

ORIGINAL ARTICLE

HELICOBACTER PYLORI INFECTION IN PATIENTS WITH CALCULAR CHOLECYSTITIS: A HOSPITAL BASED STUDY

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Background: *Helicobacter pylori*, a gram negative bacillus has been recognised as a public health problem and approximately half of the world population has *H. pylori* infection causes chronic gastritis, peptic ulcer disease and gastric malignancies. Objective of this study was to determine the frequency of *H. pylori* infection in patients of chronic calculous cholecystitis. **Methods:** This cross-sectional descriptive study was conducted at Liaquat University Hospital, Hyderabad, Pakistan from April 2010 to September 2010. All patients with history of gallstone presented with acute abdominal pain, dyspepsia, bloating and epigastric discomfort and diagnosed as calculous cholecystitis were further evaluated for the detection of *H. pylori* by serology and histopathology. Frequency and percentage of *H. pylori* infection in patients with calculous cholecystitis was calculated. **Result:** Total 100 patients of cholelithiasis underwent laparoscopic cholecystectomy were recruited. The pain in upper right part of the abdomen was observed in all 100 patients, fever in 75%, nausea and vomiting in 68%, loss of appetite in 45%, feeling of tiredness or weakness in 22%, headache in 38%, chills in 52%, backache in 58%, pain under the right shoulder in 45%, heartburn in 67%, belching in 54%, indigestion in 80%, dyspepsia in 90%, bloating in 88%, and epigastric discomfort in 85% patients. Eighty-two percent patients had family history of gallstones. The mean age of overall study population was 48.72±8.78 years and mean age of *H. pylori* infected calculous cholecystitis patients was 47.98±5.43 years in male and 48.76±6.68 years in females. The *H. pylori* infection was identified in 55% patients with calculous cholecystitis, of which 32.7% were males and 67.3% were females ($p=0.03$, statistically significant). Majority of females (60%) had ≥ 40 U/ml antibody titre ($p=0.917$, non-significant). **Conclusion:** A possible relationship was identified between *Helicobacter pylori* and calculous cholecystitis

Keywords: Gallstones, cholelithiasis, calculous cholecystitis, cholelithiatic cholecystitis, *Helicobacter pylori*

INTRODUCTION

Cholecystitis is defined as inflammation of the gallbladder that occurs most commonly because of an obstruction of the cystic duct from cholelithiasis. Ninety percent of cases involve stones in the cystic duct, (i.e., calculous cholecystitis) with the other 10% of cases representing acalculous cholecystitis.¹ The blocking of the cystic duct leads to thickening of bile, bile stasis, and secondary infection by gut organisms predominantly *E. coli* and *Bacteroides* species.² As the gallbladder becomes distended, blood flow and lymphatic drainage are compromised leading to mucosal ischemia and necrosis. Cholecystitis mainly presents with pain in the right upper quadrant which is usually a constant severe pain and radiates to the back or tip of right shoulder.^{3,4} Chronic cholecystitis manifests with non-specific symptoms such as nausea, vague abdominal pain, belching, and diarrhoea. Uncomplicated cholecystitis has an excellent prognosis with a very low mortality rate. Once complications such as perforation/gangrene develop the prognosis becomes less favourable and around 25–30% of patients either requires surgery or develops such complications. Perforation occur in 10–15% of cases.⁵ Patients with acalculous cholecystitis have a mortality ranging from 10–50% which far

exceeds the expected 4% mortality observed in patients with calculous cholecystitis.⁶ In patients who are critically ill with calculous cholecystitis and perforation or gangrene, mortality can be as high as 50–60%.⁶

