increased ultrasonography use and shifting dietary and socio-economic patterns, alongside risk factors such as obesity, diabetes, rapid weight loss, and hormone exposure.[6,7,8]

Parallel to this, Helicobacter pylori has emerged as one of the most studied bacterial pathogens in gastroenterology. This gram-negative, spiral-shaped organism colonizes the gastric mucosa of over half the world's population, with infection rates reaching eighty to ninety percent in developing regions, typically acquired in childhood through oral-oral or fecal-oral transmission under crowded, poor-sanitation conditions. H. pylori is the principal cause of chronic gastritis and peptic ulcer disease and is classified as a Group 1 carcinogen due to its causal link with gastric adenocarcinoma and association with MALT lymphoma.[9,10]

Beyond gastric pathology, growing literature implicates H. pylori in extragastric conditions including cardiovascular disease, iron deficiency anemia, and hepatobiliary disorders such as non-alcoholic fatty liver disease and hepatocellular carcinoma. Of particular relevance here is the proposed relationship between H. pylori and gallbladder disease: investigators have detected H. pylori DNA in bile and gallbladder tissue of cholecystectomy patients, suggesting possible biliary colonization beyond its conventional gastric niche.[11] Proposed mechanisms include H. pylori-induced chronic inflammation disrupting bile homeostasis, promoting cholesterol supersaturation, and impairing gallbladder motility, plausibly predisposing to stone formation and complications.[11,12]

Despite these observations, existing literature on this association remains inconsistent, with many prior studies relying on the comparatively insensitive rapid urease test rather than molecular methods, limiting reliability. Polymerase chain reaction, the gold-standard technique for H. pylori identification, offers superior sensitivity and specificity but has been underutilized in gallbladder-focused research. Given the large, heterogeneous patient population at AJ Institute of Medical Sciences and Research Centre, a tertiary referral center, a rigorous PCR-based evaluation was considered necessary to clarify this relationship. The rationale for the present study rests on the need for more definitive, molecularly validated evidence regarding the presence and clinical relevance of H. pylori within the gallbladder mucosa of symptomatic gallstone patients. Accordingly, this study aims to determine the incidence of Helicobacter pylori infection in the gallbladder mucosa of patients with symptomatic cholelithiasis necessitating cholecystectomy, and to evaluate its association with clinical, demographic, and histological factors.

MATERIALS AND METHODS

Study Design and Setting: This study was designed as a cross-sectional analysis conducted in the Department of General Surgery, A.J. Institute of Medical Sciences and Research Centre, Mangaluru. The research involved patients admitted for symptomatic cholelithiasis who were scheduled to undergo cholecystectomy at this tertiary care center. The study was conducted over a period spanning April 2023 to April 2025.

Study Population: Patients above 18 years of age with a confirmed diagnosis of symptomatic gallstone disease, scheduled for cholecystectomy in the Department of General Surgery, A.J. Institute of Medical Sciences, Mangaluru. Patients who had undergone any hepatobiliary surgery within the preceding one year, and patients who had received H. pylori eradication therapy within the past one year, were excluded to avoid confounding of the primary outcome.

Sample Size Estimation: The sample size was calculated based on a comparable study by Attaallah et al,[13] which reported an estimated prevalence (p) of 22% for H. pylori positivity in gallbladder samples. Using a 95% confidence interval and an allowable error (L) of 5%, the minimum required sample size was calculated as approximately 69 patients; a total of 71 patients were ultimately enrolled in the present study.

Ethical Considerations: Ethical clearance for the study was obtained from the Institutional Ethics Committee of A.J. Medical College prior to commencement. All participants were informed of their rights, and voluntary, written informed consent was secured from every eligible patient before any study-related procedure. No financial compensation was provided to participants, involvement was

entirely voluntary, and confidentiality of patient data was maintained throughout the study.

Data Collection Procedure:

Patient Selection and Consent: Patients admitted for symptomatic cholelithiasis were screened against the inclusion and exclusion criteria. Informed consent was obtained from eligible patients following counselling regarding the study objectives and their involvement, with assured confidentiality and documented consent.

Preoperative Evaluation: Each patient underwent a comprehensive clinical evaluation, including detailed medical history and physical examination. Preoperative investigations included standard laboratory tests and abdominal ultrasonography to confirm the diagnosis of gallstone disease, followed by a pre-anesthetic checkup for surgical clearance.

