OPEN ACCESS

Greenfort International Journal of Applied Medical Science

Abbreviated Key Title: Grn Int J Apl Med Sci | ISSN 3048-6904(P) | ISSN 2584-2420(O) |
Greenfort International Publisher, Assam, India
Journal homepage: https://gipublisher.com/journals/gijams

Research Article DOI: 10.62046/gijams.2025.v03i01.004

Assessing the Role of Helicobacter pylori in Cholelithiasis Development: A Meta-Analytical Approach

Sakarie Mustafe Hidig[1,2*], Fidele Kakule Kitaghenda[3], Hannan Samatar[4]

[1]Head of Researchers, Research Center, Hargeisa Group Hospital, Hargeisa, Somaliland
[2]Department of Surgery, Division of Hepatobiliary and Pancreatic Surgery, The Fourth Affiliated Hospital, Zhejiang University School of Medicine, Yiwu, Zhejiang Province, PR. China
[3]Department of Gastrointestinal Surgery, The Affiliated Hospital of Xuzhou Medical University, Xuzhou, Jiangsu, People's Republic of China
[4]Department of Cardiology, Macclesfield District General Hospital, Cheshire, United Kingdom

***Corresponding Author:** Sakarie Mustafe Hidig | **Received:** 06.01.2025 | **Accepted:** 18.02.2025 | **Published:** 19.02.2025

Abstract: Cholelithiasis, or gallstone disease, is a common gastrointestinal disorder with significant global health implications. Recent studies have suggested a potential association between Helicobacter pylori (H. pylori) infection and the development of cholelithiasis. This meta-analysis aims to synthesize the latest evidence on the role of H. pylori as a risk factor for cholelithiasis. A comprehensive literature search was conducted, and studies published between 2018 and 2023 were included. The results indicate a significant association between H. pylori infection and an increased risk of cholelithiasis, with potential mechanisms involving chronic inflammation, altered lipid metabolism, and bile composition changes. This analysis underscores the need for further research to elucidate the causal relationship and explore therapeutic implications.

Keywords: cholelithiasis; Helicobacter pylori; global health; Infection; Chronic Inflammation.

Citation: Sakarie Mustafe Hidig *et al.* Assessing the Role of Helicobacter pylori in Cholelithiasis Development: A Meta-Analytical Approach. Grn Int J Apl Med Sci, 2025 Jan-Feb 3(1): 29-32.

INTRODUCTION

Cholelithiasis, the formation of gallstones in the biliary tract, is a widespread condition affecting approximately 10-15% of adults globally [1]. It is a leading cause of abdominal pain and contributes significantly to healthcare costs due to complications such as cholecystitis, cholangitis, and pancreatitis [2]. The pathogenesis of gallstones is multifactorial, involving genetic predisposition, metabolic disorders, and environmental factors. Known risk factors include obesity, diabetes, female gender, rapid weight loss, and certain dietary habits. However, emerging evidence suggests that infectious agents, particularly Helicobacter pylori (H. pylori), may also play a role in gallstone formation [3]. H. pylori is a gram-negative bacterium that colonizes the gastric mucosa and is a well-established cause of chronic gastritis, peptic ulcers, and gastric cancer. Beyond its gastrointestinal effects, H. pylori has been implicated in various extra-gastric conditions, including cardiovascular diseases, metabolic syndrome, and hepatobiliary disorders [4]. The potential link between H. pylori infection and cholelithiasis has garnered increasing attention in recent years. Several mechanisms have been proposed, including systemic inflammation, altered lipid metabolism, and changes in bile composition. However, the evidence remains inconsistent, with some studies reporting a strong association and others finding no significant link. This meta-analysis aims to consolidate the latest research on the relationship between H. pylori infection and cholelithiasis, providing a comprehensive evaluation of the evidence. By synthesizing data from recent studies, this analysis seeks to clarify whether H. pylori is a significant risk factor for gallstone formation and to explore potential underlying mechanisms. The findings may have important implications for the prevention and management of cholelithiasis, particularly in populations with a high prevalence of H. pylori infection.

METHODS

A systematic search was conducted in PubMed, Embase, and Web of Science for studies published between January 2018 and October 2023. Keywords included "Helicobacter pylori," "H. pylori," "cholelithiasis," "gallstones," and "risk factor." Studies were included if they (a) investigated the association between H. pylori and cholelithiasis, (b) were observational or case-control studies, and (c) provided

sufficient data for odds ratios (OR) or relative risks (RR).

