

# Clinicopathological Study of Gallbladder Lesions: Two Years Study

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## ABSTRACT

**Background:** Gallbladder is one of the most frequently surgically resected organs which stores and concentrates the bile and is involved by both non neoplastic as well as neoplastic diseases. Chronic calculous cholecystitis is the most common benign lesion of gallbladder and pain abdomen is the commonest clinical presentation. Both non neoplastic and neoplastic lesions have similar clinical presentation and overlapping radiological findings.

**Methods:** Total 550 cholecystectomy specimens were received in pathology department. Grossly, formalin fixed specimens were examined carefully and section were given from neck, fundus and body of gallbladder. Whenever it was necessary, additional sections were given. After processing, the H&E stained sections were studied thoroughly. All the clinical details were taken from case papers.

**Result:** The commonly seen non neoplastic lesions were chronic calculous cholecystitis (405 cases), chronic cholecystitis (85 cases), Acute on chronic cholecystitis with or without stones (18 and 3 cases), acute necrotizing cholecystitis (2 cases), eosinophilic cholecystitis (3 cases), follicular cholecystitis (3 cases), lymphoplasmacytic cholecystitis (1 case), xanthogranulomatous cholecystitis (9 cases), cholesterosis (4 cases), mucocele of gall bladder (2 cases), adenomyomatosis (3 cases) and gallbladder cholesterol polyp with cholecystitis (2 cases). Among neoplastic lesions 1 case was adenoma with severe dysplasia and 9 cases were adenocarcinoma.

**Conclusion:** Chronic calculous cholecystitis was the most common lesion and out of 9 cases of carcinoma, 7 cases were diagnosed incidentally. Therefore, histopathological evaluation plays a critical role in identifying incidental gallbladder carcinoma for proper management of patients.

**Keywords:** Chronic Calculous Cholecystitis, Gall Stones, Pain Abdomen, Incidental Gallbladder Carcinoma

## Introduction

Gallbladder is the organ where bile is stored and concentrated, which helps in digestion of fat.<sup>[1]</sup> Gallbladder lesions are most commonly encountered conditions among biliary tract lesions affecting a significant proportions of the world's population. The various gallbladder lesions range from congenital anomalies, inflammatory to neoplastic which include both benign and malignant lesions. The non neoplastic lesions are encountered more frequently than the neoplastic lesions. Gall stones are the commonest biliary pathology accounting for more than 95% of gall bladder lesions. Other gallbladder diseases include cholecystitis, cholesterolosis, gall bladder polyp and adenomyomatosis.

Gallbladder lesions are very common in fatty, fertile female of fourty to fifty years age group but equally affects male and children.<sup>[2]</sup> The incidence of cholelithiasis and cholecystitis appear to be increasing over past couple of decades in India and Western world due to sedentary lifestyle, intake of fatty, high calorie diet and consumption of alcohol.<sup>[2,3]</sup>

Gallbladder carcinoma is the most common cancer of the biliary tree and 5th most common gastrointestinal

malignancy. It is characterised by rapid progression and high mortality rate. Cancers at an early stage are limited to the mucosa. Since early malignancies clinically present as benign lesion, they need to be diagnosed on histopathology for proper management of patients and for better prognosis.<sup>[4]</sup>

## Materials and Methods

The study was observational prospective study and was carried out in the department of pathology of a tertiary care centre in Mumbai for a period of 2 years (from July 2014 and June 2016). The patients coming to the surgery department from clinical outpatient department as well as patients admitted in wards with clinical diagnosis of gallbladder lesions were included in the study. All the cases with cholecystectomy from the material sources were included in the study. Clinical details of all patients were taken from case papers as well as from record section. Both intact as well as already cut open specimens were received in the surgical pathology department. Detailed gross examination of 10% formalin fixed specimens were carried out with respect to size, external surface, mucosal surface, wall thickening, presence of gallstones and type of gallstones. Important gross features of the specimen were

noted. After gross examination minimum three sections, one each from neck, body and fundus of the gallbladder were given. Also additional sections were given whenever it was necessary. The sections were subjected to routine paraffin processing, cutting with microtome and staining with Hematoxylin and Eosin (H&E). Detailed microscopic study of sections was done under the light microscope and then the final diagnosis was given. Both clinical details of the patients and histomorphological findings of the cholecystectomy specimen were studied thoroughly.