Helicobacter pylori, a gram negative bacillus has been recognised as a public health problem and approximately half of the world population has *H. pylori* infection causes chronic gastritis, peptic ulcer disease and gastric malignancies.^{7,8} The prevalence is thought to be 80% in developing countries and 30–50% in developed countries and has been recognised as a public worldwide.⁹ The prevalence appears to be higher in African-American and Hispanic populations although this is likely related to socio-economic rather than racial factors, the lower rate of infection in the West is largely attributed to higher hygiene standards and widespread use of antibiotics.¹⁰ The reported prevalence of *H. pylori* in Pakistan by Devrajani, *et al* was 49%.⁹ Recently, the bacterium has been implicated as a risk factor for various extraintestinal diseases including hepatobiliary diseases ranging from calculous cholecystitis and primary biliary sclerosing cholangitis to gall bladder cancer and primary hepatic carcinomas.¹¹ Many researchers have demonstrated the presence of *Helicobacter* in gall bladder of patients with calculous cholecystitis.^{12–15}

We planned the present clinical study to see the frequency of *H. pylori* in patients with calcular cholecystitis. Early detection and eradication of *H. pylori* infection can prevent the patients to acquire life threatening complications.

PATIENTS AND METHODS

This cross-sectional study was conducted at Liaquat University Hospital, Hyderabad, Pakistan from April 2010 to September 2010. The patients with calcular cholecystitis presenting with acute abdominal pain, dyspepsia, bloating and epigastric discomfort were further evaluated for *H. pylori* infection. History of all patients was taken and complete physical and relevant clinical examinations were performed. Routine investigations were also sorted. The calcular cholecystitis was diagnosed by abdominal ultrasound performed by expert sonologist. The referred patients from different units of hospital had history of abdominal pain and diagnosed as cases of cholelithiasis were also included in the study. For detection of *H. pylori*, 2–3 ml venous blood sample was collected in a disposable syringe from every relevant patient a day before laparoscopic cholecystectomy and sent to laboratory for analysis. The method used for *H. pylori* infection was serology and histopathology. The anti-Helicobacter pylori antibody (IgG) concentration ≥ 20 U/mL by quantitative ELISA was considered as positive. A small piece of gall bladder and bile specimen sample was collected during laparoscopic cholecystectomy with sterile measures in a bottle containing 5 ml normal saline and rest of the gall bladder tissue put in 10% formalin and sent for histopathological examination, rapid urease test and gram smear.

The exclusion criteria of the study were: patients of ≤ 12 year age, unwilling subjects, and patients already on antibiotics or *H. pylori* eradication therapy. The data was analysed using SPSS-10. The frequency and percentage of *H. pylori* was calculated in calcular cholecystitis and for gender distribution. Mean and standard deviation was calculated for age. The Chi-square test was applied between categorical variables at 95% confidence interval and the $p \leq 0.05$ was considered as statistically significant.

RESULTS

During the study period total 100 patients of calcular cholecystitis were recruited. Seventy-eight (78%) patients were admitted in surgical ward whereas remaining twenty-two (22%) were referred from different units and OPD of the hospital. Out of 100, 42 (42%) were males and 58 (58%) were females. Majority (70%) of patients presented through causality outpatient department (COD). The pain in upper right part of the abdomen was observed in all patients, fever in 75%, nausea and vomiting in 68%, loss of appetite in 45%,

feeling of tiredness or weakness in 22%, headache in 38%, chills in 52%, backache in 58%, pain under the right shoulder in 45%, heartburn in 67%, belching in 54%, indigestion in 80%, dyspepsia in 90%, bloating in 88%, and epigastric discomfort in 85% patients. Eighty-two patients had family history of gallstones. The mean age of overall study population was 48.72 ± 8.78 years and the mean age of male and female population was 43.33 ± 5.45 and 45.88 ± 8.65 years respectively. The overall mean age of *H. pylori* infected cholelithiasis patient was 52.77 ± 8.58 years, 47.98 ± 5.43 years in males and 48.76 ± 6.68 years in females. Gender distribution of *H. pylori* infection in patients with calcular cholecystitis is shown in Table-1. Helicobacter organisms were also isolated from the tested bile or gallbladder tissue, histopathological examination of resected gallbladder containing stones revealed chronic cholecystitis with mononuclear cell infiltrate. The erosions and ulcers were found in 78% and 65% of examined gallbladder specimens respectively.

