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H.Pylori in Chronic Cholecystitis- Histopathological and Immunohistochemical Assessment

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Conflict of interest: Nil

Abstract

Introduction

Gallstones are the most commonly occurring disease in surgical practice, with a prevalence of 10-15% in the European population and 3-5% in the Asian and African populations. [1]The overwhelming majority of cholecystectomies are performed for chronic cholecystitis. The cause of cholecystitis is multifactorial and still remains unclear.

Helicobacter pylori are gram negative, spiral-shaped bacilli typically present in the microaerophilic environment of the gastric epithelium. [2]There are two types of helicobacters: gastric helicobacter and enterohepatic helicobacter.[3]

H pylori gastritis is known to have complications like gastroduodenal ulcers, gastric atrophy, intestinal metaplasia, gastric cancer and mucosa associated lymphoid tissue (MALT) lymphoma.[4] Both invasive and non-invasive methods like histopathological examination, rapid urease test (RUT), microbiological culture, and polymerase chain reaction (PCR) and stool antigen tests, serology, urea breath testing (UBT) respectively are employed to identify H. pylori infection.[5]

In 1996, Chang et al. [6] unintentionally found Helicobacter pylori in the mucosa of the gallbladder of a patient suffering from cholecystitis. Since then, numerous studies have found Helicobacter species such as H. pylori, H. pullorum, H. hepaticus, H. ganmani and H. bilis, in the bile extracted from the gallbladder and in gallbladder tissue [7,8]

However, despite conflicting findings from multiple research, it is still unclear how cholecystitis or cholelithiasis relate to H. pylori infection in the gallbladder.

The objectives of this study were to conduct a histopathological examination of chronic cholecystitis cases and to investigate the frequency of H. pylori association with chronic cholecystitis. Also to evaluate specific morphological finding if any with H pylori positive chronic cholecystitis.

Keywords: Epithelial Atrophy, Cholesterolosis, Lymphoma, Urea Breath Testing

Materials and method

Ours was a retrospective study conducted on 50 cases of cholecystectomy received during the period of August 2022-January 2022 (6 months) in the Department of Pathology, Bangalore Medical college and Research Institute. The current study was approved by the ethical committee.

Relevant clinical data of the patients were recorded in the Performa .Gross examination of the gall bladder specimens were carried out. The presence of gall stones were recorded. After tissue processing, 5-7 micron thick sections were stained using hematoxylin and eosin. The sections so stained were studied thoroughly through light microscopy. All HPE results were documented like inflammation, severity of inflammation, hyperplastic changes, atrophy, cholesterolosis, intestinal metaplasia and fibrosis.

Following that, the representative tissue block was subjected to a primary monoclonal antibody directed against H pylori and its expression was analysed and studied. H pylori positive gastric biopsy was taken as the control slide. Following the use of appropriate statistical tests, these results (HPE and IHC) were associated with a number of parameters and compiled. The acquired data was transformed into a straightforward percentage format, and the chi square test was employed for statistical evaluation.

Results

A total of 50 cholecystectomy cases were analysed out of which female were 70% and males 30% with a mean age group of 43 years (43± 13.5) Gall stones were present in 86% of the cases. Chronic cholecystitis was present in 94% and acute on chronic cholecystitis in 6% cases. Mild – moderate inflammation was noted in 96% of cases while 4% showed severe inflammation. Additional microscopic characteristics seen were intestinal metaplasia, epithelial atrophy, fibrosis and cholesterolosis. (Figure 1-3)

H pylori immunostain was negative in 35 cases (70%) and positive in 15 cases (30%) (Graph 1). In my study, H pylori immunostain was seen significant in male patients with a p value of <0.001. (Figure 4-6). There was no apparent association between H pylori and age group, gallstones, or other histological characteristics. Association of H pylori with all the other parameters is given in table 1.

Discussion

The presence of H.pylori is frequently documented in various extra-gastric sites. Human Helicobacter species have been linked to a variety of hepatobiliary disorders, including malignancies like hepatocellular carcinomas, gallbladder carcinomas as well as benign conditions like chronic cholecystitis, hepatolithiasis, primary biliary cirrhosis and primary sclerosing cholangitis. [9]

A clear correlation between cholecystitis and an H. pylori infection has not yet been found and the precise route by which the H. pylori bacteria enter the hepatobiliary system is also unknown.[10]

The large intestine, skin, ears, nose, and even the eyes showed signs of H. pylori infection, according to a study by Testerman TL et al. Using the culture method, the same study revealed that H pylori was present in the gallbladder. [11]

The IHC/immunostaining method is used to examine the frequency of H. pylori association with chronic cholecystitis in our study of 50 cholecystectomy specimens. Additionally, any particular morphological features that may be linked to H. pylori-positive cholecystitis are studied as well.

