

## A Study of Spectrum of Histopathological Lesions in Gall Bladder in Cholecystectomy Specimens

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### Abstract

**Introduction:** Gall bladder pathology is one of the most encountered in surgery opd and hence constitute a major part of specimen in pathology labs worldwide. This study is done to determine the incidence of various histopathological spectrum in cholecystectomy specimens and to emphasize the importance of histopathological examination of specimen of gallbladder. Histopathological study of gall bladder is important diagnostic modality for differentiation of benign from malignant tumours.

**Material and Methods:** It is a hospital based combined retrospective and prospective study for 5 years. All the surgically excised specimens of gall bladder submitted constituted the material for study.

**Results:** We studied total 2221 samples. The mean age of the study group was 45.86±15.08 years. There was female predominance with 1818 (81.9%) cases and 403 (18.1%) were males, with male to female ratio of 4.5: 1. Maximum number of cases were in age group of 41 – 60 with 892 (40.16%) cases. Non-neoplastic lesions were the most common (n=2190, 98.6%), followed by malignant cases (n=30, 1.4%) and 1 benign case. In non-neoplastic cases chronic non-specific cholecystitis 1820 (81.9%) was the most common finding followed by acute on chronic cholecystitis 207 cases (9.3%) and xanthogranulomatous cholecystitis 97 cases (4.4%). There were 2 cases of tubercular granulomatous cholecystitis. In malignant lesions there were adenocarcinoma 24 cases (1.1%), papillary adenocarcinoma 3 cases (0.1%), mucinous adenocarcinoma 2 cases (0.1%) and adenosquamous carcinoma 1 case (0.05%).

**Conclusion:** The present study emphasised the need to examine all the cholecystectomy specimens and thorough sampling of thickened portion as well as any suspicious area in the gallbladder specimen should be done, in order to avoid missing gallbladder carcinoma cases.

**Keywords:** Gall bladder, Histopathology, Adenocarcinoma.

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## Introduction

Pathologies of the gall bladder are common in surgical and medical OPDs. Biliary pain in the epigastrium and right upper quadrant of the abdomen that radiates to the interscapular area, the right scapula, and the shoulder, along with nausea, vomiting, jaundice, anorexia, fever, and chills, are symptoms of gallbladder diseases.[1]

Non-neoplastic and neoplastic gall bladder lesions can be separated into two types. Congenital lesions like Choledochal cyst, atresia, multiseptated gall bladder, pharyngeal cap, and acquired lesions like chronic calculous cholecystitis, acute cholecystitis with or without stones, follicular cholecystitis, and xanthogranulomatous cholecystitis are included in the category of nonneoplastic lesions.[2]

Cholelithiasis is the most typical pathology observed in the gall bladder, followed by cholecystitis. One of the most frequent medical conditions requiring surgical treatment is gallstone disease.[3] Different histological alterations, such as acute and chronic inflammation, granulomatous inflammation, glandular hyperplasia, metaplasia, dysplasia, and cancer, are brought on by cholelithiasis in the gallbladder mucosa.[4] 70% to 90% of those who develop gallbladder cancer have a history of cholelithiasis. Abdominal discomfort is the primary symptom of acute cholecystitis more than three times more frequently in people over 50 (20.9%) than in younger people (6.3%).[5] The presence and severity of fibrosis and inflammation in chronic cholecystitis determine its histological appearance, which is usually invariably accompanied with gallstones. As chronic calculus cholecystitis is the most common gall bladder illness, the vast majority of cholecystectomies have been performed for this condition.[6] Fat, fertile women

over forty are at risk for developing cystic duct stones in 90% of instances, while acalculous cholecystitis is present in 10% of cases.