Surgical and Sample Collection Procedure: Patients were kept nil per os (NPO) for at least eight hours before surgery. During cholecystectomy, gallbladder mucosa samples were collected intraoperatively from the excised specimen. Samples of the mucosa were preserved appropriately and transported for laboratory processing and analysis.

Laboratory Analysis: The collected gallbladder mucosa samples were analyzed using Polymerase Chain Reaction (PCR) to detect the presence of H. pylori DNA. PCR was selected for its high sensitivity and specificity in detecting H. pylori infection in tissue samples, offering superior accuracy compared to alternative detection methods such as the rapid urease test or histological staining. In parallel, histopathological examination of the gallbladder specimens was performed to assess the degree of chronic inflammation, fibrosis, and stone composition.

Outcome Measures: Incidence of H. pylori infection in the gallbladder mucosa, as detected by PCR. Correlation of H. pylori presence with patient demographics (age and sex); analysis of the relationship between H. pylori infection and clinical presentation (symptoms such as biliary colic, nausea, vomiting, fever, and jaundice); and association of H. pylori with histological findings, including degree of inflammation and fibrosis in the gallbladder wall, stone composition, and clinical outcomes such as acute cholecystitis and pancreatitis.

Statistical Analysis: Categorical variables were summarized as frequencies and percentages, continuous variables as means with standard deviations. Inferential analyses included the binomial test (observed vs. expected prevalence), chi-square test (categorical comparisons), independent-samples t-test (mean age comparison), and odds ratios with 95% CIs to quantify associations. Statistical significance was set at $p<0.05$, with analysis performed using SPSS/R software.

RESULTS

Overview of Study Population

Between April 2023 and April 2025, 71 patients with symptomatic cholelithiasis undergoing cholecystectomy at A.J. Medical College Hospital, Mangaluru, were enrolled and analyzed as per the study protocol. All 71 patients completed intraoperative gallbladder mucosal sampling and PCR analysis for *Helicobacter pylori* (H. pylori) DNA, alongside histopathological evaluation of resected specimens.

Incidence of H. pylori in Gallbladder Mucosa

Using polymerase chain reaction (PCR), *H. pylori* DNA was detected in the gallbladder mucosa of 16 of 71 patients (22.5%). A binomial test comparing this observed proportion against the expected prevalence of 22% reported by Attaallah et al. showed no significant difference ($p = 0.89$), confirming concordance with prior literature. The 95% confidence interval for the incidence of *H. pylori* infection was 13.8% to 33.8%.

Table 1: Incidence of H. pylori in Gallbladder Mucosa (N = 71)

H. pylori Status	Number of Patients	Percentage (%)	95% CI	p-value
Positive	16	22.5%	13.8–33.8%	0.89
Negative	55	77.5%	—	—
Total	**71**	**100%**	—	—

p-value derived from binomial test comparing observed prevalence against the expected prevalence of 22% (Attaallah et al., 2013).

These findings confirm the study hypothesis that *H. pylori* is present in the gallbladder mucosa of a substantial minority of patients with symptomatic gallstone disease, at a rate statistically consistent with previously published estimates.

Clinical Presentation Stratified by H. pylori Status

H. pylori-positive patients presented with a distinct symptom profile compared to *H. pylori*-negative patients. Biliary colic was the most frequent symptom overall, but fever and vomiting were significantly more common among *H. pylori*-positive patients on chi-square testing.

Table 2: Clinical Presentation of Patients by H. pylori Status

Symptom	H. pylori Positive (n=16)	H. pylori Negative (n=55)	p-value	Odds Ratio (95% CI)
Biliary Colic	15 (93.8%)	48 (87.3%)	0.45	2.1 (0.4–10.5)
Nausea	13 (81.3%)	40 (72.7%)	0.48	1.6 (0.5–5.2)
Vomiting	11 (68.8%)	30 (54.5%)	0.03*	1.8 (1.1–3.0)
Fever	5 (31.3%)	10 (18.2%)	0.04*	2.1 (1.1–4.0)
Jaundice	3 (18.8%)	8 (14.5%)	0.67	1.4 (0.3–5.8)

Statistically significant at p<0.05.

