

## Study of Various Histopathological Lesions In Resected Gall Bladder Specimen: A Study In Consecutive 898 Cholecystectomies

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### Abstract

The histopathological spectrum of gall bladder is extremely variable depending on sex, race, age, countries and institutes. There is a wide spectrum of pathologies affecting the gall bladder ranging from congenital anomalies, calculi and its complications, non inflammatory, inflammatory to the neoplastic lesions. Gallstones are one of the major causes of morbidity and mortality all over the world. Cholelithiasis is very common particularly in fatty, fertile and female of forty to fifty and affects male and children also. Gallstone may lead to several complications such as cholecystitis, hydrops, mucocele, internal biliary fistula and carcinoma. Other histological alterations include acute cholecystitis, chronic cholecystitis and its variants such as lymphoplasmacytic and sclerosing cholecystitis, follicular cholecystitis, eosinophilic cholecystitis and xanthogranulomatous cholecystitis. Gall bladder carcinoma ranks 6<sup>th</sup> in the gastrointestinal malignant tumour and due to non specific clinical presentation it is rarely diagnosed at an early stage. Most of the incidentally detected carcinoma are surgically resectable, with a good survival rate. Though simple cholecystectomy is said to be sufficient in stages T<sub>is</sub> and T<sub>1a</sub> carcinomas, radical resection is strongly recommended in stages beyond that. This reflects the importance of histopathological study of all cholecystectomy specimens, irrespective of clinical impression. Cholecystectomy performed with provisional diagnosis of benign disease based on clinical, ultrasonological and computerized tomographic scanning misses a significant numbers of early malignant lesions of gall bladder, as histopathological detection of carcinoma is a gold standard and will continue to be superior to clinical and radiological examination

**Keywords:** Gall bladder carcinomy, Histopathology, Cholecystectomy, Cholelithiasis

### Introduction

Gall bladder is the organ which stores and concentrate the bile which helps in digestion of fat. It is among the most commonly surgically resected organs, and the number of cholecystectomy has increased more than 50% in the past decade [1]. Various lesions occur in the gall bladder. The most common is gall stone.

Cholelithiasis appears to be increasing in incidence over past couple of decades in India and western world due to increased intake of fatty and high calorie diet and increased consumption of alcohol, and obesity [2]. It is known to produce diverse histopathological changes in gall bladder ranging from acute or chronic inflammation to

metaplasia and even malignancies. Carcinoma gall bladder carries one of the worst of cancer mortalities. India is a highly populated country with a major fraction of population of lower socioeconomic status having less access to proper health facilities, a reason why early stage malignancy may escape detection leading to poor survival.

To avoid such blunders with bad consequences, therefore every cholecystectomy specimen be routinely examined histologically. The purpose of this study is to determine the various histopathological lesions involving the gall bladder.

### Materials And Methods

This was a prospective study from January 2015 to December 2016, in the department of pathology, S.P.Medical college, Bikaner, Rajasthan.

Cholecystectomy specimens received were fixed in 10% neutral buffered formalin and embedded in paraffin. Three full thickness sections were obtained from fundus, body, and neck of the gall bladder. Additional sections were taken from any grossly abnormal area if present. Sections were then stained with H and E stain and examined microscopically.

**Results**

A total of 898 cholecystectomies were received during the period of January 2015 to December 2016. This included open cholecystectomy, laproscopic cholecystectomy, and partially resected specimens. The age of patient ranged from 11 years to 90 years with mean age 44.53 years (Table 1). Male to female ratio was 1 : 3.91 (Table 2). Of these 674 cases (83.4%) had association with stone (Table 3). Chronic cholecystitis alone was the most common pathology reported in 679 cases (75.6%), out of which 540 were females and 139 were males, out of 679 cases, gall stone was associated with 508 cases (56.6%). (Fig. 1)

Table-1 Distribution of Cases According to Age Group (Years)

Age Group	No. of Cases	Percent
<20	28	3.1
21-30	199	22.2
31-40	186	20.7
41-50	181	20.2
51-60	165	18.4
61-70	108	12.0
>70	31	3.5
Total	898	100.0
Mean age (years)	44.53±15.41	