The IgG antibody titre of *H. pylori* in patients with calcular cholecystitis patients in relation to gender distribution is shown in Table-2. Of 55 *H. pylori* infection patients, 38 (69%) belonged to urban areas and 17 (31%) were from rural areas of Sindh.

Table-1: Gender distribution of *H. pylori* infected patients with cholelithiasis

Cholelithiasis	<i>Helicobacter pylori</i>		Total	p-value
	Positive	Negative		
Male	18 (32.7%)	24 (53.3%)	42 (42%)	0.03*
Female	37 (67.3%)	21 (46.7%)	58 (58%)	
Total	55 (100%)	45 (100%)	100 (100%)	

*Significant

Table-2: Gender distribution of *H. pylori* IgG antibodies

IgG U/ml	Gender		Total	p
	Male	Female		
20	1 (5.6%)	2 (5.4%)	3 (5.5%)	0.917*
21–30	3 (16.7%)	6 (16.2%)	9 (16.4%)	
31–40	2 (11.1%)	8 (21.6%)	10 (18.2%)	
41–50	6 (33.3%)	11 (29.7%)	17 (30.9%)	
>50	6 (22.2%)	10 (27.0%)	16 (29.1%)	
Total	18 (100%)	37 (100%)	55 (100%)	

*Non-significant

DISCUSSION

The *H. pylori* has been implicated as a risk factor for different extraintestinal disorders.¹⁶ Like *Salmonella typhi*, these Helicobacter organisms are tolerant to bile, colonise bile canaliculi and the gallbladder and cause hepatitis and cholecystitis. Chronic cholecystitis is commonly associated with gallstone disease and some studies have shown that cholecystitis and gallstones can cause epithelial hyperplasia of the gallbladder mucosa or cancer and various bacterial genomes have been detected in gallbladder carcinoma tissue.^{17,18} *H. pylori* can damage human gallbladder epithelial cells and could be the key

factor that leads to clinical cholecystitis.¹⁹ A meta-analysis of published work has shown strong association between *Helicobacter* and gall bladder disorders.²⁰

The present study was done to ascertain whether *H. pylori* could be identified in serum and resected gallbladder tissue and bile collected from patients with chronic calculous cholecystitis. Majority of the subjects were female with cholelithiasis, the female population was also predominant in relation to *H. pylori* infection in patients with calculous cholecystitis. This is an important information suggesting that majority of patients with calculous cholecystitis in the study group were positive with higher titres anti- *H. pylori* antibodies.

It has been observed that a fat, fertile, female of forty is at risk of cholelithiasis. We found that overall mean age of female individuals was 45.88±8.65 whereas it is 48.76±6.68 in *H. pylori* infected calculous cholecystitis patient which is consistent with the study by Apostolov *et al.*²¹ In the present study, statistically significant differences were found between prevalence of anti- *H. pylori* IgG in the study group which is consistent with the study by Deeba *et al.*²² and Karagin *et al.*^{22,23} Some studies found no significant differences in prevalence of anti- *H. pylori* IgG antibodies in patients with cholelithiasis and controls.^{24,25}

In our study majority of patients had symptoms like acute abdominal pain, dyspepsia, bloating, and epigastric discomfort, and it seem that they had coexisting acid peptic disease with calculous cholecystitis that can be correlated with observation of the study by Nilsson *et al.*²⁶ In the present study, it was observed that 60% of the patients had titres of ≥40 U/ml, of which female were predominant but the differences were not statistically significant. It is consistent with the study by Maurer *et al.*²⁷

In present study the sole identification of *H. pylori* in serum and resected gallbladder tissue among patients with cholelithiasis provides a strong evidence of association of the organism with chronic calculous cholecystitis and its possible implication in the disease pathology.

CONCLUSION

H. pylori infection in the gallbladder may be one of the aetiological factors leading to chronic cholecystitis. These observations highlight the need to take preventive, appropriate and eradication measure for growth of *H. pylori* in gallbladder.

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