## Result

The present study was prospective study conducted for a period of two years (July 2014- June 2016). Total 550 gallbladder specimens were received during the study period.

The geographical distribution of cases was studied based on whether they were from urban or rural population. Total 85.27% cases were from urban population and 14.73% cases were from rural population.

Among 550 cases, 548 (99.64%) cases presented with pain abdomen. In 87.23% cases pain was dull aching type while in 12.77% cases it was colicky. The most common site was right hypochondrium (446 cases). Other sites of involvement were epigastrium (29 cases), right hypochondrium and epigastrium (45 cases), diffuse abdomen (27 cases). 1 case had pain in right hypochondrium radiating to left iliac fossa. 52 cases were having nausea, 17 cases flatulence, 9 cases dyspepsia, 6 cases bloating, 20 cases were having nausea and vomiting and 3 cases were having pruritus. Breathlessness and constipation were found in 2 cases each. 2 cases presented with only burning micturition. The typical features of cholelithiasis were absent in 2 cases.

Many cases were found to have other metabolic disorders like diabetes mellitus and hypertension which is considered as risk factors for gall bladder lesion in the literature. In our study 34 cases were having hypertension while diabetes mellitus was seen in 12 cases. Both diabetes mellitus and hypertension was seen in 12 cases. 6 cases were having retroviral disease (RVD). One case of ischemic heart disease (IHD) was also found.

Both clinically as well as radiologically, the most common diagnosis was cholelithiasis.

Grossly among 550 cases, total 437 cases were having gallstones and two cases were having sludge in the gallbladder. 51.03% of cases had pigment stones. Cholesterol stones and mixed stones were seen in 30.89% and 18.08% cases respectively. Among neoplastic lesions total five cases were associated with stones. 3 cases were

having pigment stones and 2 cases were having cholesterol stones. Wall thickening of the gallbladder was within normal limit (1-3mm) in 375 cases (68.18%) whereas in 175 cases (31.82%) wall thickening was more than 3mm. Other findings were edema, congestion, ulceration of mucosa, necrosis, edema with mucus infiltration into the wall (mucocele), linear yellow streaks with strawberry like appearance protruding into the lumen (cholesterosis), diverticula formation within the thickened wall (adenomyomatosis) and polypoid lesion with stalk. Cases of xanthogranulomatous cholecystitis were found as diffuse wall thickening with yellowish nodule. Since xanthogranulomatous cholecystitis has similar gross appearance as carcinoma, their diagnosis was confirmed on histopathological examination. Out of 10 cases of gallbladder neoplasm, 1 case had polypoid lesion while rest of the 9 cases had infiltrative and exophytic pattern. Infiltrative growth pattern was common and seen in 8 cases while exophytic pattern was seen in 1 case. Necrotic, hemorrhagic and ulcerated areas were also noted in the luminal portion. 1 case of gallbladder carcinoma presented with gallbladder perforation.

On microscopy, the most commonly seen lesion was chronic calculous cholecystitis (405 cases, 73.64%). Other lesions were chronic cholecystitis (85 cases, 15.45%), Acute on chronic cholecystitis with stones (18 cases, 3.27%) and without stones (3 cases, 0.55%), acute necrotizing cholecystitis (2 cases, 0.36%), eosinophilic cholecystitis (3 cases, 0.55%), follicular cholecystitis (3 cases, 0.55%), lymphoplasmacytic cholecystitis (1 case, 0.18%), xanthogranulomatous cholecystitis (9 cases, 1.64%), cholesterosis (4 cases, 0.73%), mucocele of gall bladder (2 cases, 0.36%), adenomyomatosis (3 cases, 0.55%) and gallbladder cholesterol polyp with cholecystitis (2 cases, 0.36%). The variants of chronic cholecystitis include eosinophilic cholecystitis, follicular cholecystitis, lymphoplasmacytic cholecystitis and xanthogranulomatous cholecystitis.

