

## Clinical and Histological Spectrum of Gall Bladder Lesions after Cholecystectomy

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### Abstract

**Background:** Chronic cholecystitis is one of the most commonly encountered lesions in India and worldwide. Cholecystitis, cholelithiasis and tumors of gall bladder constitute the bulk of gall bladder diseases among which gall stones being the most common. Long standing chronic inflammation due to gall stones is considered as an important etiological factor in carcinogenesis. This study was carried out to correlate clinical & histopathological findings of gall bladder lesions. **Materials and Methods:** This study included 120 cases that underwent for open or laproscopic cholecystectomy for cholecystitis, cholelithiasis or suspected cases of malignancy. Clinical details were collected. Formalin fixed tissues were embedded in paraffin, cut into thin sections and stained with haematoxylin and eosin (H&E) for studying the histopathology. **Results:** Out of total 120 cases maximum were females 98 (81.66 %), and 22 (18.33 %) males. Maximum cases were seen in 4<sup>th</sup> to 6<sup>th</sup> decade. Maximum cases were diagnosed as chronic cholecystitis. Other associated findings like xanthogranulomatous change, intestinal metaplastic change, and follicular cholecystitis were seen. Total six cases of adenocarcinoma was diagnosed out of which five cases showed features of well differentiated adenocarcinoma and one case showed papillary pattern. on histopathology examination. **Interpretation and conclusion:** Gall bladder diseases can have a varied presentation on both clinical and histopathological examination. The present study showed a female predominance. Cholelithiasis proved to be a major risk factor for inflammatory diseases. Constant erosion of the gall bladder wall by gallstones over a long period may constitute a risk for malignancy.

**Keywords:** Gall Bladder Histology; Gall Bladder Lesions; Cholecystitis; Adenocarcinoma.

### Introduction

Chronic cholecystitis is the most commonly encountered lesions in India and worldwide with more than 78-90% associated with gall stones. Cholecystitis, cholelithiasis and tumors of gall bladder constitute the bulk of gall bladder diseases among which gall stones being the most common. Gall stones may remain for years without producing any symptom [1-3]. Incidence of cholelithiasis is increasing due to change in dietary habits and sedentary life style [4]. Pathological changes related to gallstone formation are still the focus of intensive

research. The hypothesis most widely accepted is the stasis of bile caused by gallbladder dyskinesia, while dyskinesia may be the result of pathological changes in the gallbladder wall [5].

Presence of gall stones has been associated with development of carcinoma. Carcinoma gall bladder is one of the most common causes of cancer mortality. Long standing chronic inflammation by gall stones plays an important etiological role in carcinogenesis [6,7]. Incidental gall bladder carcinoma is found in about 0.3-1.5 % of cholecystectomies for gall stone disease formalin [8]. Therefore present study was carried out to correlate clinical & histopathological findings of gall bladder lesions.

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### Materials and Methods

This retrospective study of gall bladder lesions was carried out during the period from July 2014 to June 2015 in the department of pathology at tertiary health

care centre. Total 120 cholecystectomy specimens were studied. We received the specimens after open cholecystectomy as well as laproscopic cholecystectomy procedures which were performed in the department of surgery. The cases were operated for cholecystitis, cholelithiasis and suspected cases of malignancy. Clinical notes, radiological findings and operative findings were collected from hospital record. Gross examination of each gall bladder was carried out. Detail description like gall bladder size, wall thickness, presence of gall stones were noted. Representative section from the lesions was taken. The formalin fixed tissues were embedded in paraffin, cut into thin sections and stained with haematoxylin and eosin (H&E) for studying the histopathology.