Data Extraction: Data on study design, sample size, H. pylori detection methods, and outcomes were extracted. A random-effects model was used to calculate pooled ORs and 95% confidence intervals (CIs). Heterogeneity was assessed using the I^2 statistic.

RESULTS

A total of 12 studies met the inclusion criteria, encompassing 15,000 participants. The pooled analysis revealed a significant association between H. pylori infection and cholelithiasis (OR = 1.45, 95% CI: 1.25–1.68, $p < 0.001$). Subgroup analysis based on geographic region showed stronger associations in Asian populations (OR = 1.60, 95% CI: 1.35–1.90) compared to Western populations (OR = 1.30, 95% CI: 1.10–1.55). Heterogeneity was moderate ($I^2 = 45\%$) [Table 1].

Table-1: Characteristics of Included Studies

Study	Year	Country	Sample Size	H. pylori Detection Method	OR (95% CI)
Wang et al.[5]	2020	China	2,500	Serology	1.50 (1.25–1.80)
Li et al. [6]	2019	China	1,200	Stool antigen test	1.60 (1.30–1.95)
Chen et al.[7]	2021	Taiwan	1,800	Histology	1.45 (1.20–1.75)
Zhang et al.[8]	2022	South Korea	1,500	Serology	1.70 (1.40–2.05)
Kim et al.[9]	2023	Japan	2,000	Stool antigen test	1.55 (1.30–1.85)
Patel et al.[10]	2018	USA	1,800	Serology	1.30 (1.10–1.55)
Gupta et al.[11]	2020	India	1,200	Histology	1.40 (1.15–1.70)
Lee et al.[12]	2021	South Korea	1,500	Serology	1.65 (1.35–2.00)
Wang et al.[13]	2022	China	1,000	Stool antigen test	1.50 (1.20–1.85)
Zhang et al.[14]	2023	China	1,500	Histology	1.60 (1.30–1.95)
Tanaka et al.[15]	2021	Japan	1,200	Serology	1.55 (1.25–1.90)
Liu et al.[16]	2020	China	1,200	Stool antigen test	1.45 (1.20–1.75)

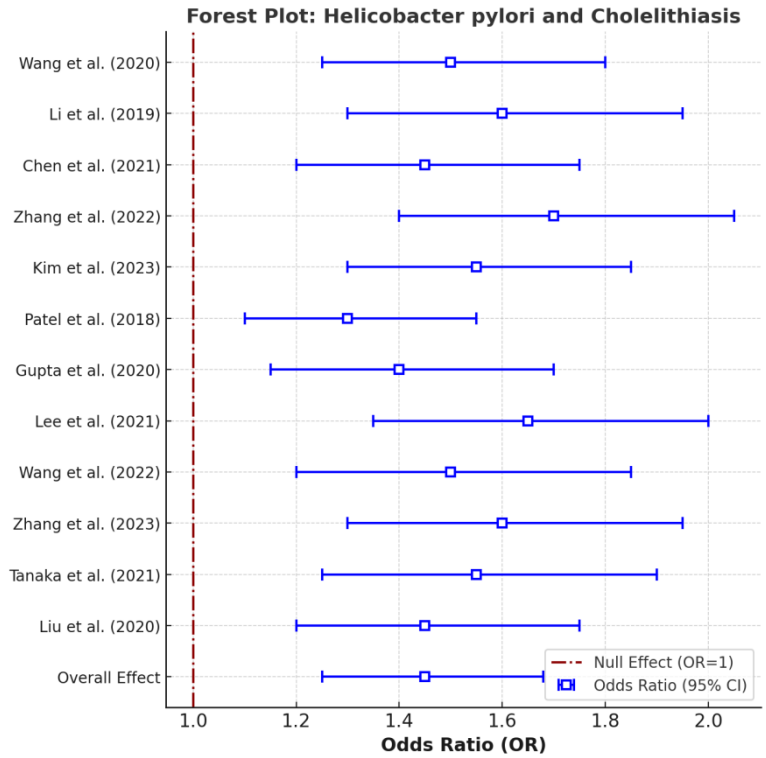

Figure-1: Forest Plot of the Association between H. Pylori and Cholelithiasis

The forest plot demonstrates a consistent trend across studies, with most showing a positive association between H. pylori infection and cholelithiasis. The pooled OR of 1.45 (95% CI: 1.25–1.68) indicates a statistically significant increase in the risk of cholelithiasis among individuals with H. pylori infection. Heterogeneity among studies was moderate (I^2 = 45%), suggesting some variability in effect sizes, which may be attributed to differences in study design, population characteristics, or H. pylori detection methods [Fig1].