Among gallbladder neoplasm cases, one case was adenoma with severe dysplasia on histopathology. Adenoma with severe dysplasia is benign neoplastic lesion of gallbladder. 8 cases were primary malignancy of gallbladder while one case was secondary tumor metastasizing from carcinoma head of pancreas. All the cases of malignant lesions were adenocarcinoma of gallbladder with well, moderate and poor differentiation. 6 cases were having well differentiated adenocarcinoma, of which one case presented with metastasis to liver. 1 case was having well differentiated adenocarcinoma of gallbladder with metastasis to bilateral ovaries. 1 case was of moderately differentiated adenocarcinoma. 2 cases were having poor

differentiation. Among poorly differentiated morphology, one case was poorly differentiated adenocarcinoma of head of pancreas with metastasis to the gallbladder.

Out of 9 cases of gallbladder carcinoma, total 7 cases were diagnosed incidentally on histopathological examination of specimens resected for benign pathology.

**Table1: Distribution of various gallbladder lesions with common clinical features.**

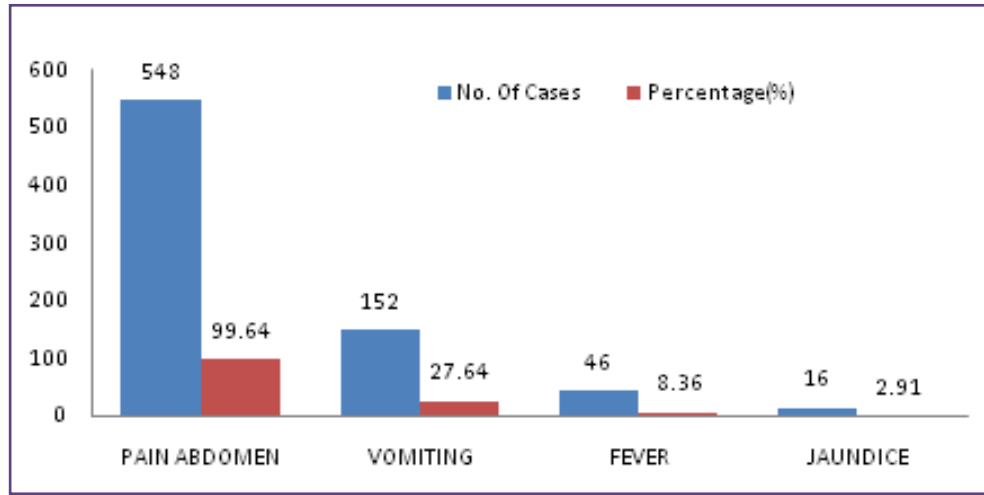
Non Neoplastic lesions	No. Of Cases	Percentage (%)	Common age group (years)	Predominant Sex	Common clinical presentation	Common site
Acute on chronic cholecystitis	3	0.55	41-60	M	Pain abdomen	Right hypochondrium
Acute on chronic calculous cholecystitis	18	3.27	41-60	M	Pain abdomen	Right hypochondrium
Acute necrotizing cholecystitis	2	0.36	41-60	M	Pain abdomen	Right hypochondrium
Adenomyomatosis of GB	3	0.55	61-80	F	Pain abdomen	Right hypochondrium
Chronic cholecystitis without stones	85	15.45	41-60	F	Pain abdomen	Right hypochondrium
Chronic calculous cholecystitis	405	73.64	41-60	F	Pain abdomen	Right hypochondrium
Eosinophilic cholecystitis	3	0.55	41-60	F	Pain abdomen	Right hypochondrium
Follicular cholecystitis	3	0.55	41-60	F	Pain abdomen	Right hypochondrium
Lymphoplasmacytic cholecystitis	1	0.18	41-60	M	Pain abdomen	Right hypochondrium
Cholesterosis	4	0.73	21-40	F	Pain abdomen	Right hypochondrium
GB cholesterol polyp with cholecystitis	2	0.36	21-40	F	Pain abdomen	Right hypochondrium
Mucocele of gall bladder	2	0.36	21-40	F	Pain abdomen	Right hypochondrium
Xanthogranulomatous cholecystitis	9	1.64	41-60	M	Pain abdomen	Right hypochondrium
Neoplastic lesions	10	1.82	21-40	F	Pain abdomen	Right hypochondrium
<b>Total</b>	<b>550</b>	<b>100</b>				