Table-2. Distribution of cases according to sex

Sex	No. of Cases	Percent
Female	715	79.6
Male	183	20.4
Total	898	100.0

Table 3 Distribution of Cases According to Stones

Association with Stone	Sex				Total	
	Female		Male		No.	%
	No.	%	No.	%		
No	168	18.7	56	6.2	224	24.9
Yes	547	60.9	127	14.1	674	75.1
	715	79.6	183	20.4	898	100

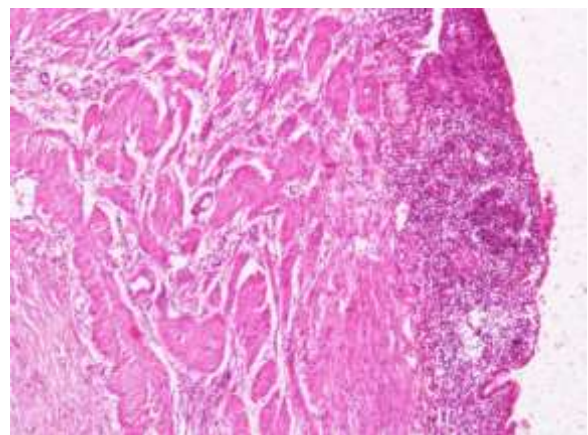


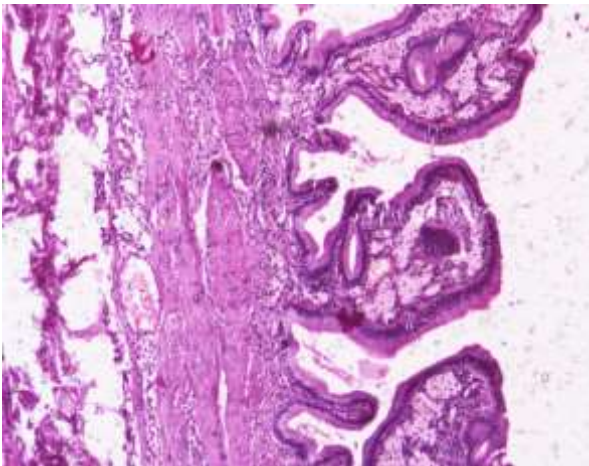
Figure 1: Chronic Cholecystitis. (H&E, 40X) showing dense infiltrate of closely packed inflammatory cells (lymphocytes, plasma cells and eosinophilic leucocytes). The eosinophilic muscle coat is thick from hypertrophy, and infiltrated by chronic inflammatory cells.

One case of chronic cholecystitis with formation of foreign body giant cell granuloma against vegetable cell was reported.

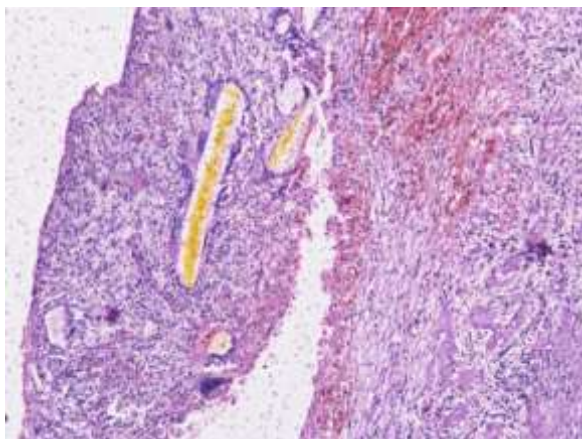
A total 87 (9.7%) patients had acute cholecystitis, out of which 70 cases (7.8%) were associated with stone.

Cholesterosis was identified in 60 cases (6.7%), of which 54 were females and 6 were males. All cases of cholesterosis were associated with chronic cholecystitis. 41 (4.6%) patients had coexisting gallstones, whereas 19 (2.1%) were reported to have acalculous cholesterosis. (Fig. 2)



