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Research Article

Is *H. Pylori* the New Risk Factor for GB Cancer?

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Abstract

To find out the various clinicopathological presentations of gall stone disease with special relation to *H. pylori* infections of Gall Bladder. Institution based observational study in a tertiary care center. A total of 50 patients were selected who were admitted with the diagnosis of cholelithiasis and planned for cholecystectomy. Gallbladder specimen was then sent for routine H&E stain and additional Giemsa stain. Patients were grouped under two categories based on result of Giemsa stain. Out of which 10% showed the presence of *H. pylori* in the GB wall specimen. The presence of *H. pylori* in gall bladder wall was mostly seen in patients depicting chronic cholecystitis features on histopathological examination. Chronic cholecystitis is one of the most common risk factors for development of GBC. And inflammation being an important predisposing factor for development of cancer, could help us establish a relationship between GB cancer and *H. pylori*. Thus, in areas of high prevalence of GBC, like the gang belt *H. pylori* should further be evaluated as an etiological agent for the development of gall bladder cancer.

Keywords: *H. pylori;* Cholelithiasis; Gall bladder cancer (GBC); Cholecystitis

Introduction

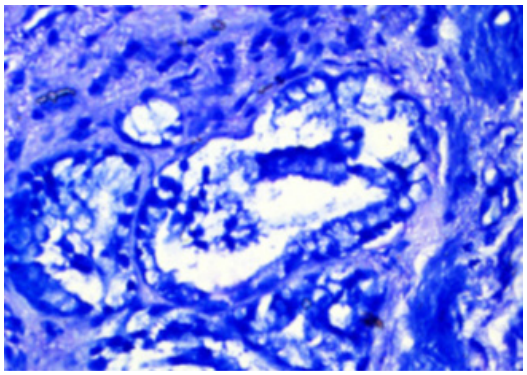

Figure 1: Chronic cholecystitis with positive *H. pylori* in mucosal glands.

India is a high incidence area for GBC. GBC is one of the three leading cancers among women of North and North-east India. The incidence has been steadily rising in India among women as well as men. India accounts for 10% of the global burden of GBC. In India, the incidence of GBC is 10 times higher in north India compared to the southern Indian states [8.9/100,000 population (Delhi) VS. 0.8/100,000 population (Chennai)] [1]. Gallbladder Cancer (GBC) arises from the epithelial lining of the Gall Bladder (GB) and the cystic duct (Figure 1). It is the most common biliary tract malignancy worldwide and manifests as either diffuse thickening of the GB wall or as a GB mass arising from the fundus, neck or body of the GB [2]. *Helicobacter* species has been associated with increased risk of GBC. *H. pylori* was first described in the gallbladder mucosa in patients with gallstones 1996, and a relationship between *H. pylori* and gallstone formation was reported [3]. All studies from India have shown a definite but small risk of *H. pylori* in the causation of GBC. It is hypothesized that a relationship like that of *H. pylori* and gastric carcinoma exists in the gall bladder (Figure 2). According to this, *H. pylori* is a causative agent of gallbladder cancer by causing chronic cholecystitis due to gall stones and

later developing dysplasia, metaplasia and carcinoma. A history suggestive of chronic cholecystitis is present in approximately 50 % of the GBC patients. Recently, inflammation was distinguished as a hallmark of cancer. Increasing proof demonstrated that a large number of tumors originate from sites of chronic inflammation, which supports the perspective that chronic inflammation can incline to cancer [4]. Chronic inflammation plays a serious role in evoking cancer development in the gallbladder.

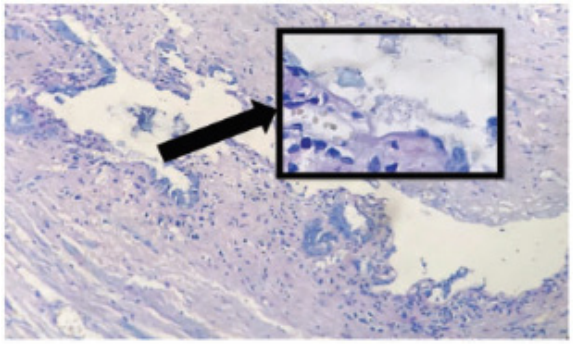

Figure 2: Gallbladder biopsy stained for *H. pylori* using Giemsa staining.

Aims and Objective

To study the presence of *H. pylori* in cholecystectomy specimen of patients of gall stone disease and its co-relationship with histopathological changes.

