

Helicobacter Pylori and Metaplastic Changes in Chronic Cholecystitis: A Correlation Study

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ABSTRACT

Introduction: Various types of metaplastic changes, such as gastric metaplasia (foveolar type or antral type) and intestinal metaplasia, are observed in chronic cholecystitis but not in normal mucosa. Helicobacter species can be detected in the bile and gallbladder tissue of patients with benign gallbladder disease. **Objective:** The present study aimed to observe the correlation between chronic cholecystitis and the presence of Helicobacter pylori as well as the different types of metaplastic changes in gallbladder mucosa. **Materials and Methods:** This descriptive, observational study was conducted at the Departments of Pathology and Surgery at a tertiary care medical college and hospital from April 2021 to March 2022, using a cross-sectional design. All confirmed cases of chronic cholecystitis, with or without cholelithiasis, were included in the study. **Results:** Intestinal metaplasia was the most common type of metaplastic change in the gallbladder epithelium in chronic cholecystitis in this region. PAS and Alcian Blue positivity were significantly higher in cases with metaplasia compared to those without metaplasia. H. pylori was detected in 3 cases (1.55%) of chronic cholecystitis in this study population. **Conclusion:** Mucin histochemistry may help identify early metaplastic changes in gallbladder epithelium. The use of a combination of methods for the detection of H. pylori in gallbladder tissue may increase the detection of positive cases.

KEYWORDS: Helicobacter pylori, PAS, Alcian Blue, chronic cholecystitis, metaplasia

INTRODUCTION

Chronic cholecystitis is a chronic inflammatory lesion that may be a sequela of repeated bouts of acute cholecystitis, and it is mostly associated with cholelithiasis.^[1] The chronically inflamed gallbladder may show hyperplastic, metaplastic, and atrophic changes. The three important mucosal changes, namely hyperplasia, metaplasia, and dysplasia, are considered precursor lesions of malignancy.^[2] Gallbladder malignancy, mostly adenocarcinoma, is the most common malignancy of the extrahepatic biliary tract and is more frequent in females than males (3 to 4:1 ratio).^[2] Cholelithiasis is the most important risk factor (about 95% of cases) associated with carcinoma of the gallbladder.^[2] Different types of metaplastic changes are seen in gallbladder epithelium in chronic cholecystitis. Various studies have been done and are ongoing to show different types of metaplastic changes and whether they have any role in the histogenesis of gallbladder adenocarcinoma.^[1-3]

Chronic cholecystitis is the most commonly encountered disease of the gallbladder, and the overwhelming majority of cholecystectomies are performed for chronic cholecystitis.^[4-6] It is associated with cholelithiasis in more than 90% of the cases. Therefore, as with gallstones, there is a female predominance. Data regarding the prevalence of metaplastic changes in gallbladder epithelium in chronic cholecystitis and the types of metaplasia commonly seen in this part of the country are lacking. Different types of metaplastic changes like gastric metaplasia (foveolar type or antral type) and intestinal metaplasia are seen in chronic cholecystitis, not observed in normal mucosa. Moreover, squamous metaplasia is rarely found in the mucosa of chronic cholecystitis but not seen in the nor-

mal gallbladder. *Helicobacter pylori*, a helical-shaped gram-negative microaerophilic bacterium, is commonly found in the stomach. [7] It infects the stomach, affecting about two-thirds of the world's population and about 30% to 40% of people in the United States. *H. pylori* causes chronic inflammation in the stomach (gastritis) or duodenitis. It also causes gastric cancer or a rare type of stomach lymphoma. *Helicobacter* species can be detected in bile and gallbladder tissue of patients with benign gallbladder disease. Bile-resistant *Helicobacter* species like *H. hepaticus*, *H. bilis*, *H. pullorum*, and *H. ganmani* have been discovered in humans and also in animals. There has been no significant advancement in research works in this area due to the lack of gold-standard diagnostic methods for these organisms in bile, although a few published works have shown a strict association between *Helicobacter* and gallbladder disease. [7] Identification of *H. pylori* by DNA PCR assay showed that *H. pylori* was identified in hepato-biliary mucosa including gallbladder, bile duct, etc. [8] Maurer et al. reported that a mouse model of cholelithiasis was induced by infection with enterohepatic *Helicobacter* species; studies by other observers showed that the prevalence of *H. hepaticus* infections in samples from patients with gallstones or cholecystitis was higher than in samples from patients with other diseases. A meta-analysis of some published work has shown a strong association between *Helicobacter* and gallbladder disease. [7]