In a study by Dar et al, a significant association was found between h pylori and hepatobiliary stones. [12,13] However no such association was seen in the present study.

45 patients made up the study population in another study by Rashmi Patnayak et al., and the mean age was 47±13.5 years (Min-20 and Max-77). Most of them (27 out of 45) had many pigmented stones. In three cases, cholesterol stones were observed. The majority of the specimens (37/45) had a diagnosis of chronic calculus cholecystitis. The H. pylori immunostain was positive in 10 of the patients. H pylori immunostaining did not significantly correlate with gallstones.[14] These results were consistent with our research.

In another study conducted in Iran by Fatemi et al., DNA from 10 Helicobacter species—including two H. bilis and eight H. pylori—was found in the bile of 77 patients with acute and chronic cholecystitis. However, Acute gallstone cholecystitis was found to be strongly correlated with H. pylori DNA here, which our analysis did not account for.[15]

In our study we found a significant correlation of H pylori with chronic cholecystitis in male patients. However in contrast such an association was not found in other research articles. In the current study, no clinicopathological characteristics were associated with H pylori. Similarly in the studies by Khan S A et al and Motie M et al the association of H. pylori with gender, cholecystitis, gall stones, histological features and age distribution were non-significant. [16,17]

Despite all of these conclusions, a research by Bashir S. et al. found that none of the 150 chronic cholecystitis samples tested positive for H pylori using the Giemsa staining method. Only 35 patients had IHC, and those results were likewise negative. [18]

Legend Figures

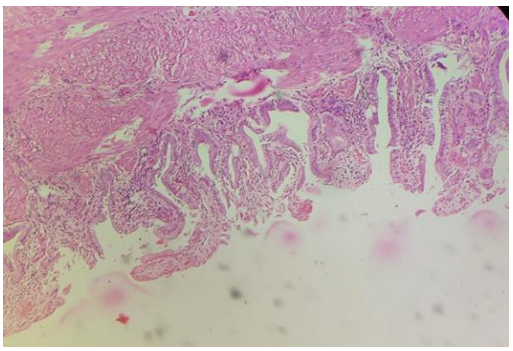


Figure 1: Chronic Cholecystitis (HPE-20X)

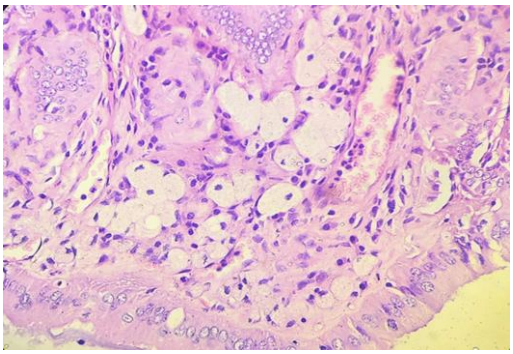


Figure 2: Cholesterolosis (HPE-40X)

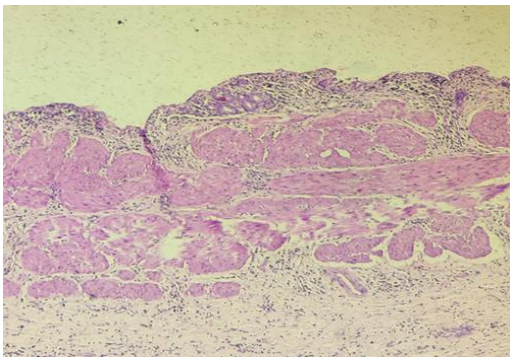


Figure 3: Atrophy (HPE-10X)

