



The Histopathological Spectrum Of Gallbladder Diseases In Cholecystectomy Specimens – An Observational Cross - Sectional Study

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Abstract

Introduction: Gallbladder diseases are a common surgical health issue requiring cholecystectomy worldwide. Histopathological examination of gallbladder specimens is an important step in the confirmation of clinical and radiological diagnosis of gallbladder diseases.

Objective: To study the histopathological spectrum of the gallbladder diseases in cholecystectomy specimens.

Materials and methods: A 2 year observational cross sectional study was conducted at a tertiary care hospital, after Institutional Ethics Committee approval. Total 105 cholecystectomy (either by laparoscopic or open procedure) specimens were included in the study. The clinical details, investigations of the patients undergoing cholecystectomy as well as gross and histopathological findings in gallbladder specimens were studied.

Result: Out of 105 cholecystectomy specimens, 68 were female (64.76%) and 37 male (35.24%). Thus, the female to male ratio being 2:1. Age groups from 11 to 80 years were included of which 31-40 and 41-50 years age group comprised of majority of the patients. The following diagnoses were made on histopathology – chronic cholecystitis with cholelithiasis 68 cases (64.76%), chronic cholecystitis (acalculous) 14 cases (13.33%), choledochal cyst and adenocarcinoma 06 cases each (5.71% each), adenomyomatosis and xanthogranulomatous cholecystitis 04 cases each (3.81 % each). Adenoma, empyema and mucocele 01 case each (0.95% each).

Conclusion: Most of the gall bladder diseases occur due to cholelithiasis where females are affected more. Thorough sampling of the cholecystectomy specimens and routine histopathological examination is of utmost importance to detect non neoplastic complications and incidental gallbladder carcinoma. This study gives a comprehensive picture of different histopathological patterns.

Keywords: cholecystectomy, gallbladder diseases

Introduction

Histopathological examination of gallbladder specimens is an important step in the confirmation of clinical and radiological diagnosis of gallbladder diseases. Gallbladder disease is one of the common health problems. It includes neoplastic and non neoplastic lesions. Gallbladder is among one of the most commonly resected organs.¹ Cholecystectomy is

the most commonly performed procedure for gallbladder diseases.¹ Nowadays, the number of cholecystectomies has increased.¹

Cholecystitis, cholelithiasis and benign tumours of the gall bladder constitute majority of the cholecystectomies.¹ Most of the cholecystectomies

are done for cholelithiasis i.e gallstone disease. Gallstone appears to be the most important risk factor for carcinoma gall bladder.²

Various histopathological appearances such as chronic cholecystitis, cholelithiasis, benign tumours or tumour like lesions are seen in gallbladder specimens.^{2,3} Unexpected carcinoma gallbladder can also be detected which has some chance to be missed during pre-operative imaging studies for diagnosis.² In this way, histopathology holds an important place in diagnosing incidental gallbladder carcinoma as well.

Aim And Objective

To study the histopathological spectrum of the gallbladder diseases in cholecystectomy specimens.

Material And Methods

A 2 year observational cross sectional study was conducted at our tertiary care hospital, after Institutional Ethics Committee approval. Cholecystectomy (either by laparoscopic or open procedure) specimens kept in 10% formalin and sent for histopathological examination, were included in the study. The clinical details, investigations of the

patients as well as gross and histopathological findings in gallbladder specimens were studied carefully. 105 gallbladder specimens were included. All the gallbladder specimens were studied grossly as well as histologically.

Ethics

The study was approved by the Institutional Ethics Committee. All patients gave informed consent to participate in this study.

Results

The total number of gallbladder specimens studied after cholecystectomy were 105, with 68 females (64.76%) and 37 males (35.24%). Average age of the patients ranged from 12 to 77 years with mean of 43.11 years and standard deviation of 13.48 years. Maximum no. of cases were found between age group of 31- 40 and 41-50 years, 26 cases each (25 % for each group) followed by 21-30 years, 22 cases (21% of total cases) and 51-60 years, 19 cases (18% of total cases).

Table 1 shows clinical features of patient of gall stone diseases.

Table 1: Clinical features of patients

Sr No	Symptoms	No. of patients	Percentage
1	Pain in abdomen (right upper hypochondrium)	99	94%
2	Nausea and vomiting	10	9.50%
3	Lump in abdomen	5	5%
4	Loose stool	2	2%
5	Jaundice	2	2%

Table 2 shows that in our study, chronic cholecystitis with cholelithiasis was the most common histopathological diagnosis.

Table 2: Distribution of histopathological varieties of cholecystectomy specimens

	Histopathological diagnosis	Number of cases	Percentage (%)
A]	NON-NEOPLASTIC LESIONS		
	Chronic cholecystitis with cholelithiasis (Calculous cholecystitis)	68	64.76

	Chronic cholecystitis (Acalculous cholecystitis)	14	13.33
	Choledochal cyst	6	5.71
	Adenomyomatosis	4	3.81
	Xanthogranulomatous cholecystitis	4	3.81
	Empyema	1	0.95
	Mucocele	1	0.95
B]	NEOPLASTIC LESIONS		
	Benign		
	Adenoma	1	0.95
	Malignant		
	Adenocarcinoma	6	5.71
	TOTAL	105	100.00

Table 3: Distribution of cases according to the wall thickness (on macroscopic examination)

Wall Thickness	Number of cases (Total cases N=105)	Percentage (%)
Increased (> 3 mm)	26	24.76
Normal (≤3 mm)	79	75.24
TOTAL	105	100.00

Figure 1: Specimen of gallbladder with thickened wall and single black stone in the lumen (chronic cholecystitis)