Vomiting (p = 0.03) and fever (p = 0.04) were the only symptoms showing a statistically significant excess among *H. pylori*-positive patients, with roughly twofold higher odds for both. Fever, an indicator often associated with acute cholecystitis, occurred with 2.1-fold higher odds (95% CI: 1.1–4.0) in the *H. pylori*-positive group, suggesting a link between bacterial colonization and more severe inflammatory presentations.

Demographic Correlates of H. pylori Infection

Demographic comparisons between *H. pylori*-positive and -negative groups revealed a numerically higher prevalence of infection among women and older patients, though neither difference reached statistical significance.

Table 3: Demographic Characteristics by H. pylori Status

Demographic Factor	H. pylori Positive (n=16)	H. pylori Negative (n=55)	p-value
Gender			0.520
Male	5 (31.2%)	22 (40.0%)	
Female	11 (68.8%)	33 (60.0%)	
Age (years)			0.320
Mean ± SD	52.3 ± 8.7	49.7 ± 9.2	
Range	38–65	35–68	

An independent-samples t-test showed no significant difference in mean age between groups (p = 0.32), and a chi-square test showed no significant difference in gender distribution (p = 0.52). While *H. pylori* positivity was more common among women (68.8% vs. 60.0%) and slightly older patients, these trends did not achieve statistical significance, likely reflecting the modest sample size.

Histological Findings

Histopathological analysis of resected gallbladder mucosa demonstrated significantly greater inflammatory and fibrotic changes in *H. pylori*-positive specimens.

Table 4: Histological Findings in Gallbladder Mucosa by H. pylori Status

Histological Feature	H. pylori Positive (n=16)	H. pylori Negative (n=55)	p-value	Odds Ratio (95% CI)
Inflammation			0.02*	3.6 (1.2–10.8)
Mild	4 (25.0%)	30 (54.5%)		
Moderate to Severe	12 (75.0%)	25 (45.5%)		
Fibrosis			0.04*	2.9 (1.0–8.4)
Present	10 (62.5%)	20 (36.4%)		
Absent	6 (37.5%)	35 (63.6%)		
Stone Composition			0.48	1.6 (0.5–5.2)
Cholesterol Stones	13 (81.3%)	40 (72.7%)		
Pigment Stones	3 (18.8%)	15 (27.3%)		

Statistically significant at p<0.05.

Moderate to severe chronic inflammation was present in 75.0% of *H. pylori*-positive specimens compared with 45.5% of *H. pylori*-negative specimens (p = 0.02; OR 3.6, 95% CI 1.2–10.8). Fibrosis followed a similar pattern, present in 62.5% versus 36.4% of specimens, respectively (p = 0.04; OR 2.9, 95% CI 1.0–8.4). Stone composition did not differ significantly by *H. pylori* status, although cholesterol stones were numerically more frequent in the *H. pylori*-positive group.

Correlation Between H. pylori Infection and Clinical Outcomes

Postoperative and clinical course data were analyzed to determine whether *H. pylori* positivity was associated with disease complications.

Table 5: Correlation Between H. pylori Infection and Clinical Outcomes

Clinical Outcome	H. pylori Positive (n=16)	H. pylori Negative (n=55)	p-value	Odds Ratio (95% CI)
Acute Cholecystitis	6 (37.5%)	10 (18.2%)	0.03*	2.7 (1.1–6.5)
Pancreatitis	2 (12.5%)	6 (10.9%)	0.85	1.2 (0.3–5.0)
No Complications	8 (50.0%)	39 (70.9%)	0.10	0.4 (0.1–1.1)

Statistically significant at p<0.05.

Acute cholecystitis was significantly more frequent among H. pylori-positive patients (37.5% vs. 18.2%; p = 0.03; OR 2.7, 95% CI 1.1–6.5), whereas the incidence of pancreatitis was similar between groups (12.5% vs. 10.9%; p = 0.85). Correspondingly, uncomplicated disease courses were more frequent among H. pylori-negative patients (70.9% vs. 50.0%), although this trend did not reach statistical significance (p = 0.10).

Figure Legends

Figure 1: Incidence of H. pylori in Gallbladder Mucosa.