The present study was conducted to observe the correlation between chronic cholecystitis and the presence of *Helicobacter Pylori* as well as different types of metaplastic changes in gallbladder mucosa.

METHODS

The study was conducted at the Department of Pathology and General Surgery at a tertiary care medical college and hospital in eastern India. The study period was from April 2021 to March 2022. It was a descriptive, observational study with a cross-sectional design.

Study Population: Patients of all age groups and both sexes who underwent cholecystectomy were provisionally included in the present study after explaining the study and obtaining informed consent.

Inclusion Criteria: All confirmed cases of chronic cholecystitis with or without cholelithiasis were included in the study.

Exclusion Criteria: All patients who underwent cholecystectomy due to carcinoma gallbladder, cholelithiasis without chronic cholecystitis, mucocele of the gallbladder, and porcelain gallbladder were excluded from the study.

A total of 194 patients fulfilled the inclusion criteria and gave valid consent to participate in the study. Specimens of gallbladder were collected after cholecystectomy and received at the Department of Pathology. These specimens were examined grossly, sections were stained with Haema-

toxylin and Eosin (H&E), Periodic Acid Schiff (PAS), Alcian Blue (AB) (pH 2.5), combined Alcian Blue-Periodic Acid Schiff, Giemsa, and Warthin-Starry stain (WS).

Procedure: Fresh tissue was immediately fixed by placing it in 10% neutral buffered formalin for 24 hours and, after appropriate processing, embedded in paraffin 5-micron thick sections and stained by the Haematoxylin and Eosin method. Separate paraffin-embedded sections were stained using PAS, Alcian Blue, combined Alcian Blue-Periodic Acid Schiff, Giemsa, and Warthin-Starry staining. Schiff reagent results: neutral and sialomucin—magenta, nuclei—blue. By studying the PAS, AB, and combined AB-PAS stained sections, the mucin staining pattern of the gallbladder epithelium was observed and recorded.

Statistical Analysis: Data were entered in a Microsoft Excel datasheet. Statistical analysis was done using Epi Info 3.5. The association between different variables was tested using the Chi-Square test. For statistical significance, a *p*-value less than 0.05 was considered significant.

RESULTS

A predominance of female patients was found in this study, with the male-to-female ratio being 1:4.5 (*n* = 194, *M* = 35, and *F* = 159). The mean age of the patients was 43.54 years, with a standard deviation of 12.94 years. The median age of the patients was 44.5 years. The maximum number of patients was in the age group 41 to 50 years, while the lowest number of patients was in the less-than-20-years age group.

Grossly, the average length of gallbladders in the study population was 6.57 cm, with a standard deviation of 1.03 cm. Serosal congestion was present in 17 cases (8.76%). The mucosa was bile-stained in 146 cases (75.26%); cholesterolosis was present in 26 cases (13.40%), and mucosal ulceration in 18 cases (9.28%). Most of the cases had stones in their gallbladder. Among the 194 patients, 161 (82.99%) had gallbladder stones, while only 33 cases (17.01%) had no stones. Among the 194 cases of chronic cholecystitis, xanthogranulomatous cholecystitis was present in 7 cases (3.61%), eosinophilic cholecystitis in 1 case (0.51%), and follicular cholecystitis in 11 cases (5.67%). Mild inflammation was present in 48 cases (24.74%), moderate inflammation in 95 cases (48.97%), and severe inflammation in 51 cases (26.29%).