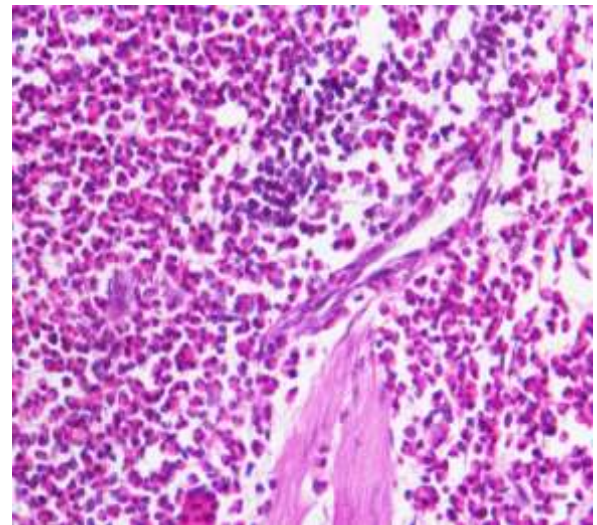


**Figure-2:**Gallbladder-Cholesterolosis,(H&E,10X)showing numerous foamy macrophages in the lamina propria. Xanthogranulomatous cholecystitis was reported in 32 cases (3.6%) out of which 28 cases (3.1%) were associated with stone. The mean age was 52.6 years in our study and male to female ratio of 3:1. Grossly this entity showed marked thickening of gall bladder.(Fig.3)



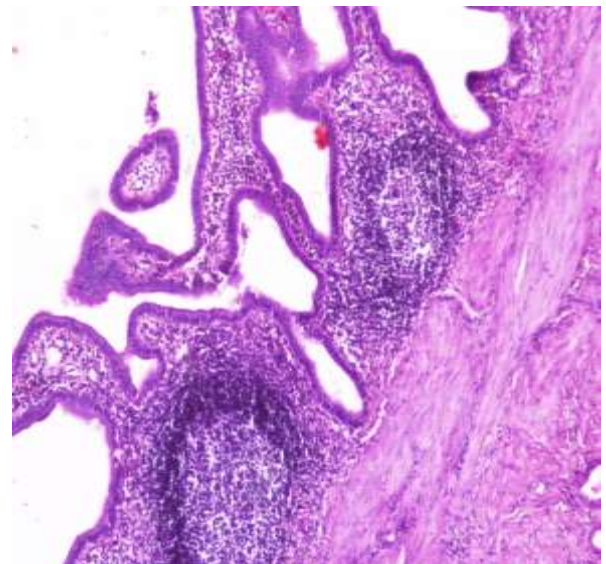
**Figure-3:**Xanthogranulomatous Cholecystitis.(H&E10x).The inflammatory infiltrate in the thickened gall bladder wall is composed predominantly of foamy macrophages,admixed with foreign-body type giant cells & pigments Eosinophilic cholecystitis was identified in 15 cases (1.67%) aged between 20 to 60 years. The patients with EC comprised of 9 females and 6 males with median age of 39.8 years. Seven out of 15 cases of Eosinophilic cholecystitis had

associated gallstone. One patient had bilious perforation with peritonitis.(Fig.4)



**Figure-4:**Eosinophilic Cholecystitis .Histopathological slide of patient showing eosinophilic infiltration of gall bladder wall. (H&E,40X)

Follicular cholecystitis was found in 2 cases (0.2%), both of which were female(Fig.5). Adenomyomatosis change was present in 0.1% of case.



**Figure-5:**Follicular Cholecystitis.Histopathological slide of patient showing prominent lymphoid follicles in the lamina propria(H&E,10X).

Twenty one cases (2.3%) of carcinoma were diagnosed out of which 18(2%) were females and 3(0.3%) were males(Table4&5).



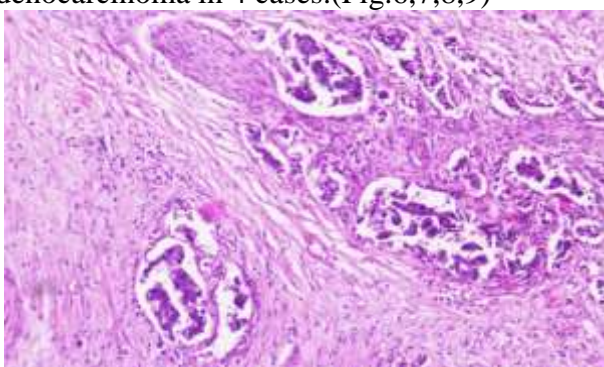
**Table-4** Clinicopathological features of gall bladder carcinoma found in this study