A pie/bar chart depicting the proportional distribution of PCR-confirmed H. pylori status among the 71 study participants: 22.5% (16/71) H. pylori-positive versus 77.5% (55/71) H. pylori-negative, corresponding to the data in Table 1.

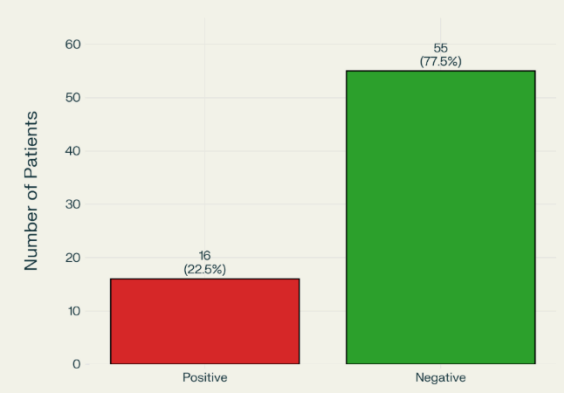


Figure 1: Incidence of H. pylori in Gallbladder Mucosa

Figure 2: Comparative Clinical and Histological Profile by H. pylori Status.

A grouped bar chart comparing the percentage frequency of key clinical symptoms (vomiting, fever), histological features (moderate–severe inflammation, fibrosis), and the clinical outcome of acute cholecystitis between *H. pylori*-positive and *H. pylori*-negative patients, illustrating the consistently higher frequency of each parameter in the *H. pylori*-positive group.

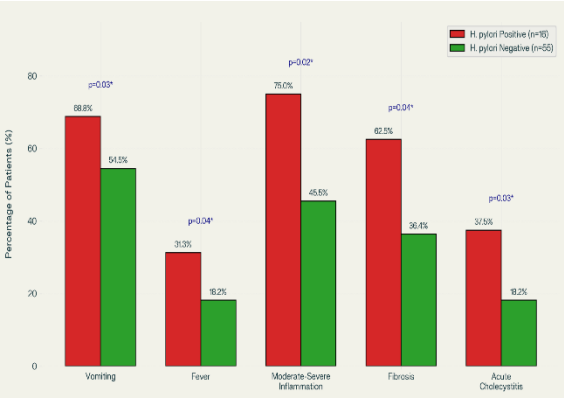


Figure 2: Comparative Clinical and Histological Profile by H. pylori Status

DISCUSSION

Gallstone disease remains a major gastrointestinal burden worldwide, and although its pathogenesis is classically attributed to cholesterol supersaturation, biliary stasis, and genetic predisposition, accumulating evidence has implicated Helicobacter pylori as a possible extragastric contributor to gallbladder inflammation and lithogenesis.[8,11] Since prior investigations largely relied on the comparatively insensitive rapid urease test, this study employed the gold-standard PCR technique to determine the incidence of H. pylori in gallbladder mucosa of patients with symptomatic cholelithiasis undergoing cholecystectomy, and to evaluate its correlation with clinical, demographic, and histological parameters.

In the present study, H. pylori DNA was detected in 22.5% (16/71) of gallbladder mucosa samples, with a 95% confidence interval of 13.8% to 33.8%, closely matching the 22% prevalence reported by Attaallah et al., against which our sample size was calculated, with a binomial test confirming no significant deviation (p=0.89).[13] Our finding is broadly consistent with the pooled Asian estimates of Wang et al., whose meta-analysis reported an odds ratio of 4.30 for gallbladder H. pylori positivity in Asian populations compared with 2.13 in non-Asian populations (Wang et al., 2021, and with Cen et al., whose earlier meta-analysis of 18 studies similarly found a stronger association in Asian-region studies (OR 3.75) than non-Asian ones (OR 2.25).[14,15] Notably, our incidence is markedly higher than the 0% gallbladder PCR positivity recently reported in a South Indian cohort undergoing cholecystectomy, despite 20.4% gastric positivity in the same patients, and considerably lower than the 61.2% gallbladder positivity reported in a Chennai-based histopathological study.[16,17] Other Indian studies have reported even lower rates, such as 5.6% by histology and detection in only a single case among 35 patients, while an earlier RUT-based Indian study reported an 18% association with cholelithiasis.[18,19,20] This wide variability across Indian cohorts likely reflects differences in detection method, sample type, and regional H. pylori strain prevalence, and supports Lim et al.'s observation that the organism may reach the gallbladder via hematogenous spread or ascending biliary migration, producing a chronic low-grade inflammatory state that is inconsistently captured by less sensitive assays.[21]