Both benign and malignant gall bladder neoplasms are possible. Adenoma, adenomyomatosis, inflammatory polyps, etc. are examples of benign lesions. The two types of gall bladder cancers are mesenchymal and epithelial, respectively. In addition to this, the gall bladder can develop paragangliomas, lymphomas, and other cancers. Abdominal ultrasonography frequently reveals gallbladder polyps, which can affect up to 4.5% of adult population. The majority are believed to be benign, however a small percentage (4%–10%) are adenomas, which are benign. According to surgical studies, the biggest risk factor for malignancy is the size of the polyp, with adenomatous polyps 10 mm and greater having a 37% to 55% chance of becoming malignant.[7]

Epithelial growth and muscle hypertrophy on the gallbladder wall, as well as mucosal outpouching into or through the thickened muscular layer, similar to Rokitansky-Aschoff sinuses, are the hallmarks of the condition gallbladder adenomyomatosis. Gall bladder adenomyomatosis was first identified as a precancerous lesion by Aldridge et al.[8] Later, it was claimed in a number of articles that segmental adenomyomatosis had a greater incidence rate and was the cause of gallbladder cancer.[9,10] Due to its vague clinical manifestation, gall bladder carcinoma, which ranks fifth among gastrointestinal malignant tumours, is rarely identified at an early stage.[11] A extremely uncommon kind of cancer, gall bladder cancer typically affects people who are older than 70 and develops when the gall bladder is constantly inflamed. It is an extremely aggressive cancer, and because it has spread to nearby organs like the liver, the prognosis is very bad.[12]

Adenocarcinoma, squamous cell carcinoma, small cell carcinoma, and sarcomas are the most prevalent types of gall bladder cancer.[13]

0.3-1.5% of cholecystectomy specimens show histological evidence of gall bladder cancer.[14] In 15–30% of patients, there is no indication of malignancy prior to or during surgery, and the illness is discovered postoperatively through microscopic examination. When investigating the cause of jaundice or vague gastrointestinal problems, ultrasonography is a helpful first line of investigation since it sensitively identifies bile duct occlusion. Differential diagnosis and determining the extent of the tumour locally are crucial in the diagnosis of gall bladder cancer. Imaging techniques such as endoscopic ultrasonography, CT, MRI, and magnetic resonance cholangiopancreatography are helpful for these goals. Following surgical excision, the complete specimen is sent for histological analysis, the most accurate way for determining the precise pathological process—in particular, malignancy at play.

Our study's objective is to assess the prevalence of different histological spectra in cholecystectomy specimens and to highlight the significance of histopathologically examining gallbladder specimens. Gall bladder histopathological analysis is a crucial diagnostic tool for separating benign from malignant tumours.

### Methods

This is a prospective and retrospective study of 5 years duration, 3 years retrospective and 2 years prospective from January 2018 to December 2022 at Department of Pathology, Sardar Patel Medical College, Bikaner. The cholecystectomy specimens received at Department of Pathology at Sardar Patel Medical College and associated group of

hospital; Bikaner constituted the sample for study. Autolyzed specimens and inadequate and poorly preserved resected specimen were excluded from the study. Patient's clinical data comprising of clinical features & laboratory investigation reports were collected from medical records in surgically resected specimens. Cholecystectomy specimens received were examined grossly for presence of pus, fibrin, hemorrhage, hyperemia, perforation, and presence of any localized lesion. Measurement of the specimen were noted. The specimen was fixed in 10% buffered formalin overnight. After fixation, the specimen was sectioned, if gall stones are present as per protocol. Gross findings of the mucosa and any other gross lesions were noted. Sections were taken from the fundus, body and neck of the gallbladder, additional sections were taken from abnormal appearing mucosa.

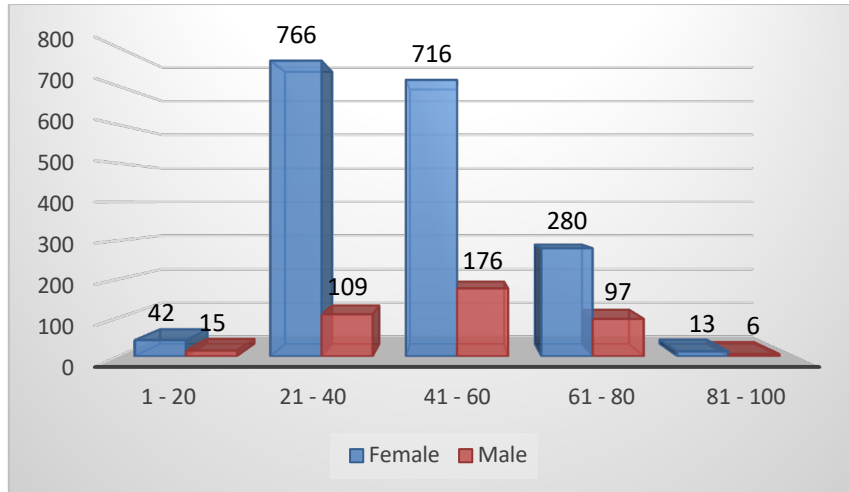
### Data analysis:

