ORIGINAL ARTICLE

Frequency of helicobacter pylori infection in patients presenting with symptomatic cholilithiasis at tertiary care hospital, Karachi

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Abstract:

Background: Gallstones represent a significant burden for health care systems worldwide and are one of the most common disorders presenting to emergency room. It is becoming an increasingly common cause of morbidity, leading to hospital admission in the developing world. The bacterium Helicobacter pylori (H. pylori)has been implicated as a risk factor for various diseases including chronic gastritis, gastric ulcer, duodenal ulcer, and gastric cancer. Helicobacter pylori are believed to be a mediating factor for gastric and extragastric diseases. The gallbladder and bile duct may be two of the targets of chronic H. pylori infection.

Aim: To study the frequency of helicobacter pylori infection in patients presenting with symptomatic cholelithiasis at tertiary care hospital, Karachi.

Material and Methods: The study is conducted in Surgical Unit III, Abbasi Shaheed Hospital, Karachi to clarify the prevalence and investigate the correlation between H. pylori infection and gallstones. All patients with symptomatic gall stones admitted for laparoscopic or open cholecystectomy were included in the study. The method for H. pylori infection detection is stool antigen test.

Results: 165 patients were admitted in Surgical Unit III, Abbasi Shaheed Hospital, Karachi from January 2018 to July 2021 with symptomatic gallstones for Laparoscopic / Open cholecystectomy. 29(17.57%) are males and 136(82.41%) are females. 149(90.30%) patients had laparoscopic cholecystectomy and 16(9.69%) patients had open cholecystectomy. 11(6.66%) patients had conversion of difficult laparoscopic to open cholecystectomy. H. pylori stool antigen was positive in 47(28.48%) and had medical therapy for H. pylori before surgery.

Conclusion: Our result showed a significant positive correlation between H. pylori infection and symptomatic gall stones. H. pylori infection is closely related to an increased risk of cholelithiasis and chronic cholecystitis.

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Introduction:

Gallstones represent a significant burden for health care systems worldwide. It was once considered a disease of western world but due to changes in food pattern and lifestyle, it is becoming an increasingly common cause of morbidity and the leading cause of hospital admission in the developing world. Its occurrence in West is 10% and in Asian population ranges from approximately 3%-15% and in Pakistan and the incidence of gall stones is about 4% and 14.2% in males and females respectively.[1] Gallstone formation may be associated with a complex interaction of genetic and environmental factors such as female sex, family history, and ethnicity.[2] Lifestyle and some other metabolic disorders, high alcohol consumption, hyperlipidemia, fatty liver, and obesity also affect gallstone formation.[3]

Helicobacter pylori, is a gram negative bacillus, it has been recognized as a public hazard and approximately half of the world population has

Table 1: Age distribution

Age in years	No of patients	%ages
<20 years	4	2.42%
20-29 years	21	12.72%
30-39 years	38	23.03%
40-49 years	43	26.06%
50-59 years	34	20.60%
>60 years	25	15.15%

Table 2: Types of Cholecystectomy

Types of Cholecystectomy	No of patients
Laparoscopic Cholecystectomy	149 (90.30%)
Open Cholecystectomy	16 (9.69%)

Table 3: Frequency of H.Pylori infection

H.Pylori infection stool antigen test	Frequency	Percentages
Yes	47	28.48%
No	118	71.51%
Total	165	100.0%

H. pylori infection. The prevalence is thought to be 60%- 80% in developing countries and 30%–50% in developed countries and has been recognized as a public hazard worldwide.[4] The reported prevalence of H. pylori in Pakistan was 49%.[5] The other study showed the prevalence of H. pylori infection as 12.06%.[6]

Recently, the bacterium has been implicated as a risk factor for various extra-intestinal diseases including hepatobiliary diseases ranging from calcularcholecystitis and primary biliary sclerosing cholangitis to gallbladder cancer and primary hepatic carcinomas.[7] Helicobacter pylori are believed to be a mediating factor for various gastric and extragastric disease. The gallbladder and bile duct may be two of the targets of chronic H. pylori infection and gallstones formation.

The study is designed to determine the frequency of H. pylori in patients presenting with symptomatic cholelithiasis in order to establish the local perspective as there is paucity of local data. Early detection would help in establishing the magnitude of problem and on the basis of which effective and timely management can be done which would impact upon the progression of disease and its complications. Moreover, data from this study would provide the much needed local perspective as there is wide variation in prevalence of H. pylori infection in different regions of the world. We are burdened with a large population of patients with symptomatic cholelithiasis.

Material and Methods:

The study was conducted after permission from the institutional ethical review committee. Consenting cases, meeting inclusion criteria were enrolled in the study from the Surgical Unit III, Abbasi Shaheed Hospital, Karachi. Informed consent was obtained from all the patients for assigning them to the study and using their data in research. Brief history about duration of illness and demographic information was taken at the time of admission.