S.N.	Clinicopathological features	Number of Cases
1.	Incidence	21/898
2.	Female:Male	6:1
3.	Mean Age	44.53±15.41 years
4.	Association with Gall stones	15/21

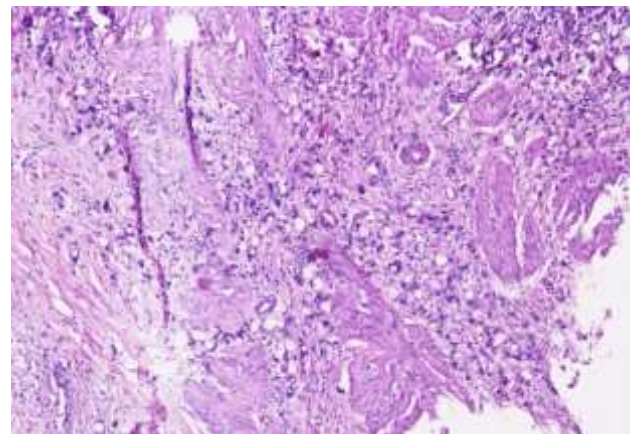
**Table 5.** Histological diagnosis of gall bladder carcinoma found in this study

Histopathological Diagnosis	Sex				Total	
	Female		Male			
	N	%	No.	%	No	%
Adenocarcinoma	12	1.3	2	0.2	14	1.5
Mucin.Secreting Adenocarcinoma	3	0.3	0	-	3	0.3
Papillary Adenocarcinoma	3	0.3	1	0.1	4	0.4
Total	18	2.0	3	0.3	21	2.3
Mean Age of Carcinoma Patients	44.53±15.41 years					

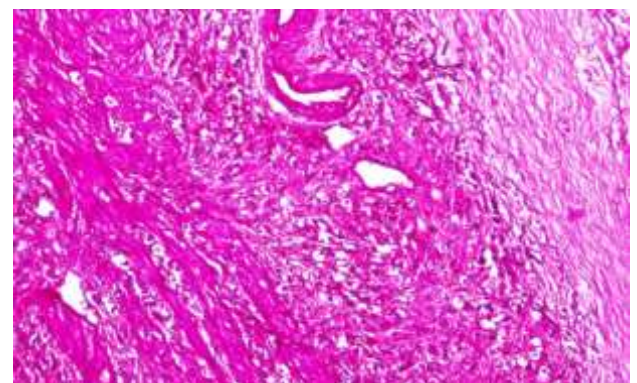
Among 21 cases of carcinoma, adenocarcinoma not otherwise specified (with well, moderate and poor differentiation) was found in 14 cases, mucin secreting adenocarcinoma in 3 cases and papillary adenocarcinoma in 4 cases.(Fig.6,7,8,9)



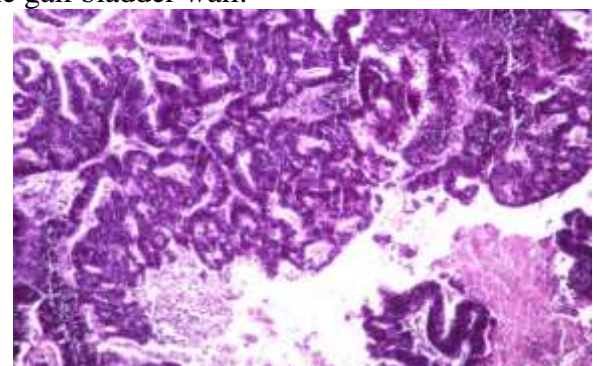
**Figure-6:** Gallbladder Adenocarcinoma (H&E, 10X) showing clusters of malignant glands invading the gall bladder wall.



**Figure-7:** Gallbladder-Mucin secreting Adenocarcinoma (H&E, 10X) showing tumour cells in small clusters, invading the gall bladder wall with signet ring appearance due to intracytoplasmic mucin accumulation.



**Figure-8;** Gallbladder-Mucin secreting Adenocarcinoma (PAS, 10X) showing clusters of PAS+ tumour cells invading the gall bladder wall.