After entering data into Excel worksheet, it will be analyzed with the help of frequency, proportion, mean, standard deviation and tests of significance wherever applicable

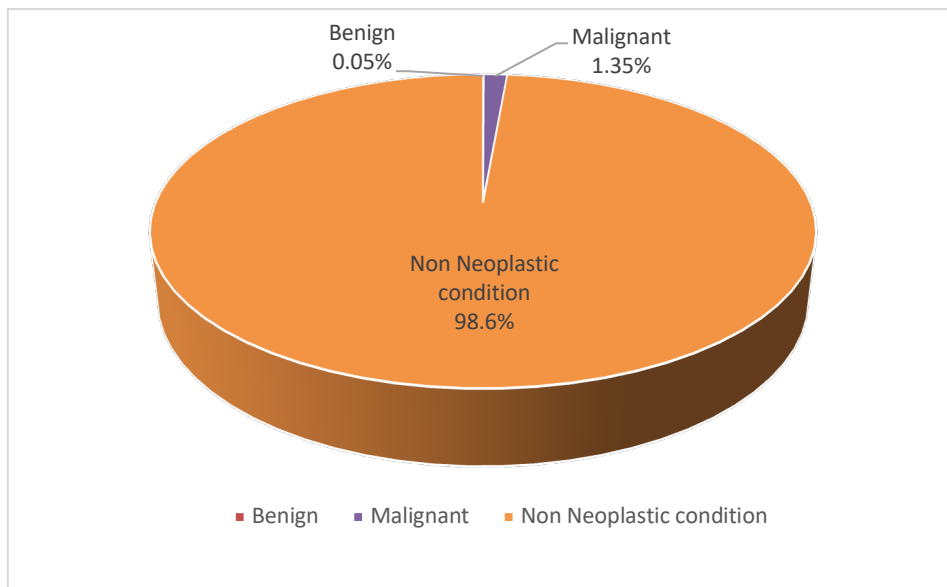
### Results

In the present study, we included total 2221 cholecystectomy samples received at our department. The mean age of the study group was  $45.86 \pm 15.08$  years. Maximum number of cases were in age group of 41 – 60 with 892 (40.16%) cases followed by 21 – 40 with 875 (39.39%) cases. There was female predominance in our study with 1818 (81.9%) were females and 403 (18.1%) were males, with female to male ratio of 4.5: 1.

On histopathological examination, non-neoplastic cases were most common with 2190 cases (98.6%), and we observed 30 (1.35%) samples with malignant lesions and only 1 case was reported as benign.



**Figure 1: Age and gender wise distribution of cases.**



**Figure 2: Distribution of cases according to category of lesion**

**Table 1: Histopathological diagnosis in present study**

Diagnosis	Count	%
Acute on Chronic Cholecystitis`	207	9.3%
Adenomyomatous hyperplasia	8	0.36%
Chronic Non-Specific Cholecystitis	1820	81.95%
Eosinophilic cholecystitis	25	1.13%
Follicular Cholecystitis	1	0.05%
Gangrenous Cholecystitis	3	0.14%
Ischemic Cholecystitis	17	0.77%
Lympho-Eosinophilic cholecystitis	2	0.09%
Necrotic Cholecystitis	7	0.32%
Perforated gall bladder	1	0.05%
Tubercular Granulomatous Cholecystitis	2	0.09%
Xanthogranulomatous Cholecystitis	97	4.37%
Papillary Adenoma Biliary type with choledochal cyst	1	0.05%

Adenocarcinoma	24	1.08%
Adenosquamous Carcinoma	1	0.05%
Mucinous Adenocarcinoma	2	0.09%
Papillary Adenocarcinoma	3	0.14%
Total	2221	100.0%

**Table no. 2: Malignant lesions reported in present study**

Diagnosis	Count	%
Adenocarcinoma	24	80%
Adenosquamous Carcinoma	1	3.33%
Mucinous Adenocarcinoma	2	6.67%
Papillary Adenocarcinoma	3	10%
Total	30	100%

As shown in table no. 1, maximum cases were of inflammatory nature with chronic non-specific cholecystitis 1820 (81.9%), followed by acute on chronic cholecystitis 207 cases (9.3%). Xantho-granulomatous cholecystitis was reported in 97 cases (4.4%), eosinophilic cholecystitis in 25 cases (1.1%). Tubercular granulomatous cholecystitis was reported in 2 cases (0.1%). Among malignant lesions, adenocarcinoma was reported in 24 cases (1.1%), papillary adenocarcinoma in 3 cases (0.1%), mucinous adenocarcinoma in 2 cases (0.1%).