Among the 194 cases, only intestinal metaplasia was seen in 61 cases (31.44%), only pyloric metaplasia in 23 cases (11.86%), both intestinal and pyloric metaplasia in 36 cases (18.56%), focal squamous metaplasia in 2 cases (1.03%), and no obvious metaplasia in 72 cases (37.11%) (Figures 1 and 2). Intestinal metaplasia was the most common in this study, with a total of 97 (50%) patients having intestinal metaplasia, while 59 (30.41%) patients had pyloric metaplasia. No relation was found between metaplasia and the sex of the patients. Among 159 female

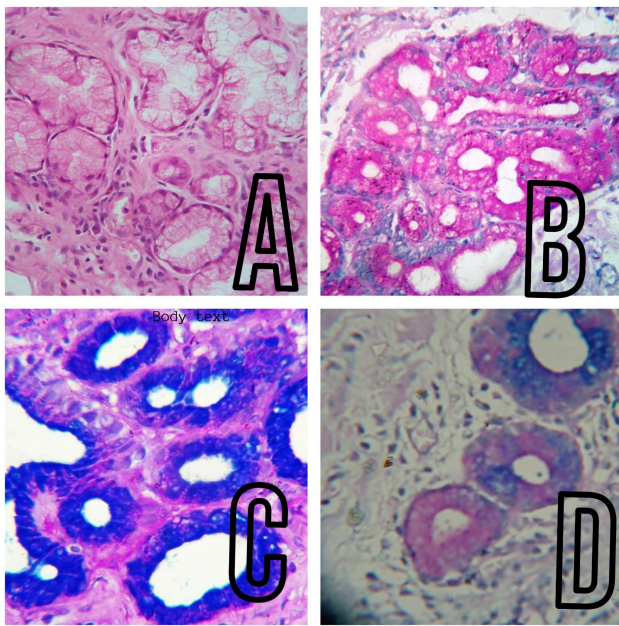


Figure 1: Pyloric metaplasia A: Pyloric metaplasia – abundant pale cytoplasmic mucin compressing the nucleus to the abluminal aspect of the cell: H&E stain, 400X, B: Pyloric metaplasia, mucins are Alcian blue positive; Alcian blue (pH 2.5) stain, 400X, C: Pyloric metaplasia, mucins are PAS positive; PAS stain, 400X, D: Pyloric metaplasia, both Alcian blue & PAS positive; combined Alcian blue – PAS stain, 400X

patients, 99 had metaplastic changes (62.26%), and among 35 male patients, 23 had metaplastic changes (65.71%), which was statistically insignificant (p -value = 0.702).

No relation was found between the presence of metaplasia and the presence of stones (p -value = 0.060). Metaplasia was present in 65.84% of cases where gallstones were present (n = 161) compared to 48.48% of cases where gallstones were absent (n = 33) (Table 1).

The presence of metaplasia with the severity of inflammation was compared, and there was no statistically significant association (p -value = 0.448). In mucin histochemistry, 62 cases (31.96%) were only periodic acid-Schiff positive, 42 cases (21.65%) were only Alcian blue (pH 2.5) positive, and 63 cases (32.47%) were positive for both periodic acid-Schiff and Alcian blue.

Periodic acid-Schiff positivity was most commonly seen in cases where metaplastic changes were present. Among 122 cases with metaplasia, periodic acid-Schiff positivity was seen in 91 cases (74.59%), whereas among 72 cases with no metaplastic changes, periodic acid-Schiff positivity was seen in only 34 cases (47.22%), which was statistically significant (p -value < 0.001) (Table 1). Similarly, Alcian blue positivity was also most commonly seen in cases where metaplastic changes were present. Among 122 cases with metaplasia, Alcian blue positivity was seen in 74 cases (60.66%), whereas among 72 cases with no metaplastic changes, Alcian blue

positivity was seen in only 31 cases (43.05%), which was statistically significant (p -value = 0.017) (Table 1).