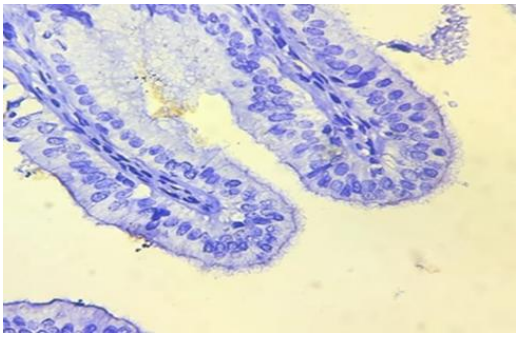


Figure 4: H pylori IHC immunostaining positive (20x)

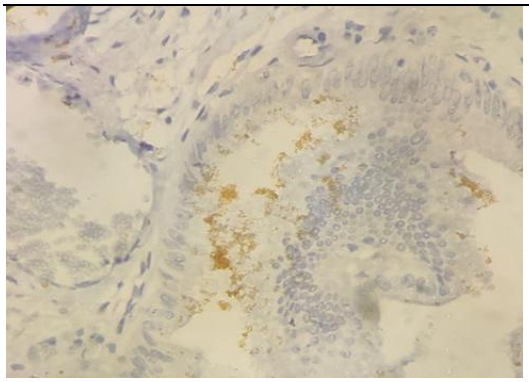


Figure 5: H pylori IHC immunostaining positive (40x)

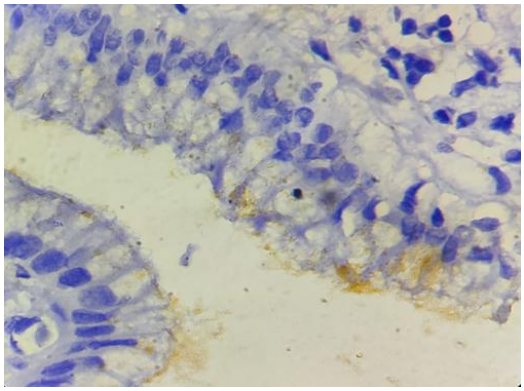
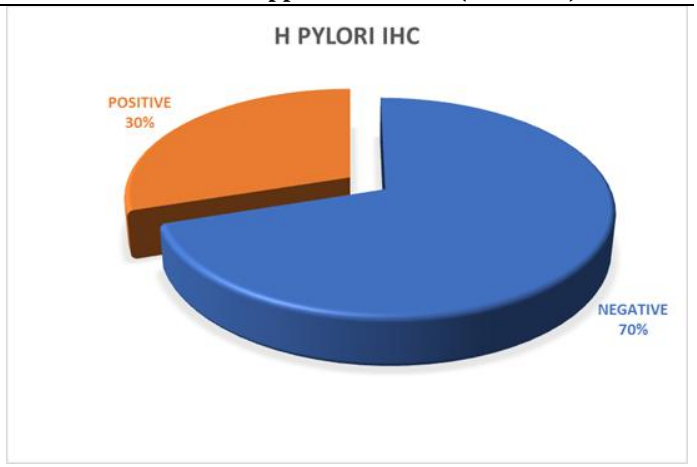


Figure 6: H pylori IHC immunostaining positive (100x)



Graph 1: H Pylori IHC Positivity

Table 1:

	H Pylori Positive	**H Pylori Negative**	**P Value**
	N (%)	**N (%)**	
1. Gender			
Females	5 (14.3%)	30(85.7%)	
Males	10 (66.7%)	5(33.3%)	< 0.001
2. Age			
<30	4(36.4%)	7(63.6%)	
30 - 40	1(10.0%)	9(90.0%)	0.025
40 - 50	6(35.3%)	11(64.7%)	
50 - 60	3(60.0%)	2(40.0%)	
>60	1(14.3%)	6(85.7%)	
3. Diagnosis			
Chronic Cholecystitis	14 (93.3%)	33 (94.3%)	0.085
Acute On Chronic Chole	1(6.7%)	2(5.7%)	

4. Gall Stones			
Gall Stones	12(80%)	31(88.6%)	0.886
No Gall Stones	3(20%)	4 (11.4%)	
5. Severity Of Inflammation			
Mild	12(80%)	29(82.8%)	
Moderate	2(13.3%)	5(14.3%)	0.819
Severe	1(6.7%)	1(2.9%)	

Conclusion

According to our study H pylori was seen in 30% of chronic cholecystitis cases. Even though the incidence of chronic cholecystitis in males is less, since significant association was seen with male patients in present study - the cause of chronic cholecystitis can be attributed to H pylori. But due to limitation of sample size this association requires further research for confirmation.

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