### Discussion

The present study on histopathology of surgically removed gallbladder was undertaken with an objective of studying the various histopathological findings encountered in gallbladders, to determine the age and sex distribution among

patients with the gallbladder lesions and to study the association of gallstones with cholecystitis and carcinoma of gallbladder. We received a total of 2221 cases of cholecystectomies during the study period.

Most (81.9%) of the cases included in the present study were female patients with Male: Female ratio being 1:4.5. Mondal B et al [15] did a similar study to know the histopathological spectrum of lesions encountered in the gallbladder. Majority (80.8%) of them were from female patients with Male: female ratio of 1: 4.2, which agrees with our study. Results of the present study correlated with similar study done by H Mohan et al [16] (1:6.4). However, studies of Beena D et al [17] (1:1.2) and Awasthi N [18] (1: 2.6) also show female predominance but the ratio was not as high as our study. Overall results of all studies showed female predominance.

**Table 3: Comparison of age group of patients in the present study with other studies**

Study by	Beena D et al [17]	Mondal B et al [15]	H Mohan et al [16]	Murmu S et al [19]	Mittal R et al [20]	Present study
Age range (years)	17-83	13-76	10- 90	21- 70	14-84	1- 88
Age group with maximum cases (years)	41- 50	20- 29	31- 40	41- 50	41-50	41- 60

Age of patients in the present study ranged from 1 year to 88 years with a mean of  $45.86 \pm 15.08$  years. The highest number of cases were seen in 41 - 60 age group

(892 cases, 40.16%). The results were similar to the results obtained by Awasthi N [18], Beena D et al [17], Murmu S et al [19], and Mittal R et al [20] where

maximum number of cases were found in 5<sup>th</sup> decade. However, Mondal B et al found

maximum cases in comparatively younger age of 20 – 29 years.

**Table 4: Comparison of presence of calculi in the present study with other**

Study by	Total number of gallbladders studied	Total number of gallbladders with calculi	Percentage
Awasthi N [18]	732	697	95.2%
Beena D et al [17]	200	130	65%
H Mohan et al [16]	1100	1050	95.45%
Karlatti SS et al [21]	143	104	72.73%
Present study	2221	2051	92.34%

In our study, 92.34% of the cases were associated with gallstones. Previous studies conducted by Karlatti SS et al [21] et al, Awasthi N [18] and H Mohan et al [16] showed similar percentage of gallbladder with calculi 72.73%, 95.2%,

and 95.45% respectively. However, Beena D et al [17] reported a lower percent of gall stones in their study. Surgeons sending gallbladder specimens without including gallstones may be the cause for the lower values.

**Table 5: Comparison of incidence of non-neoplastic lesions in the present study with other studies**

Study by	Total number of gallbladders studied	Total number of non-neoplastic gallbladders	Percentage
Murmu S et al [19]	106	104	98.1%
Awasthi N [18]	732	732	100%
Beena D et al [17]	200	199	99.5%
Mondal B et al [15]	786	781	99.36%
H Mohan et al [16]	1100	1086	98.72%
Mittal R et al [20]	1305	1282	98.23%
Present study	2221	2190	98.6%

Non-neoplastic conditions of gallbladders formed the major group of pathological lesions in the present study constituting 2190 cases (98.6%) which included spectrum of lesions consisting of acute cholecystitis, acute on chronic cholecystitis, chronic cholecystitis, eosinophilic cholecystitis and xanthogranulomatous cholecystitis which was similar to the studies done by Murmu S et al [19] in which the non-neoplastic conditions of gallbladder formed the major group with an incidence of 98.1%. The present study also correlated well with other studies by Mittal R et al [20] (98.23%), Beena D et al [17] (99.5%), Mondal B et al [15] (99.36%).