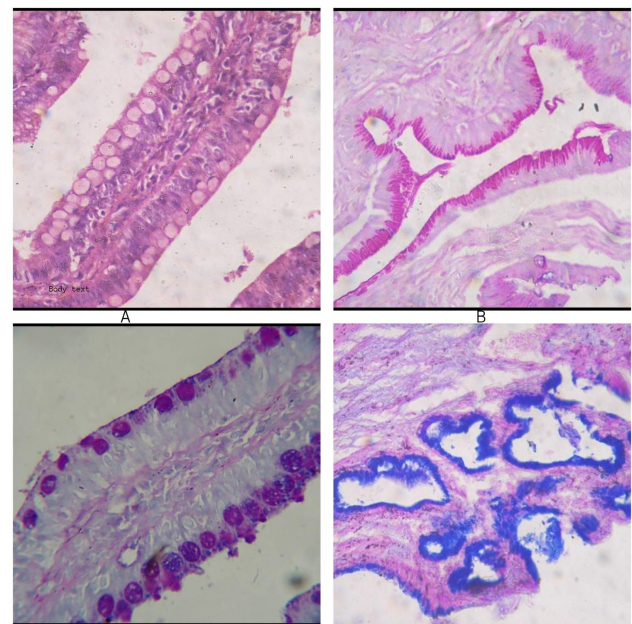


Figure 2: Intestinal metaplasia A: Intestinal metaplasia with plenty of goblet cells; H&E stain, 400X, B: Intestinal metaplasia with some goblet cells, mucins are PAS positive; PAS stain, 100X, C: Intestinal metaplasia, mucins are Alcian blue positive; Alcian blue (pH 2.5) stain, 100X, D: Intestinal metaplasia, mucins are combined Alcian blue – PAS positive; combined Alcian blue – PAS stain, 400X

Among the 61 cases of only intestinal metaplasia, 46 (75.41%) were only periodic acid-Schiff positive, 41 (67.21%) were only Alcian blue positive, and 30 (49.18%) were positive for both Alcian blue and periodic acid-Schiff. Among 23 cases of only pyloric metaplasia, 17 (73.91%) were only periodic acid-Schiff positive, 10 (43.48%) were only Alcian blue positive, and 4 (17.39%) were positive for both periodic acid-Schiff and Alcian blue. Among 36 cases of both intestinal and pyloric metaplasia, 28 (77.78%) were only periodic acid-Schiff positive, 23 (63.89%) were only Alcian blue positive, and 15 (41.67%) were positive for both periodic acid-Schiff and Alcian blue (Table 2).

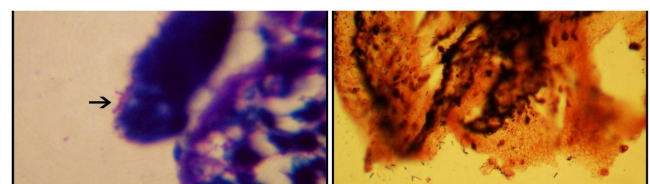


Figure 3: A: H. pylori – dark blue, curved bacilli at mucosa; Giemsa stain, 1000X, B: H. pylori – multiple black, curved bacilli; Warthin-Starry stain, 400X

Helicobacter pylori was not found in most cases. In this study, among a total of 194 cases, curved bacilli

Metaplasia	PAS-positive	PAS negative	Total	Statistical significance
Present	91 (74.59)	31 (25.41)	122	$\chi^2=14.80, p <0.001$
Absent	34 (47.22)	38 (52.78)	72	
Total	125 (64.43)	69 (35.57)	194	
Metaplasia	Alcian Blue positive	Alcian Blue negative	Total	
Present	74 (60.66)	48 (39.34)	122	$\chi^2=5.65, p =0.017$
Absent	31 (43.05)	41 (56.95)	72	
Total	105 (54.12)	89 (45.88)	194	

Table 1: Distribution of patients a) according to presence of metaplasia and PAS positivity, b) according to the presence of metaplasia and Alcian Blue positivity