All patients with symptomatic gallstones admitted for laparoscopic or open cholecystectomy were included in the study. Non-consenting patients, patients who have taken H-pylori eradication therapy within 4 weeks duration, patients with history of perforated peptic ulcer or patients unfit for general anesthesia and Surgery were excluded.

Stool sample was sent before surgery for H. pylori stool antigen test (SATs). The stool immunoassay test uses a polyclonal anti-H. pylori and is developed to identify current infection by detecting antigen(s) that are producedand shed into the stool by live H. pylori bacteria. All H pylori stool antigen positive patients were treated with triple therapy for 14 days before surgery.

Results:

165 patients were admitted in Surgical Unit III, Abbasi Shaheed Hospital, Karachi from January 2018 to July 2021 with symptomatic gallstones for Laparoscopic/Open cholecystectomy. 29(17.57%) were males and 136(82.41%) were females. Mean age of 43.87±11.21. Majority of

patients were between 30- 50 years 81(49.09%). [Table 1]

149(90.30%) patients had laparoscopic cholecystectomy and 16(9.69%) patients had open cholecystectomy. [Table 2]11-patients had conversion of laparoscopic to open cholecystectomy due to difficult anatomy, 3-patients with Hepatitis C viral marker positive and deranged clotting profile, 2-patients had Mirizzi syndrome and impacted stone at the neck had open cholecystectomy. In cholecystectomy patients 41(24.84%) were diabetics and 54(32.72%) were hypertensive.

H. pylori stool antigen was positive in 47(28.48%) and treated by medical therapy before surgery. Data was analyzed on SPSS Version 20. Mean and standard deviation was calculated for continuous variables such as age and duration of symptoms.

Discussion:

Incidence of gallstones increases with age in all racial groups.[8] In addition to ethnicity and genetics, advancing age, obesity and female gender are also risk factors for gallstones. Because of female sex hormones and increased cholesterol levels, females with obesity are more likely to get gallstones.[9] However, the most significant risk factors for gallstone disease were patients with age >65 years and being overweight BMI>25.[10] The incidence of H. pylori increases with age and the probability of detecting H. pylori in the bile increased steadily with increasing age.[11] In our study the gallstone disease is more common in females. 17.57% were male and 82.41% were female.

Helicobacter species have not been proved to induce histological injury to the biliary epithelium or liver parenchyma. The strongest association of the presence of these organisms in bile is with cholestatic conditions.[12] The presence of H. pylori in gallbladder wall mucosa might indicate a big risk for cholelithiasis. Several studies showed variable incidence of H.Pylori in symptomatic gallstones 10%-55%.[13]

In another study the presence of H. pylori in the gallbladders ranges from 33% to 37% of patients with symptomatic gallstones.[14] In our study the infection rate of H.pylori in symptomatic gall stones is 47/165 (28.48 %).(Table 3) Helicobacter pylori infection of the gallbladder was significantly associated with cholelithiasis an increased risk of chronic cholecystitis and cholecystitis when compared with the control group. (24.98% vs. 8.28%, P<0.05).[15]

Several factors have been reported to play roles in the formation of gallstones, including bacterial infections in the gallbladder and bile ducts.[16] It is known that increased incidence of hepatobiliary disease and risk of hepatobiliary cancer is associated with chronic carriage of Salmonella typhiin the gallbladder. Whether or not H. pylori has a similar relationship in patients with chronic cholecystitis can only be proved by a prospective study of hepatobiliary disease using appropriate tests for H. pylori diagnosis.

H. pylori was first described in the gallbladder mucosa in patients with gallstones in 1996, and a relationship between H. pylori and gallstone formation was reported. Bacteria closely similar to Helicobacter pylori detected immunohistologically and genetically in resected gallbladder mucosa.[17] The survival of H. pylori is documented to be more favorable in low pH areas mostly in stomach.[18] It remains unclear if H. pylori reaches the gallbladder and biliary tree via an ascending route from the duodenum, or via the portal venous system.[19] Patients undergoing Endoscopic retrograde Cholangiopancreatography (ERCP) specially sphincterotomy reported that the procedure could result in contamination of the gallbladder with helicobacter strains via the ascending pathway from the duodenum. The stomach was colonized in nearly all patients with infected bile, and it is likely that the bacteria may have entered the bile ducts by reflux from the duodenum. Even the stones retrieved from common bile duct during ERCP may harbor H. pylori.[20]

Hematogenous spread via the portal venous system to the liver and the excretion of the or-

ganisms into the bile is another pathway for the H. pylori spread. After translocation of Helicobacter species may colonize the biliary tract. Bile and gallbladder tissue samples were obtained from patients who underwent cholecystectomy for chronic cholecystitis with cholelithiasis. Patients with gallstones were 3.5 times as likely to have H. pylori in the bile compared with patients in a control group.[21]

Different mechanisms are responsible for the formation of pigmented gallstones and cholesterol gallstones. Recently, studies showed that H. pylori infection could have an important role in the formation of cholesterol gallbladder stones.[22] Since Helicobacter species was detected from the gallbladder tissue, gallstone, and bile taken from the gallbladder specimen, and results have shown that H. pylori, may contribute to the formation of cholesterol gallstones.[23] Due to bile stasis H. pylori is relatively more colonized in bile in gallstone diseases and support the role of H. pylori in the development of cholecystitis in humans.[24] Dar et al,[25] also pointed an association between the presence of H. pylori and hepatobiliary stone diseases.