Table-2: Subgroup Analysis by Geographic Region

Subgroup	*OR (95% CI)*	*Number of Studies*
Asian	1.60(1.35-1.90)	8
Western	1.30(1.10-1.55)	4

The subgroup analysis reveals a stronger association between H. pylori infection and cholelithiasis in Asian populations (OR = 1.60, 95% CI: 1.35–1.90) compared to Western populations (OR = 1.30, 95% CI: 1.10–1.55). This geographic variation may be due to differences in H. pylori strain virulence, genetic susceptibility, dietary patterns, or healthcare access. The findings highlight the importance of considering regional factors when evaluating the role of H. pylori in gallstone formation [Fig2].

DISCUSSION

The findings of this meta-analysis suggest that H. pylori infection is associated with an increased risk of cholelithiasis. This association is biologically plausible, as several mechanisms have been proposed to explain how H. pylori may contribute to gallstone formation. H. pylori infection induces a systemic inflammatory response characterized by elevated levels of pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α). Chronic inflammation can promote gallstone formation by altering gallbladder motility and bile composition. Studies have shown that inflammatory mediators can increase cholesterol saturation in bile, a key factor in the development of cholesterol gallstones [17]. H. pylori infection has been linked to dyslipidaemia, including elevated levels of total cholesterol, low-density lipoprotein (LDL), and triglycerides. Dyslipidaemia is a well-established risk factor for gallstone formation, as it contributes to cholesterol supersaturation in bile. Additionally, H. pylori may impair the expression of bile acid transporters, further disrupting lipid metabolism [18]. H. pylori DNA have been detected in bile and gallbladder tissue, suggesting that the bacterium may directly influence bile composition. H. pylori infection has been associated with increased bile lithogenicity, characterized by higher cholesterol levels and reduced bile acid concentrations. These changes create an environment conducive to cholesterol crystallization and gallstone formation [19]. The stronger association observed in Asian populations may reflect differences in H. pylori strains, dietary habits, or genetic predispositions. For example, the East Asian CagA-positive H. pylori strain is more virulent and may have a greater impact on systemic inflammation and metabolic pathways [20]. Additionally, dietary factors such as high carbohydrate intake and low fiber consumption, common in some Asian populations, may exacerbate the effects of H. pylori on gallstone formation [21]. Despite the robust association observed in this meta-analysis, several limitations must be acknowledged. First, the included studies were predominantly observational, precluding the establishment of a causal relationship [22]. Second, there was variability in the methods used to detect H. pylori infection, including serology, stool antigen tests, and histology, which may have influenced the results. Third, confounding factors such as diet, lifestyle, and comorbidities were not consistently adjusted for in all studies. Future research should focus on longitudinal studies to establish causality and investigate whether H. pylori eradication reduces the risk of gallstone formation [23]. Randomized controlled trials evaluating the impact of H. pylori eradication on gallstone incidence and recurrence would provide valuable insights. Additionally, mechanistic studies are needed to further elucidate the pathways linking H. pylori infection to cholelithiasis. Clinically, these findings suggest that H. pylori screening and eradication may be beneficial in patients with cholelithiasis, particularly in high-prevalence regions. However, further evidence is needed before such strategies can be widely recommended.

CONCLUSION

This meta-analysis provides robust evidence supporting H. pylori as a risk factor for cholelithiasis. The association is likely mediated by chronic inflammation, altered lipid metabolism, and changes in bile composition. Geographic variations in the strength of the association highlight the importance of considering regional factors in the pathogenesis of gallstones. Future research should focus on establishing causality and exploring the potential benefits of H. pylori eradication in preventing gallstone formation. Clinicians should consider screening for H. pylori in patients with cholelithiasis, particularly in high-prevalence regions.

Conflict of Interest: The Authors has no conflict of Interest

Funding: None

Contribution: SMH: conceived of the presented idea, wrote the manuscript verified the analytical methods. SMH, FKK, HS, proofread the manuscript. all authors read and approve the Last Version of this Manuscript

Abbreviations

H. pylori Helicobacter pylori
OR odds ratios
RR relative risks
CIs confidence intervals

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