**Figure9:** Gallbladder Papillary adenocarcinoma (H&E, 10X) showing papillary formation with fibrovascular core covered by malignant cells. There is

significant cytologic atypia with disorganization of the lining epithelium.

On pathological staging, this study revealed T<sub>2</sub> (13 cases, 61.9%) and T<sub>1b</sub> (7 cases, 33.3%) and T<sub>is</sub> (1 case, 4.7%). Perineural invasion was seen in 1 case.

## Discussion

In our study, the age of the patients ranged from 11 years to 90 years with mean age 44.53±15.41 years slightly higher than that reported in other studies[3]

The histopathological spectrum of gall bladder disease after cholecystectomy is found to be quite diverse. In present study, lesions of gall bladder were more common in females than in males with a male to female ratio of 1:3.91 which was similar to other study carried out by Rahul et al[4], Asuquo et al[5], Tantia et al[6] and John et al[7], reported male to female ratio of 1:4.8; 1:5, 1:2.8 and 1:4 respectively.

Most of the patients presented with pain upper abdomen, nausea and/or vomiting, which is consistent with findings by Laghari et al[8].

The most common histopathological finding in our study was chronic cholecystitis : 679(75.6%) specimens were reported as chronic inflammation with mucosal ulceration, denudation and wall infiltration by chronic inflammatory cells like neutrophils, macrophages, plasma cells and varying degree of fibrosis. Out of 679 cases of chronic cholecystitis, gall stone was associated with 508 cases (56.6%). A similar study by Memon[9] also reported chronic cholecystitis as major histopathological finding, identified in 64.8% cases.

In the presents series, acute cholecystitis was found in 87(9.7%) of cases out of which 70(7.8%) cases were associated with stone. They were characterized by phlegmanous nutrophilic infiltration with frequent ulcer formation, gangrenous changes, and abscess formations. Two cases showed acute perforation of gall bladder. In a study made by Meirelles-Costa et al[10] in 2010 to determine histological alterations in gall bladder specimens found acute cholecystitis in 174 patients out of 1091 patients (10.3%). Cholesterosis was identified in 60 cases (6.7%) of which 54 were females and 6 were males. All

cases of cholesterosis were associated with chronic cholecystitis. 41(4.6%) patients had coexistent gall stones, whereas 19(2.1%) were reported to have acalculous cholesterosis. Our incidence was slightly low compared to the study of Mohan et al[11] and Tadashi-Terada[12] who reported an incidence of 10.1% and 11% respectively.

In the present study, xanthogranulomatous cholecystitis was reported in 32 cases (3.6%) out of which 28 cases were associated with stone. The mean age was 52.6 years and with female to male ratio of 3:1. It is characterized by diffuse infiltration of macrophages and other inflammatory cells. On macroscopic examination, this entity showed marked thickening of gall bladder.

In a study made by Sujata et al[13] to determine spectrum of histopathological lesion in cholecystectomy specimens found 0.5% cases of follicular cholecystitis. In the present study 2 cases (0.2%) of follicular cholecystitis were found. Our study was slightly lower compared to above study.

The incidence of eosinophilic cholecystitis is low in India. Studies across the world showed its prevalence to be 0.25 to 6.4% with average age of presentation being 37 years[14]. In our study 15 out of 898 cholecystomies patients (1.7%) aged between 20 to 60 years showed eosinophilic cholecystitis. The patients with eosinophilic cholecystitis comprised of 9 females and 6 males with median age of 39.8 years.

In the present study adenomyomatous changes was present in 0.1%. It was associated with acute cholecystitis. This was characterized by many RASs and muscular hypertrophy. No international metaplasia was recognized in the present series.

In our study 21 (2.3%) case of carcinoma out of which 18 were females and 3 were males. Mean age of patients was 44.53 years.

This study revealed T<sub>2</sub> (13 cases 61.9%) and T<sub>1b</sub> (7 cases 33.3%) and T<sub>is</sub> (1 case 4.7%). Perineural invasion was seen in 1 case.

Histological examination of the tumors revealed findings similar to other study[15]. Among all 21 cases, we found adenocarcinoma not otherwise specified with well, moderate and poor differentiated in 14

cases, mucin secreting adenocarcinoma in 3 cases, and papillary adenocarcinoma in 4 cases.

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