



## Helicobacter Pylori Infection and Gallbladder Diseases: a Mini-review

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### Abstract

Helicobacter pylori is recognized as one of the most common chronic bacterial infections worldwide. It's proved to be the main pathogenic agent in chronic gastritis, peptic ulcer, and gastric cancer, as well as the proposed etiology in diseases of the organs other than the stomach and duodenum like liver, biliary system, heart and vascular system, and skin. In this mini-review, we aimed to discuss shortly about the association of H. pylori infection in gallbladder diseases, such as chronic cholecystitis, cholelithiasis, and gall bladder cancer. Our study shows that H. pylori infection in the gallbladder may be one of the etiological factors leading to the gallbladder diseases. The precise mechanism requires further verifications.

**Keywords:** Helicobacter pylori, gallbladder, Chronic cholecystitis, Cholelithiasis, Gallbladder cancer

### Introduction

Helicobacter pylori (H. pylori) is a spiral shaped, gram-negative, microaerophilic rod with 4-7 flagella [1]. It is recognized as one of the most common chronic bacterial infections worldwide, infecting approximately half of the global population. And is proved to be the main pathogenic agent in chronic gastritis, gastric ulcer, duodenal ulcer, chronic[2]. Atrophic gastritis, gastric Mucosa-Associated Lymphoid Tissue (MALT) lymphoma, gastric adenocarcinoma, non-ulcer dyspepsia and Gastro Esophageal Reflux Disease (GERD) [3].

The relationship of H. pylori with diseases of organs other than the stomach and duodenum has also been investigated and reported [4]. H. pylori antibody was detected in liver in patients with chronic liver diseases, non-alcoholic fatty liver diseases, non-alcoholic steatohepatitis, liver fibrosis, primary sclerosing cholangitis, primary biliary cirrhosis, intrahepatic stones, hepatic encephalopathy in patients with cirrhosis, and hepatic carcinoma[5 6], in biliary tract and gallbladder in biliary epithelial inflammation [7 8]. Cholelithiasis in heart and vessels in atherosclerosis, acute coronary ischemia (biopsies from aorta and internal mammary artery), Coronary Heart Disease (CHD), and atheroma [9 10]. And in the skin in acne rosacea, chronic urticaria, and Sweet's Syndrome [11 12]. To add more, H. pylori is associated with iron deficiency anemia in children, Cobalamin deficiency, vitamin B-12 deficiency, and megaloblastic anemia [13 14].

In this mini-review, we aimed to discuss shortly about the association of H. pylori infection in gallbladder diseases, such as chronic cholecystitis, cholelithiasis, and gall bladder cancer.

### Results

#### Chronic cholecystitis

Sabbaghian showed that GERD and gastritis are mostly seen in biliary dyskinesia [15] and this observation raised the question if colonization of the gallbladder with H. pylori would be the cause of chronic inflammation similar to the association of H. pylori in Chronic gastric inflammation. Moricz. Found a high prevalence of H. pylori infection in the patients with chronic cholecystitis and proposed this bacterial infection may be associated with pathological mechanism [16]. Chen DF showed the association of gastric metaplasia of gallbladder mucosa with chronic cholecystitis which this might be related to the H. pylori infection in the gallbladder. Moreover, they showed that there was a significant association between H pylori positivity and Interleukin-1 (IL-1), IL-6 and IL-8 levels in the gallbladder, indicating that these ILs may participate in pathogenesis of chronic cholecystitis [17]. This result is consistent with the role of ILs in the pathogenesis of H pylori-related gastritis and gastric ulcer[18].

#### Cholelithiasis

Kawaguchi first detected H. pylori in the gallbladder's mucosa of a patient with gallstones and cholecystitis who underwent cholecystectomy in 1996 for the first time. There are controversial results from different studies, showing in favor of or against the theory of role of H. pylori in gallstone formation. In the in-favor group, we could propose that the biliary obstruction and subsequent bile stasis can lead to bacterial overgrowth and to the development of gallstones [19 20].

## Gallbladder cancer

Risk factors for the development of gallbladder cancer are patient demographics, gallbladder abnormality, patient exposure, and Salmonella and Helicobacter infections. The association between H[21 22]. pylori infection and biliary tract carcinoma (gallbladder cancer, and cholangiocarcinoma) is still controversial Hassan howed that the H. pylori infection could aggravate gallbladder mucosal lesions which are potentially precancerous (mucosal hyperplasia, metaplasia, and lymphoid infiltration). There are multiple possible mechanisms explaining the association of H. pylori infection and gallbladder cancer: 1. promoting cell inflammation (IL-8 production) 2. Disturbing cell proliferation and apoptosis 3. The perigenetic pathway: inflammation and increased TNF- $\alpha$  and IL-6 production, causing change in cell adhesion and lead to dispersion and migration of mutated epithelial cells 4. Cag PAI which is a H. pylori virulence factor activates the proinflammatory signaling pathways in hepatobiliary cells (as the same effect on gastric epithelial cell) [23 24].

## Conclusions

Our study shows that H. pylori infection in the gallbladder may be one of the etiological factors leading to gallbladder diseases. The precise mechanism requires further verifications [25].

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