## Results

Out of total 120 cases maximum were females 98 (81.66 %), and 22 (18.33 %) males. Maximum cases were seen in 4<sup>th</sup> to 6<sup>th</sup> decade. Common symptoms with which cases were presented were abdominal pain, followed by history of vomiting, fever, jaundice and oral contraceptive. On examination, clinician noticed abdominal tenderness, guarded rigidity and in a few cases palpable gall bladder. Duration of the symptoms was varied from 6 months to 5 years. Intraoperative diagnosis of chronic cholecystitis was made in 110 cases by operating surgeon. Out of which gall stones were found in maximum number of cases as shown in table 2.

On gross examination, gall bladder with stones were seen in 103 (chronic calculous cholecystitis in 98 and suspicious of malignancy in 5) cases. Gall bladder size was normal in 102 (85%), enlarged in 16 (13.33 %) and fibrotic in 2 (01.67%) specimens. The average gall bladder wall was found to be normal (<3 mm) in 113 (94.17 %) cases while it was thickened >3 mm) in the remaining 7 (05.83%) cases. The number of gall stones was ranging from single to multiple (Figure 1 A).

On microscopic examination normally gall bladder shows, mucosa which consists of single layer of uniform, tall columnar epithelial lining with

microvilli, basal nuclei and pale cytoplasm. Lamina propria contains loose connective tissue with capillaries. Muscular layer consists of circular, longitudinal and oblique smooth muscle fibers without distinct layers. Adventitia consists of perimuscular connective tissue composed of collagen, elastic tissue, fat, vessels, lymphatics, nerves and paraganglia. In the present study, out of 120 cases maximum cases were diagnosed as chronic cholecystitis and two cases (01.67%) were diagnosed as acute on chronic cholecystitis. In some cases, gallbladder epithelium was normal; it covered lamina propria and protruded with it into the lumen of gallbladder (Figure 1B). Rokitansky-Aschoff sinuses with deep penetration of muscularis layer and moderate hypertrophy of muscularis externa were observed in some cases.

In the entire tissue material, the typical connective tissue of lamina propria with congested blood vessels was characteristic. Inflammatory infiltrate comprised of lymphocytes, eosinophils, mast cells, macrophages and neutrophils as noticed in chronic cholecystitis (Figure 1C). In one of the cases goblet cells were present in a fragment of the epithelium, features suggestive of intestinal metaplasia (Figure 1D). Lamina propria showed dense inflammatory cell along with lymphoid follicle formation, suggestive of follicular cholecystitis. In one case (0.83%), changes of adenomyomatosis noted like extensively fibrotic gallbladder wall with numerous Rokitansky-Aschoff sinuses but few/no smooth muscle bundles and an expanded subserosal layer containing abundant nerve-trunks.

In six cases (5%) gall bladder carcinoma was observed, all of them diagnosed as adenocarcinomas (one papillary and five well differentiated patterns). Tumor cell were arranged in glandular patten and individual cell with features of malignancy (Figure 1E). All diagnosed carcinoma cases were females. The youngest was 40 years old while the oldest was 67 years of age. Five cases were clinically suspected for malignancy and the sixth case was diagnosed on histological examination. The remaining one was incidental finding, which was diagnosed on microscopic examination.