The incidence of xanthogranulomatous cholecystitis in the present study was 4.4% (97 cases). These results were comparable to their results obtained from the study done by H Mohan et al [16] (26 cases, 2.3%) and Mittal R et al [20] (42 cases 3.2%). However, Murmu S et al [19] (1 case, 0.94%), Beena D et al [17] (2 cases, 1%), showed a lower incidence when compared to the present study.

Eosinophilic cholecystitis is a rare condition. The incidence of it in the present study was 1.1% (25 cases), which was comparable to the results obtained from the studies conducted by H Mohan et al [16] (6 cases, 0.5%). A slightly lower incidence was obtained from the

study done by Sharma I et al [22](1 case, 0.31%). Though rare condition a higher incidence of eosinophilic cholecystitis was seen in the study by Selvi TR et al [23](4 cases, 3.8%) and this might be due to lesser sample size in their study or different study region compared to the present study (Salem, Tamil Nadu).

### Carcinoma of gallbladder

**Table 6: Comparison of incidence of gall bladder carcinoma in the present Study with other studies**

Study by	Incidence of gallbladder carcinoma	Incidence of gallbladder carcinoma in Percentage
Murmu S et al [19]	2cases	1.88%
Awasthi N [18]	0cases	0
Beena D et al [17]	1case	0.5%
Mondal B et al [15]	5cases	0.6%
H Mohan et al [16]	12cases	1.09%
Mittal R et al [20]	13cases	1%
Sharma I et al [22]	22 cases	0.86%
Present study	30cases	1.35%

Incidence of carcinoma gallbladder found in the present study was 1.35% (30 cases), which correlated very well to the incidence found in the study conducted by Murmu S et al [19] (2 cases, 1.88%) and H Mohan et al [16] (12 cases, 1.09%). A lower incidence was observed in studies done by Beena D et al [17] (1 case, 0.5%), Mondal B et al [15] (5 cases, 0.6%), and Sharma I et al [22] (3 cases, 0.86%). The higher incidence of malignant lesions in our study may be due to tertiary care cancer center in our college.

The mean age of carcinoma gallbladder diagnosed in the present study was years (range 41-80 years) that is in elder age group. Studies done by Mittal R et al [20] (56.2 years) observed lower mean age than the present study. We observed female preponderance of carcinoma gallbladder with female to male ration of 3:1 in our study. Similarly observed in studies done by Murmu S et al [19].

The percentage of carcinoma gall bladder associated with gallstones were different in each study. We observed that out of 30

Incidence of adenoma in the present study was 0.05% (1 cases), which was of papillary type. The incidence of adenoma was higher in studies of Kumari G et al [12] (1 case, 0.18%) and H Mohan et al [16] (2 cases, 0.18%).

cases of malignant gallbladder lesions 66% (20 cases) had gall stones. The observation is closely similar to Barbhuiya MA et al [24](77.67%), and Kalita D et al [25](72%). Whereas Hamdani NH et al [26](86%) and H Mohan et al [16](100%) showed the association of gall stones with carcinoma gallbladder in significantly higher number of cases extending up to 100% cases.

According to the present study there was no statistically significant difference (at  $p < 0.05$ ) between malignancy and gallbladder calculi. Hence the association of gallstones with carcinoma gallbladder could not be considered.

### Conclusion

Gall bladder diseases have a spectrum of presentation histopathologically. In the present study an attempt was made to demonstrate the histological changes of non-neoplastic and neoplastic lesions of gallbladder.

The majority of the gallbladder lesions were non-neoplastic, of which chronic cholecystitis formed the major bulk. The

present study, in accordance with other studies showed a female predominance. Hence it might be concluded that chronic cholecystitis was the most probable diagnosis in female patients in 5<sup>th</sup> and 7<sup>th</sup> decade of life.

Incidence of gallbladder carcinoma was 1.4% in the present study. The observations from this study indicated a statistical association between increased thickness of gallbladder and carcinoma of gallbladder.

Hence, the present study emphasized the need to examine all the cholecystectomy specimens and thorough sampling of thickened portion as well as any suspicious area in the gall bladder specimen should be done, in order to avoid missing gallbladder carcinoma cases.

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