With respect to clinical presentation, H. pylori-positive patients in our cohort exhibited a higher frequency of biliary colic, nausea, vomiting, and fever, with vomiting (p=0.03) and fever (p=0.04) reaching statistical significance and odds ratios of 1.8 and 2.1, respectively. This pattern parallels the observations of Wang et al., who noted that gallbladder H. pylori colonization was linked to more complicated disease courses across their pooled

cohorts.[14] Demographically, although H. pylori positivity was more common among women (68.8%) and older patients (mean age 52.3 years) in our study, neither difference reached statistical significance (p=0.52 and p=0.32, respectively). This mirrors the findings of Raza et al., whose Southern Indian cohort also found no significant association between H. pylori and either age (p=0.63) or gender (p=0.23), despite a female predominance among positive cases, and Jahantab et al., who similarly reported no significant relationship between H. pylori positivity and age or sex in Iranian cholecystectomy patients.[18,22] Lim et al. further noted that while gallstone disease itself shows a strong female and age-related preponderance from estrogen-mediated cholesterol handling, the added contribution of H. pylori to this demographic skew remains inconsistently reported across the literature.[21]

Histologically, H. pylori-positive gallbladders in our cohort showed significantly more moderate-to-severe chronic inflammation (75% vs. 45.5%, p=0.02) and fibrosis (62.5% vs. 36.4%, p=0.04). This is strongly corroborated by Wang et al., whose meta-analysis identified greater chronic inflammatory change in H. pylori-colonized gallbladder tissue, attributed to sustained immune activation and cytokine-mediated remodeling, and by Raza et al., who reported a highly significant association between H. pylori and degree of fibrosis (p<0.0001), inflammatory mononuclear infiltrate (p<0.01), and epithelial hyperplasia (p<0.003), even though they found no overall correlation with calculous cholecystitis itself.[14,18] Vasanthbalan et al. additionally found H. pylori positivity to be significantly associated with multiple gallstones (75.9% vs. 29.6% in single-stone cases, p<0.001) and with acute-on-chronic cholecystitis, while the large multi-center Chinese study by Yao et al. demonstrated that H. pylori-positive patients had significantly higher total cholesterol and LDL-cholesterol but lower bilirubin, mechanistically supporting a role for the organism in cholesterol-mediated lithogenesis (Yao et al., 2024).[17,23]

Regarding clinical outcomes, acute cholecystitis was significantly more frequent among H. pylori-positive patients in our cohort (37.5% vs. 18.2%, p=0.03; OR 2.7), whereas pancreatitis incidence did not differ significantly (p=0.85). This selective association with gallbladder-specific rather than pancreatic complications aligns with Lim et al., who found more robust evidence linking H. pylori to gallbladder and biliary tract pathology than pancreatic disease, and is consistent with Yao et al.'s multi-center finding that H. pylori was more strongly associated with the choledocholithiasis phenotype than with straightforward cholecystolithiasis (OR 3.32).[21,23]

This study carries certain limitations, including its modest single-center sample of 71 patients and its cross-sectional design, which precludes causal inference; PCR detection of bacterial DNA, while highly sensitive, also does not confirm viable, actively replicating infection. Nonetheless, the study's strengths include its use of PCR as the gold-standard detection method, likely improving sensitivity over the RUT- or histology-based Indian comparators cited above, and its comprehensive clinical, demographic, and histopathological evaluation within a well-defined surgical cohort. Clinically, these findings suggest that H. pylori status could serve as a marker of disease severity, identifying patients at higher risk of acute cholecystitis who may benefit from closer perioperative monitoring; should future interventional studies establish causality, targeted eradication therapy could become an adjunctive strategy for reducing gallstone-related morbidity, particularly in high-prevalence regions such as India. Furthermore, the discordant findings between our study and the recent South Indian cohort by Hegde et al., which found complete absence of gallbladder H. pylori despite confirmed gastric colonization using the same PCR platform, raise an important methodological question about whether gallbladder colonization is a truly independent event rather than a simple extension of gastric infection, a question that our cross-sectional design was not equipped to resolve.[16] Taken together, the heterogeneity across Indian studies (ranging from 0% to over 60% positivity) underscores that detection method, tissue sampling technique, and possibly regional strain variation substantially influence reported prevalence, and argues strongly for standardized, multicentric protocols in future Indian research on this topic.