Material and Methods

A total of 50 patients who presented to surgery department with diagnosis of gall stone disease from the month of April 2020 to October 2020 were included in the study. The study was started after approval from the ethical committee of the medical college (Table 1). These patients were selected randomly between the age group of 18-60 years, with informed written consent and a proforma was created and filled by every patient. Patient taken treatment for *H.pylori* eradication in the past 6 months were excluded from the study. Patient underwent cholecystectomy, Gall bladder specimens was sent for histopathological examination in 10% buffered formaldehyde solution. Gross tissue processing and routine H&E staining of the sections was done as per standard lab protocol (Table 2). Additional sections were taken and subjected to Giemsa staining. The results were studied and compared according to the HPE findings. Based on HPE report, patients will be divided into two categories *H. Pylori* positive and negative group. Further the two groups shall be compared based on the histopathological findings as follows:

A. Inflammation

B. Hyperplasia

C. Pyloric and intestinal metaplasia

D. Dysplasia

E. Cancerous changes.

Table 1.

HPE Finding	Total=50	Percentage
Acute	5	10%
Chronic	40	80%
Acute on Chronic	5	10%

Table 2.

HPE Findings	Total No=50	Percentage (%)
Inflammation	48	96%
Hyperplasia	5	10%
Metaplasia	37	74%
Dysplasia	0	0%
Cancerous Changes	2	4%

Result

Among the 50 patients included in the study, 20% (10) were male and 80% (40) were females. Out of which 93% were symptomatic for gall stone disease and all of them were diagnosed for cholelithiasis based on USG findings (Table 3). The histopathological report depicted chronic inflammation/ cholecystitis in 90% (45) of the patients. 20% (10) patients showed acute and acute on chronic inflammation. Presence of inflammation of depicted in 48/50 patients, accounting for 96% patients .74% (37/50) patients showed metaplasia in GB wall on HPE. Hyperplasia was seen in 10% of the cases. Cancerous changes were evident in 4% (02) of evaluated cases. 10% patients showed presence of *H. pylori* with Giemsa staining in GB wall. Out of the 10%, every patient had chronic cholecystitis appearance on HPE.

Table 3.

GIEMSA Stain for *H. PYLORI*	Total No=50	Percentage
Positive	5	10%
Negative	45	90%

Discussion

The true prevalence and relationship of different species of Helicobacter in the pathogenesis of these diseases is not known. There is currently insufficient evidence regarding the route whereby *H. pylori* settles in the gallbladder. It may reach the gallbladder via an ascending route from the duodenum or via the portal circulation system [5]. Researchers continue to discover new associations between *H. pylori* and idiopathic diseases, as well as potential benefits of *H. pylori* infection. Zhou 14 found *H. pylori* in 20% of chronic cholecystitis cases, and also emphasized that gallbladder metaplasia and pre-malignant lesions such as adenomyomatosis were more frequent in patients positive for gallbladder *H. pylori* [6]. In another study, Hassan [7] 19 reported that *H. pylori* infection aggravated potentially precancerous mucosal lesions. Helaly [8] in their study also showed the presence of *H. pylori* in almost 40.9% of samples in patients with chronic calcular cholecystitis. They also found a significant association between gastric and gall bladder *H. pylori* positivity. The source for gall bladder infection may be

gastric colonization with *H. pylori*. They suggested that *H. pylori* may act as a lithogenic component, especially in presence of pure pigmented gallstones. Bansal, they concluded that there was a high prevalence of *H. pylori* infection in the gallbladder in northern Indian patients undergoing cholecystectomy for benign gallbladder disease which was detected only by PCR. Mishra [9] *H. pylori* may be endemic to the Varanasi region and may not play a significant role in the etiopathogenesis of gallbladder cancer in that region. They concluded that *H. pylori* colonizes areas of gastric metaplasia in gallbladder producing histological changes like those in gastric mucus. A recent study has shown that *H. pylori* can damage human gallbladder epithelial cells *in vitro* and could be the key factor that leads to clinical Cholecystitis. Histological changes, considered pre-neoplastic, were demonstrated in the mucosa of gallbladder, limited to mice infected with *Helicobacter spp* such as, intestinal metaplasia, hyperplasia, dysplasia in addition to eosinophilic inflammation and hyalinosis. Higher prevalence of cholesterol stones in the North Indian population and presence of heavy metals in the water and soil of the Indo Gangetic plains have been postulated as the reason for the same.

Conclusion

H. pylori was found in 10% of the patients included in this study. GBC being asymptomatic, is usually diagnosed in later stages. Therefore, any risk factor that could be evaluated earlier could be an added asset for the early diagnosis of GBC. It raises chances of potential prevention of this disease by eradication of *H. pylori* through medical therapy. Also, clinicians treating patients with gastric *H. pylori* infection need to be aware that associated gall bladder disease may need attention at the same time.

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