**Table 2: Comparison of various non neoplastic lesions.**

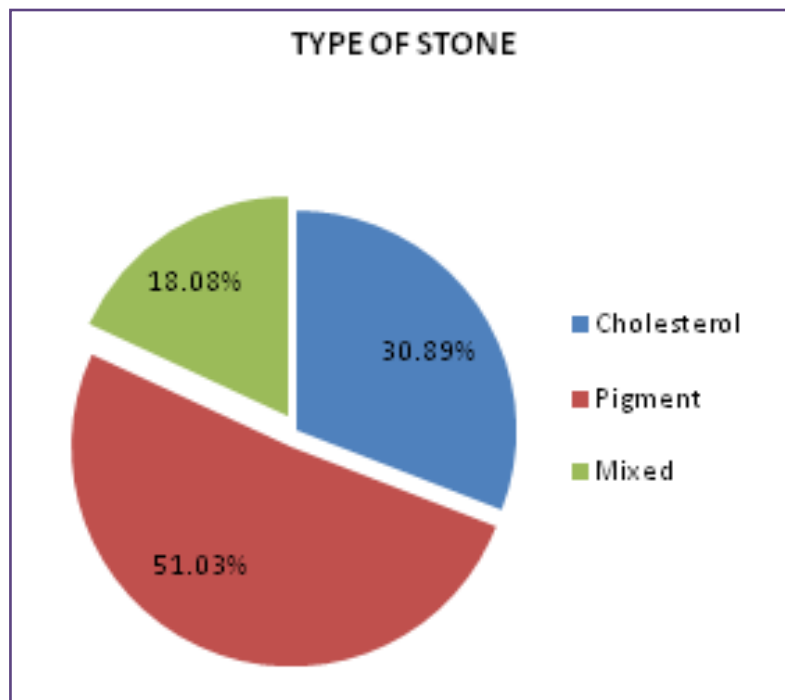
Diagnosis	Dowerah et al <sup>[5]</sup>	Awasthi N <sup>[10]</sup>	N.Sreemani K et al <sup>[11]</sup>	Present study
Acute cholecystitis	2.9%	0.80%	-	0.36%
Acute on chronic cholecystitis	-	3.20%	-	3.81%
Chronic cholecystitis	85.4%	97%	81.17%	89.18%
Eosinophilic cholecystitis	3.90%	-	0.58%	0.54%
Xanthogranulomatous cholecystitis	0.90%	1.80%	1.76%	1.63%
Follicular cholecystitis	-	3.10%	0.58%	0.54%
Cholesterosis	4.90%	6.20%	0.58%	0.72%
Adenomyomatosis	1.90%	0.10%	2.35%	0.54%

**Table 4: Comparison of incidental diagnosis of gallbladder cancer.**

Studies	No of incidental gallbladder carcinoma cases	Total no of cholecystectomies	Incidence rate
Sharma JD et al <sup>[14]</sup>	17	863	1.97%
Dipti Kalita et al <sup>[15]</sup>	18	4115	0.44%
Shreshtha et al <sup>[20]</sup>	9	570	1.4%
Mittal et al <sup>[21]</sup>	13	1305	0.9%
Present study	7	550	1.27%



**Fig. 1: The overall common clinical features of various lesions.**



**Fig. 2: The distribution of different types of gallstone.**



Fig. 3a: chronic cholecystitis with cholesterol gallstones, Fig 3b- cholesterosis, Fig 3c- gallbladder polyp, Fig 3d- gallbladder carcinoma with metastasis to liver.