CONCLUSION

This study demonstrates that H. pylori DNA is present in 22.5% of gallbladder mucosa samples from patients with symptomatic cholelithiasis, and its presence correlates significantly with more severe clinical symptoms, greater chronic inflammation and fibrosis, and higher rates of acute cholecystitis. These findings support a possible pathogenic role for H. pylori in gallstone-related morbidity, though causality remains unproven. Larger, multicentric studies using confirmatory molecular techniques are warranted to validate these associations and explore eradication therapy as a potential preventive strategy.

REFERENCES

1. Sebghatollahi V, Parsa M, Minakari M, Azadbakht S. A clinician's guide to gallstones and common bile duct (CBD): A study protocol for a systematic review and evidence-based recommendations. Health Sci Rep. 2023 Sep 12;6(9):e1555. doi: 10.1002/hsr2.1555. PMID: 37706014; PMCID: PMC10496460.
2. Behari A, Kapoor VK. Asymptomatic Gallstones (AsGS) - To Treat or Not to? Indian J Surg. 2012 Feb;74(1):4-12. doi: 10.1007/s12262-011-0376-5. Epub 2011 Dec 3. PMID: 23372301; PMCID: PMC3259178.
3. Sasmal PK, Singh PK, Sahoo A, Dutta T. Asymptomatic gallstone disease: Re-evaluating the threshold for surgical options in the era of precision medicine. World J Gastrointest Surg 2025; 17(11): 110501 [PMID: 41357627 DOI: 10.4240/wjgs.v17.i11.110501]
4. Di Ciaula A, Wang DQ, Portincasa P. An update on the pathogenesis of cholesterol gallstone disease. Curr Opin