**Table 1:** Age and sex distribution

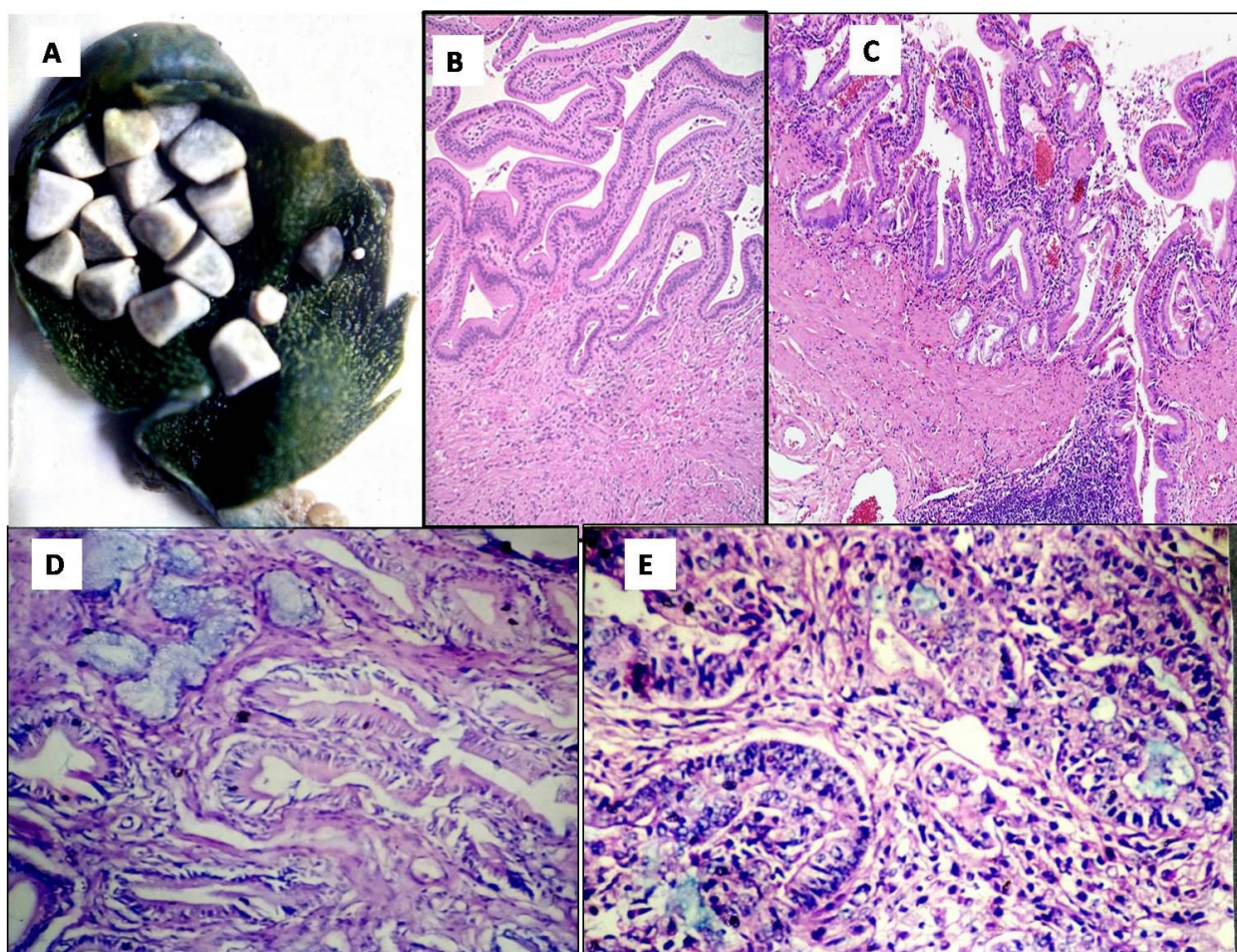
Age (years)	Sex		Total
	Male	Female	
< 30	03	11	14
31-40	08	25	33
41-50	09	30	39
51-60	01	24	25
61-70	01	06	07
>70	-	02	02
Total	22	98	120

**Table 2:** Operative findings

Operative Findings	No of Cases	Percentage
Chronic Cholecystitis	110	92.50
With stone	98	81.67
Without stone	12	10.00
Carcinoma gall bladder	06	05.00
With stone	05	04.17
Without stone	01	00.83
Dilation of common bile duct	04	03.33

**Table 3:** Histopathological diagnosis

Sr. No	Histopathological Diagnosis	No. of cases	Percentage
1	Chronic Cholecystitis	101	84.17
2	Acute on chronic cholecystitis	02	01.67
2	Follicular Cholecystitis	01	00.83
3	Xanthogranulomatous Cholecystitis	06	05.00
4	Malkoplakia	02	01.67
5	Adenomyomatosis	02	01.67
6	Adenocarcinoma	06	05.00
	Well differentiated	05	04.16
	Papillary	01	00.83