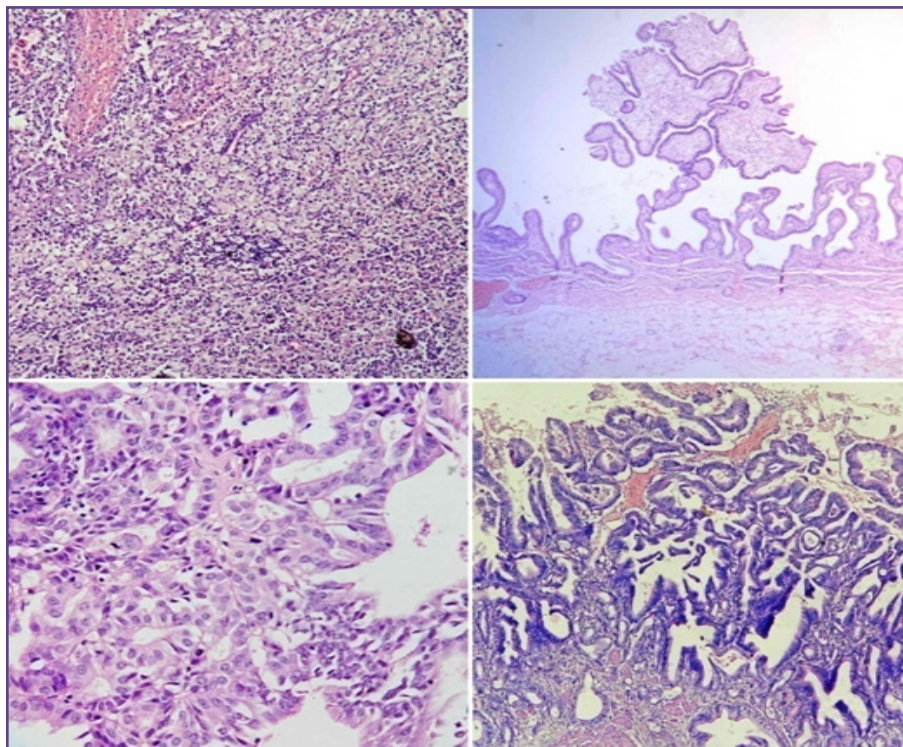


Fig. 4a: Xanthogranulomatous cholecystitis [H&E, 20X], Fig 4b- Cholesterol polyp of gallbladder [H&E, 10X], Fig 4c- Gallbladder adenoma with severe dysplasia [H&E, 40X], Fig 4d- Well differentiated adenocarcinoma of gallbladder [H&E, 20X].

## Discussion

Gall bladder lesions are among the most common lesions encountered in clinical practice and gallbladder is one of the most common surgically resected specimen.<sup>[5]</sup> In our study total 550 cases of cholecystectomy were studied in two years and a variety of both non neoplastic and neoplastic lesions were found. Due to change in life style, there is global increase in the incidence of various gallbladder lesions, so that the study was carried out to analyse various lesions of gallbladder with respect to the clinical aspects. All the cases of cholecystectomies in two years were included in the study.

Clinically, the most common presenting complaint was pain abdomen comprising 99.63% cases and was mostly located in the right hypochondrium and epigastric region which has similarity with the study of Ezhil Arasi et al<sup>[6]</sup> and Bansal et al<sup>[7]</sup> where pain abdomen was the most common symptom and was found in 55% and 100% cases respectively. Other features like nausea/vomiting, fever and jaundice was found in 27.63%, 8.36%, 2.90% cases respectively while in the study of Bansal et al,<sup>[7]</sup> it was found in 64.4%, 13.5% and 6.7% cases.

In our study, the incidence of non neoplastic lesions was peak in the age group of 41-60 years with female predominance which has similar outcome in a study done by Rakesh B.H et al.<sup>[8]</sup> The youngest age was 4 years and elder most was 84 years in our study. The mean age of non neoplastic cases was 45.09 years while in a study of Sumit Giri,<sup>[9]</sup> the mean age was 51 years. The non neoplastic lesions were more commonly encountered than the neoplastic ones and comprised of 98.18% while neoplastic lesions were 1.82%. In studies done by Ezhil Arasi et al<sup>[6]</sup> and Dr. Gudeli Vahini et al<sup>[4]</sup> there was varied proportion of neoplastic lesions and comprised of 5% and 4.5% respectively.