Gastroenterol. 2018 Mar;34(2):71-80. doi: 10.1097/MOG.0000000000000423. PMID: 29283909; PMCID: PMC8118137.
5. Sun H, Warren J, Yip J, Ji Y, Hao S, Han W, Ding Y. Factors Influencing Gallstone Formation: A Review of the Literature. Biomolecules. 2022 Apr 6;12(4):550. doi: 10.3390/biom12040550. PMID: 35454138; PMCID: PMC9026518.
6. Liu Y, Yao B, Yang X, Sun Q, Yang X, Liang L. Research progress on the role of microbiota in the pathogenesis of gallstone disease. Frontiers in Microbiology. 2025;16:1672767–7.
7. Stinton LM, Shaffer EA. Epidemiology of gallbladder disease: cholelithiasis and cancer. Gut Liver. 2012 Apr;6(2):172-87. doi: 10.5009/gnl.2012.6.2.172. Epub 2012 Apr 17. PMID: 22570746; PMCID: PMC3343155.
8. Mohite SU, Panse N, Kannan R, Tapkire R, Pradhan S, Gulia A, et al. Prevalence of gallstone disease in India: insights from a community-based cross-sectional study. BMJ Public Health. 2026 Feb 5;4(1):e004015. doi: 10.1136/bmjph-2025-004015. PMID: 41658223; PMCID: PMC12878284.
9. Lim KPK, Lee AJL, Jiang X, Teng TZJ, Shelat VG. The link between Helicobacter pylori infection and gallbladder and biliary tract diseases: A review. Ann Hepatobiliary Pancreat Surg. 2023 Aug 31;27(3):241-250. doi: 10.14701/ahbps.22-056. Epub 2023 Jun 26. PMID: 37357161; PMCID: PMC10472116.
10. Ali A, AlHussaini KI. Helicobacter pylori: A Contemporary Perspective on Pathogenesis, Diagnosis and Treatment Strategies. Microorganisms. 2024 Jan 22;12(1):222. doi: 10.3390/microorganisms12010222. PMID: 38276207; PMCID: PMC10818838.
11. Santos MLC, de Brito BB, da Silva FAF, Sampaio MM, Marques HS, Oliveira E Silva N, de Magalhães Queiroz DM, de Melo FF. Helicobacter pylori infection: Beyond gastric manifestations. World J Gastroenterol. 2020 Jul 28;26(28):4076-4093. doi: 10.3748/wjg.v26.i28.4076. PMID: 32821071; PMCID: PMC7403793.
12. Kumar S, Patel GK, Ghoshal UC. Helicobacter pylori-Induced Inflammation: Possible Factors Modulating the Risk of Gastric Cancer. Pathogens. 2021; 10(9):1099. https://doi.org/10.3390/pathogens10091099
13. Attaallah W, Yener N, Ugurlu MU, Manukyan M, Asmaz E, Aktan AO. Gallstones and Concomitant Gastric Helicobacter pylori Infection. Gastroenterol Res Pract. 2013;2013:643109.
14. Wang L, Chen J, Jiang W, Cen L, Pan J, Yu C, et al. The Relationship between Helicobacter pylori Infection of the Gallbladder and Chronic Cholecystitis and Cholelithiasis: A Systematic Review and Meta-Analysis. Canadian Journal of Gastroenterology and Hepatology [Internet]. 2021 Jan 6 [cited 2026 Aug 31];2021:e8886085. Available from: https://www.hindawi.com/journals/cjgh/2021/8886085/
15. Cen L, Pan J, Zhou B, Yu C, Li Y, Chen W, Shen Z. Helicobacter Pylori infection of the gallbladder and the risk of chronic cholecystitis and cholelithiasis: A systematic review and meta-analysis. Helicobacter. 2018 Feb;23(1). doi: 10.1111/hel.12457. Epub 2017 Dec 20. PMID: 29266548.
16. Hegde A, Gupta S, Ahamed SF, Mallipatel R, Dias M, Rosario V, Patel M, Rozario A. Correlation Between Gastric and Gallbladder Helicobacter pylori Infection in South Indian Patients Undergoing Cholecystectomy for Gallbladder Disease. Cureus. 2025 Sep 19;17(9):e92726. doi: 10.7759/cureus.92726. PMID: 41116933; PMCID: PMC12535756.
17. Vasanthbalan SB, Chandran M, Madan S, Gokul A, Krishnan K. Prevalence of Helicobacter pylori Infection in Gallbladder Specimens of Patients with Calculous Cholecystitis: A Cross-sectional Study. J Clin Diag Res. 2026;20(7):PC06-PC09.
18. Raza M, Kumar H, Gawri A. Study of association of H. pylori infection of the gall bladder and calculous cholecystitis. Int J Surg Sci. 2022;6(1):158-164.
19. Kosma V, Gole SN, Nirala SL, Siddiqui RP, Agrawal SN. A study of H. pylori infection as risk factor for the gall stone disease . Int Surg J [Internet]. 2023 May 30 [cited 2026 Aug. 31];10(6):1051-6.
20. Athavale VS, Khandalkar SN, Bhide PC, Shetty I, Lad A. A study of association of H. pylori infection and cholelithiasis. Int Surg J [Internet]. 2018 Jan. 25 [cited 2026 Aug. 31];5(2):701-4.
21. Lim KPK, Lee AJL, Jiang X, Teng TZJ, Shelat VG. The link between Helicobacter pylori infection and gallbladder and biliary tract diseases: A review. Annals of Hepato-Biliary-Pancreatic Surgery. 2023 Jun 26;27(3):241.
22. Jahantab MB, Safaripour AA, Hassanzadeh S, Yavari Barhaghtalab MJ. Demographic, Chemical, and Helicobacter pylori Positivity Assessment in Different Types of Gallstones and the Bile in a Random Sample of Cholecystectomied Iranian Patients with Cholelithiasis. Can J Gastroenterol Hepatol. 2021 Aug 9;2021:3351352. doi: 10.1155/2021/3351352. PMID: 34422710; PMCID: PMC8371640.
23. Yao SY, Li XM, Cai T, Li Y, Liang LX, Liu XM, Lei YF, Zhu Y, Wang F. Helicobacter pylori infection is associated with the risk and phenotypes of cholelithiasis: A multi-center study and meta-analysis. World J Gastroenterol. 2024 Dec 21;30(47):4991-5006. doi: 10.3748/wjg.v30.i47.4991. PMID: 39713162; PMCID: PMC11612862.