**Fig. 1:** **A.** Multiple large faceted mixed stones in thinned wall gall bladder. **B.** Normal histology: Gall bladder mucosa consists of single layer of uniform, tall columnar cells with, basal nuclei and pale cytoplasm. Lamina propria contains loose connective tissue with capillaries. Muscular layer showing smooth muscle fibers. (H & E, 100X). **C.** Chronic Cholecystitis: Ulceration of mucosa, lamina propria contains mixed inflammatory cell infiltrate and congested capillaries (H & E, 100X). **D.** Intestinal type metaplasia: Presence of goblet cell in the epithelium (H & E, 400X). **E.** Well differentiated adenocarcinoma : Normal histology of gall bladder is replaced by tumor cells arranged in glandular pattern and individual cell with features of malignancy (H & E, 400X)

## Discussion

In this study, out of total 120 cholecystectomies, gall stones were present in 103 cases (85.83%) and correlates with other studies [8, 9]. Female cases were 98 (81.66%). Other studies have also reported preponderance of females among patients of gall bladder disease but the ratio has been higher as compared to this study [1, 3, 4, 6, 9, 10]. Reason for this female predominance has been attributed to female sex hormones, sedentary habits and genetic factors in various studies [1]. In this study, age of the patients ranged from 22 to 76 years. Maximum numbers of patients were in the 4<sup>th</sup> to 6<sup>th</sup> decade of life. This was in accordance with a few studies [8], but was higher than that reported in other study [11]. In the present study, among young patients subjected to cholecystectomy 14 patients were aged less than 30 years. The group was dominated by women. The results are consistent with other study [12]. Symptoms like abdominal pain, vomiting, fever, jaundice and signs like tenderness, guarded rigidity and palpable gall bladder were also observed by other study [7].

Lymphocytes, eosinophils as a dominating type of cells in the inflammatory infiltrate were noted in a great number of patients in cases of chronic cholecystitis. Microscopic lesions of mucosa most frequently included various grading and various stage of parietal fibrosis, this is consistent with previous studies [12, 13]. Presence of goblet cells, enterochromaffin cells or antral-type (pseudopyloric) glands in gallbladder epithelium in cases were thought to represent intestinal or gastric metaplasia, and to represent premalignant lesions in the organ. In one of the case in the present study found intestinal Metaplasia, which were also noted by studies [7, 9]. The most common histopathological finding in this study was chronic cholecystitis, seen in 101 cases out of 120 (84.17%), which is consistent with previous study [13]. Follicular formation, active inflammation and antral metaplasia were associated with chronic cholecystitis in 0.83%, 1.67%, 0.83%, and 3.2%. Xanthogranulomatous change was seen in 5%. These findings were also observed by other studies [3, 9, 14].

Multiple studies have been conducted in the recent past focusing on whether gall bladder histopathology must be done routinely or selectively. Gall bladder carcinoma always presents with some gross abnormalities. Therefore specimen sent for histopathology after intra-operative inspection of the mucosa by the operating surgeon can save time and cost, supported by previous studies. [8, 9, 14, 15]. Incidental gall bladder carcinomas on microscopy,

with no evidence of gross abnormalities are not rare and therefore they advocate routine histopathology of all electively resected cholecystectomy specimens. In this series however, one case of incidental gall bladder carcinoma was seen and found consistent with the series [3, 7, 8].

## Conclusion

Gall bladder diseases can have a varied presentation both clinically and histopathologically. The present study, in accordance with other studies showed a female predominance. Majority of patients were in third to fifth decade of life. Cholelithiasis proved to be a major risk factor for inflammatory diseases of this organ. The most common histopathological diagnosis was chronic cholecystitis. Constant erosion of the gall bladder wall by gallstones over a period of time may constitute a risk factor for malignancy.

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