Type of Metaplastic Changes	Total	PAS Positive (%)	AB Positive (%)	Both PAS & AB Positive (%)
Pure Intestinal Metaplasia	61	46 (75.41)	41 (67.21)	30 (49.18)
Pure Pyloric Metaplasia	23	17 (73.91)	10 (43.48)	04 (17.39)
Both Intestinal & Pyloric Metaplasia	36	28 (77.78)	23 (63.89)	15 (41.67)
Squamous Metaplasia	02	0	0	0
Total	122	91 (74.59)	74 (60.66)	49 (40.16)

Table 2: Mucin staining pattern in metaplasia

indicative of *Helicobacter pylori* were detected in only 3 cases (1.54%). Only 1 Giemsa-stained section and 2 Warthin-Starry-stained sections showed curved bacilli indicative of *H. pylori* among a total of 194 cases (Figure 3) In these 3 cases, a moderate degree of inflammation was present, but no obvious metaplastic changes were seen.

DISCUSSION

Mohan et al. [9] found a male-to-female ratio of 1:6.4 in their study on the morphological spectrum of gallstone disease involving 1,100 patients in North India. Some other studies suggest that female sex hormones and the sedentary habits of most women in India expose them to factors that promote gallstone formation. [10-12]

Selvi et al. [11] conducted a study in India and found that the mean age of presentation was 45.90 years, with the maximum number of patients (51%) between 41-60 years. [2] This is almost similar to the findings of our study. Chronic cholecystitis is associated with cholelithiasis in more than 90% of the cases. In this study as well, most cases were associated with gallstones. Among the total 194 cases, stones were present in 161 cases (82.99%). According to Raptopoulas et al. [13], 12% to 13% of chronic cholecystitis patients do

not have gallstones and 64-84% of cholecystectomy specimens show pyloric metaplasia very frequently. [14-16] Rahul Khanna et al. [17] observed about 16% each of antral and intestinal metaplasia in their specimens, while others have found the incidence of antral metaplasia in about 50-100% of their cases with cholelithiasis. [18, 19] In a study in Essa [17], the metaplastic lesions were predominantly of the pyloric type, characterized by structures similar to the pyloric glands in the lamina propria, followed by the intestinal type, characterized by the presence of goblet cells and other intestinal-like cells. Metaplastic changes in epithelial cells are common adaptive responses and are usually associated with chronic irritation. In the gallbladder, gallstones and subsequent inflammation may induce epithelial injury and resultant metaplastic changes. [20]

In the present study, no relation was found between the presence of metaplasia and the presence of stones (p -value = 0.060). Metaplasia was present in 65.84% of cases where gallstones were present ($n = 161$) compared to 48.48% of cases that were not associated with gallstones. The sample size may be responsible for these discordant results.

In a study in North India [21], the severity and frequency of changes in mucous glands, such as hyperplasia and metaplasia, were found to increase with advancing age,

commonly observed in patients above 40 years of age. In this study, the presence of metaplasia in relation to the age of the patient showed a linear trend (p -value = 0.042). In the age group up to 30 years, metaplasia was present in 68.75% of cases, in the 31 to 40 years age group in 70.83% of cases, in the 41 to 50 years age group in 63.64% of cases, and in the more than 60 years age group in 50% of cases. The incidence of metaplasia initially showed an increasing occurrence with advancing age, but later revealed a downward trend with increasing age.