Grossly, the thickness of gallbladder is important as it is increased in both non neoplastic as well as neoplastic conditions. The thickness was between 1-3mm in 68.18% cases and >3mm in 31.82% cases in our study while in other studies done by Ezhil Arasi et al<sup>[6]</sup> and Sumit Giri,<sup>[9]</sup> the thickness was between 1-3cm in 43% and 58.15% cases and >3mm in 57% and 41.85% cases respectively. On microscopy, chronic calculous cholecystitis was the most common lesion comprising 89.18% of cases which is also a common observation reported by Dowerah et al,<sup>[5]</sup> Awasthi N<sup>[10]</sup> and N.Sreemani K et al<sup>[11]</sup> where the lesion is found in proportion of 85.4%, 97% and 81.17%. It is found that various gallbladder lesions are associated with gallstones. In our study, total 77.30% cases were associated with gallstones, which is concordant with the study of Dr. Gudeli Vahini et al<sup>[4]</sup> where gall stones were found in the same proportion. Among various gall stones, cholesterol stones, mixed stones and pigmented stones were commonly found. Mazlum M et al<sup>[12]</sup>

reported that cholesterol stones were common in gallbladder lesions in urban population while in our study pigment stones were more commonly found comprising 51.03% cases. In the study of Rakesh B.H et al<sup>[8]</sup> and Bansal et al<sup>[7]</sup> the pigment stones were found in proportion of 60% and 38%.

Among neoplastic lesions the incidence was peak in the age group of 21-40 years with slight increase in younger age while in studies of Barbhuiya et al,<sup>[13]</sup> Sharma JD et al<sup>[14]</sup> and Dipti Kalita et al,<sup>[15]</sup> the peak incidence was found in the age group 40-60 years, 41-60 years and 50-60 years respectively. This indicates that there is an increase in the frequency of gallbladder carcinoma in younger age groups. Similar to our study, females were commonly affected by gallbladder carcinoma in their study also. In our study, the neoplastic cases commonly presented with pain abdomen comprising 100% cases and the most common site of involvement was right hypochondrium. Barbhuiya et al<sup>[13]</sup> and Nissar Hussain et al<sup>[16]</sup> had similar observation for clinical behaviour of gallbladder carcinoma.

Like non neoplastic lesions, neoplastic lesions were also found to be associated with gallstones. In the studies of Barbhuiya et al,<sup>[13]</sup> Dipti Kalita et al<sup>[15]</sup> and Nissar Hussain et al<sup>[16]</sup> the gallstones were found in 77.67%, 72% and 86% cases of gallbladder carcinoma while in our study, 50% cases of gallbladder carcinoma were associated with stones. It suggests that gallstone is an important etiological factor for development of carcinoma which is also supported by the studies of Nissar Hussain et al<sup>[16]</sup> and Wang et al.<sup>[17]</sup> Pigment stones were the most common type of stones found in our study which is concordant with the finding reported by Kimura et al<sup>[18]</sup> from Japan.

Same authors Barbhuiya et al,<sup>[13]</sup> Dipti Kalita et al<sup>[15]</sup> and Nissar Hussain et al<sup>[16]</sup> did extensive study on gallbladder carcinoma and found that adenocarcinoma was the most common type microscopically which is also a common observation in our study.

Although gallbladder carcinoma is most common cancer of biliary tree, the cholecystectomy specimen is not found frequently due to its late presentation, early spread by lymphatics, hematogenous or direct route, high propensity to seed the peritoneal surface and lack of effective adjuvant therapy.<sup>[19]</sup> Many times the malignant lesions are encountered incidentally in specimens resected for cholelithiasis, inflammation, perforation or in suspected cases of xanthogranulomatous cholecystitis. In our study, 7 out of 9 cases of gallbladder cancer were found incidentally. Among carcinoma cases the proportion of incidentally diagnosed cases (77.7%) is significantly high which reflects the importance of histopathological examination of every specimen. Out of 7 cases 5 were diagnosed as case of cholelithiasis, 1 as case of perforation and 1 case as obstructive jaundice clinically as well as radiologically.

In our study, another considerable finding was that all the cases of neoplastic lesions and 85.27% cases of non neoplastic lesions were from urban population while Barbhuiya et al<sup>[13]</sup> found that rural population of northern part of India was commonly involved by gallbladder carcinoma.

### Conclusion

Although chronic calculous cholecystitis was the most common finding, other non neoplastic and neoplastic lesions of gallbladder had similar clinical presentation which mandates histopathological examination of every cholecystectomy specimen. Many cases of gallbladder carcinoma were found incidentally so, regardless of age group thorough sampling of thickened portion as well as any suspicious area of gallbladder specimen should be done followed by careful histopathological examination to avoid escape of any neoplastic change.

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