Diagnostic testing methods available for H. pylori include non-invasive and invasive techniques. Non-invasive techniques include serology, urea breath testing, and stool antigen detection of H. pylori. Serology testing is the least sensitive non-invasive technique. It has 75% to 85% sensitivity compared with 95% sensitivity for stool antigen and urea breath testing. Because of the high rate of false positives, serology test is no longer recommended in the United States.Stool antigen tests detect active infection, and excellent for pre-treatment or post-treatment testing, and are highly specific for H. Pylori infection.[26]

Stool antigen test (SAT) detects the presence of H. pylori antigen in stool samples and has a good sensitivity and specificity, 94% and 97% respectively in global meta-analysis, in the diagnosis of H. pylori infection.[27] Stool antigen tests are easy to perform and do not require specialized equipment, which make it suitable for in-office test in developing countries. Moreover, SAT is a useful tool for epidemiological study and screening programs.[28] There are two types of SATs used for H. pylori detection, enzyme immunoassay (EIA) an immunochromatography assay (ICA) based methods, using either polyclonal antibodies or monoclonal antibodies. EIA-based tests provide more reliable results than ICA-based tests.[29] With regard to cost and equipment, SAT is more suitable than urea breath test (UBT) for mass surveys. As compared with serological test, which are usually used for screening, SAT seems to provide more reliable results in diagnosis of H. pylori infection. The accuracy of SAT is influenced by several factors, like usage of antibiotic, Proto pump inhibitors, altered bowel movements and upper gastrointestinal bleeding. Preservation of the specimen, temperature, transport time before testing, and test cut-off valve also have impact on the diagnostic accuracy of SAT.[30] H. pylori stool antigen testing are recommended as non-invasive tests for active H. pylori infection, as a basis for a "test-and-treat" strategy for helicobacter pylori in regions in which the prevalence of helicobacter pylori exceeds 20%.[31]

Serum anti-H Pylori antibody test is an unreliable test for evaluating and eradication therapy because antibodies can be present in the blood for a long time even after successful eradication. Thus Serology is suboptimal for the diagnosis of active H. pylori infection.[32]

Helicobacter pylori infection may be involved in the formation of brown pigmented gallstones. Helicobacter pylori can produce oxidative stress and free radical re-actions through the reactive oxygen species (ROS) and re-active nitrogen species (RNS) system 33 and release large amounts of pro inflammatory and vasoactive sub-stances, such as interleukins (IL)-1, IL-6, and tumor necrosis factor (TNF)-α34, which are involved in gallbladder inflammatory disorders and pathogenesis of gallstones. Urease-positive Helicobacter species are capable of precipitating calcium and may also promote the risk of gall stone formation by acting as a foreign body nidus.[35] H pylori in gallbladder induces beta-glucuronidase, bacterial hydrolase, and phospholipase to deconjugate bile and hydrolyze

phosphatidylcholine, thus promoting the synthesis of free bilirubin, free bile acids, and free fatty acids. Urease positive helicobacter species precipitates free ionized calcium ion with free bilirubin to form calcium bilirubinate stones. Calcium bilirubinate, free bileacids, and free fatty acids are the major components of brown pigment stones.[36]

Since H. pylori infection promotes the formation of gallstones, Zhang et al,[37] and Takahashi et al,[38] consider whether H. pylori eradication therapy can prevent the formation of gallstones, they both found a statistically significant trend in the reduction of gallstones among the patients who received helicobacter pylori eradication.

Conclusion:
Helicobacter pylori infection is found in patients treated for symptomatic gall stones. Helicobacter pylori infection is closely related to an increased risk of chronic cholecystitis and cholelithiasis. Treatment of helicobacter pylori infection is necessary to save the patients from post cholecystectomy symptoms.

Limitations: Due to the intrinsic limitations of a single-centered study, more accurate population-specific conclusions could have been drawn with larger-scaled research.

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Role and contribution of authors:
Nimra Ali, collected the data, references and did the initial write up.

Azfaruddin Qureshi, went through the article, made useful changes in introduction, discussion and result.

Sayed Ashraf Hassan, critically went through the article and made final changes.

Ramsha Fareed, collected the data and helped in introduction writing.

Farhina Salahuddin, collected the references and helped in discussion writing.

Narmeen Farooq Panjwani, collected the data, references and also helped in interpretation of data.

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