In this study, no relationship was found between the sex of the patient and the presence of metaplastic changes (p -value = 0.702). The severity of inflammation was compared with the presence of metaplasia, but it failed to show any significant relationship (p -value = 0.448). In the present study, periodic acid-Schiff positivity was more commonly seen in cases where metaplastic changes were present than in those without metaplasia. Among 122 cases with metaplasia, PAS positivity was seen in 91 cases (74.59%), whereas among 72 cases with no metaplastic changes, PAS positivity was seen in only 34 cases (47.22%), which was statistically significant (p -value < 0.001). Similarly, Alcian Blue positivity was also more commonly seen in cases where chronic injury of the gallbladder leads to metaplastic changes that induce the appearance of neutral mucin (PAS positive), which may further dedifferentiate to sialomucins containing dysplastic or neoplastic cells if the activity and/or chronicity persists [22], as detected by Alcian Blue at pH 2.5. The results of this finding are also apparent in the work of others. [8, 23, 24]

Some researchers [24] have detected bacteria suggestive, but not diagnostic, of *Helicobacter* species using different histopathological methods (Warthin-Starry, Haematoxylin-Eosin, and Gram staining). In another study in India [25], there was no evidence of *H. pylori* infection of the gallbladder on histopathological examination using H&E, Giemsa, and Warthin-Starry stains. *H. pylori* DNA was detected in 16 patients (32.6%) and none of the 12 controls by PCR analysis (p -value = 0.025). The presence of *H. pylori* DNA in bile and/or the gallbladder was associated with a positive urea breath test (p -value < 0.0001). In a study in Karachi, Pakistan [26], *H. pylori* DNA was demonstrated in cases of chronic cholecystitis and gallbladder carcinoma associated with cholelithiasis. In another study in India, Mishra et al. [27] found that *H. pylori* colonized in 45% of cases using Loeffler's methylene blue and Warthin-Starry stain (presence of *H. pylori* was confirmed by immunohistochemistry) in areas of gastric metaplasia in the gallbladder, producing histologic changes similar to those seen in gastric mucosa.

CONCLUSION

Intestinal metaplasia was the most common type of metaplastic change in the gallbladder epithelium among chronic cholecystitis cases in this region of the country.

PAS and Alcian Blue positivity were significantly higher in cases with metaplasia than in those without metaplasia. Therefore, mucin histochemistry may help identify early metaplastic changes in the gallbladder epithelium. Further studies are necessary to confirm this. *H. pylori* was detected in 3 cases (1.55%) of chronic cholecystitis in this study population. The use of a combination of methods for detecting *H. pylori* in gallbladder tissue may reveal more positive cases. Regional differences may also contribute to this result. Further studies are needed to elucidate the role of *H. pylori* in chronic cholecystitis.

REFERENCES

1. Latio M. Early carcinoma of the gallbladder. *Beitr Pathol.* 1976;158:169–72.
2. Latio M. Histogenesis of epithelial neoplasms of the human gallbladder, I Dysplasia. *Pathol Res Pract.* 1983;178:51–57.
3. Dowling GP, Kelly JK. The histogenesis of adenocarcinoma of the gallbladder. *Cancer.* 1986;58:1702–1710.
4. Weedon D. Diseases of the gallbladder. In: RMN M, PP A, AD B, et al, editors. *Pathology of the Liver*; 1994. p. 514–534.
5. Bilhartz LE, Horton JD. Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management. 6th ed. Philadelphia: WB Saunders. M F, BF S, MH S, editors; 1998.
6. Jagannath SB, Singh VK, Cruz-Correa M. A long-term cohort study of outcome after cholecystectomy for chronic acalculous cholecystitis. *Am J Surg.* 2003;185:91–95.
7. Manoj P. *Helicobacter* species are associated with a possible increase in risk of biliary lithiasis and benign biliary diseases. *World J Surg Oncol.* 2007;5:94–94.
8. Myung SJ, Kim MH, Shim KN, Kim YS, Kim EO, Kim HJ. Detection of *Helicobacter pylori* DNA in the human biliary tree and its association with hepatolithiasis. *Dig Dis Sci.* 2000;45:1405–141.
9. Mohan H, Punia R, Dhawan SB, Ahai S, Sekhon MS. Morphological spectrum of gallstone disease in 1100 cholecystectomies in North India. *Indian J Surg.* 2005;67:140–142.
10. Tandon RK. Pathogenesis of gallstones in India. *Trop Gastroenterol.* 1988;9:83–91.
11. Baig SJ, Biswas S, Das S, Basu K, Chattopadhyay G. Histopathological changes in gallbladder mucosa in cholelithiasis: correlation with chemical composition of gallstones. *Trop Gastroenterol.* 2002;23:25–32.

12. Dhar SC, Ansari S, Saha M, Ahmad MM, Rahman MT, Hasan M. Gallstone disease in a rural Bangladesh community. *Indian J Gastroenterol*. 2001;20:223–229.
13. Raptopoulos V, Compton CC, Doherty P. Chronic acalculous gallbladder disease: Multiimaging evaluation with clinical-pathologic correlation. *AJR Am J Roentgenol*. 1986;147:721–724.
14. Barcia J. Histologic analysis of chronic inflammatory patterns in the gallbladder: diagnostic criteria for reporting cholecystitis. *Ann Diagn Pathol*. 2003;7(3):147–153.
15. Albores-Saavedra J, Alcántara-Vazquez, Cruz-Ortiz A, Herrera-Goepfert H, R. The precursor lesions of invasive gallbladder carcinoma. Hyperplasia, atypical hyperplasia, and carcinoma in situ. *Cancer*. 1980;45(5):919–927.
16. Yamaguchi K, Enjoji M. Carcinoma of the gallbladder: A clinicopathology of 103 patients and a newly proposed staging. *Cancer*. 1988;62(7):1425–1432.
17. Martinez-Guzman E, Rosa-Bayan JDL. Neoplasms and dysplasia of the gallbladder and their relationship with lithiasis: A case-control clinicopathological study. *Rev Gastroenterol Mex*. 1998;63:82–90.
18. Duarte I, Llanos O, Domke H, Harz C, Valdivieso V. Metaplasia and precursor lesions of gallbladder carcinoma: Frequency, distribution, and probability of detection in routine histologic samples. *Cancer*. 1993;72(6):1878–1884.
19. Yamagiwa H, Tomiyama H. Intestinal metaplasia, dysplasia, carcinoma sequence of the gallbladder. *Acta Pathol Jpn*. 1987;36:989–97.
20. Stancu M, Căruntu ID, Giușcă S, Dobrescu G. Hyperplasia, metaplasia, dysplasia and neoplasia lesions in chronic cholecystitis - a morphologic study. *Rom J Morphol Embryol*. 2007;48(4):335–342.
21. Khanna R, Chansuria R, Kumar M, Shukla HS. Histological changes in the gallbladder due to stone disease. *Indian J Surg*. 2006;68:201–205.
22. Gupta SC, Misra V, Singh PA, Roy A, Misra SP, Gupta AK. Gallstones and carcinoma gallbladder. *Indian J Pathol Microbiol*. 2000;43(1):147–154.
23. Lin TT, Yeh CT, Wu CS, Liaw YF. Detection and partial sequence analysis of *Helicobacter pylori* DNA in bile samples. *Dig Dis Sci*. 1995;40:2214–2223.
24. Fox JG, Dewhirst FE, Shen Z, Feng Y, Taylor NS, Paster BJ. Hepatic *Helicobacter* species identified in bile and gallbladder tissue from Chileans with chronic cholecystitis. *Gastroenterology*. 1998;114:755–763.
25. Bansal VK, Misra MC, Chaubal G, Gupta D, Das S, Ahuja B et al. *Helicobacter pylori* in gallbladder mucosa in patients with gallbladder disease. *Indian J Gastroenterol*. 2012;31(2):57–60.
26. Yakoob J, Khan MR, Abbas Z, Jafri W, Azmi R, Ahmad Z. *Helicobacter pylori*: association with gallbladder disorders in Pakistan. *Br J Biomed Sci*. 2011;68(2):59–64.
27. Misra V, Misra SP, Dwivedi M, Shouche Y, Dharne M, Singh PA. *Helicobacter pylori* in areas of gastric metaplasia in the gallbladder and isolation of *H. pylori* DNA from gallstones. *Pathology*. 2007;39(4):419–443.

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