Figure 2: Microphotograph of Adenomyomatosis of gallbladder showing hyperplasia of the muscle wall of the gallbladder and dilated benign glands. (Hematoxylin and Eosin stain, 400 X)

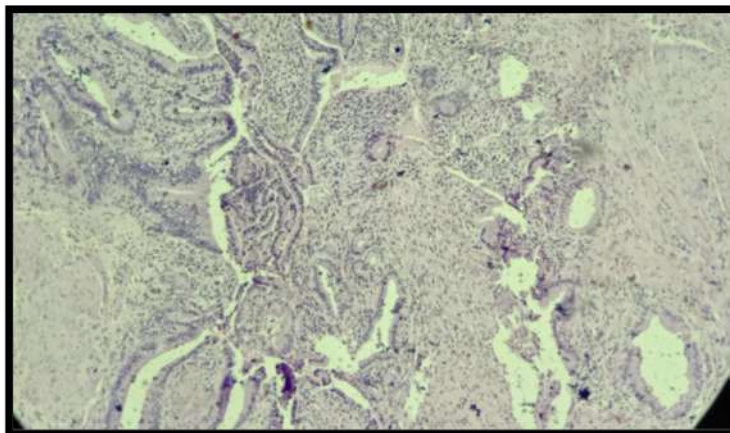


Figure 3: Microphotograph of gallbladder showing Xanthogranulomatous cholecystitis with foamy macrophages with inflammatory infiltrate (Hematoxylin and Eosin stain, 400 X)

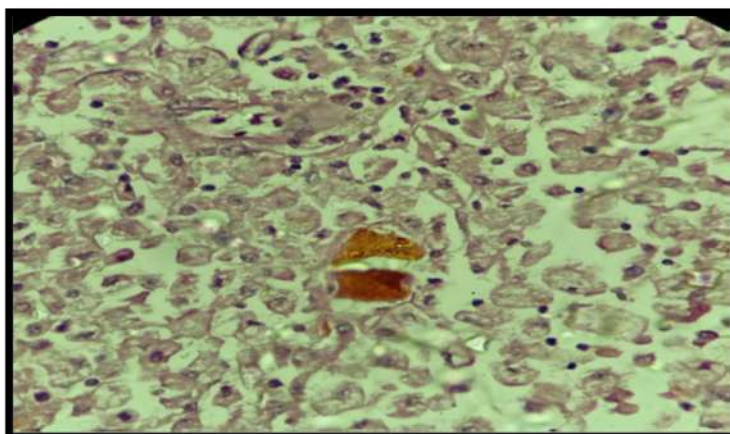
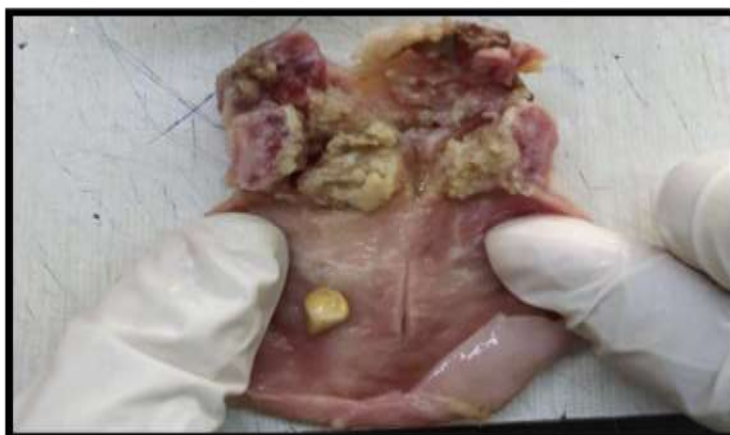


Figure 4: Specimen of adenocarcinoma gallbladder showing tumour of size 2 x 1 cm in the neck and body of gallbladder



Discussion

The present study was planned to evaluate histopathological spectrum of gallbladder diseases in cholecystectomy specimens in our institute. Clinical details and data was collected from a total of 105 cholecystectomy specimens.

Analysis of demographic profile of our study shows that mean age of the patients was 43.11 ± 13.48 years with range of 12 to 77 years. Out of all patients, percentage of females (64.76%) was more than that of males (35.24%) (Females to males ratio- 2:1) Similar findings were found in a study done by Bansode I and Baheti M1 (2019) in which lesions of gallbladder were common in the 5th decade with the mean age of presentation of 45.5 years and showed female patients (76%) more than males (24%). A study done by Thukral S *et al.*4 (2018) found that, in gall bladder lesions age range was 20 to 85 yrs and female patients (74.8 %) were more than male patients (25.2%). A study done by Giridharan *et al.*5 (2017) found that incidence of gall stone diseases was common in females (84%) than males (16%). Female sex hormones and sedentary habits of most women in India exposes them to factors that possibly promote the formation of gallstones.

The maximum number of cases were found in the fourth and fifth decade of life (25% for each). Similar findings were seen by study done by Ahadi M *et al.*6 (2020) in which maximum number of gall bladder disease cases were found in age group of 31-60 yrs (51% of all cases). Also, the study done by Sharma I *et al.*7 (2015) showed that maximum incidence of gall bladder disease were in between 21—60 yrs (86% of all cases). The average age of these patients in India is a decade younger than in the west. A study done by Barbara L *et al.*8 in Italy shows that maximum number of gall stone diseases were in between age group of 50 -65 years (50.51% of total cases). The exact cause of this is not known although it may be due to genetic predisposition.⁸

Pain in abdomen located in right upper hypochondrium region was the most common presenting symptom in 94 % of total cases of gall bladder diseases. Nausea, vomiting, loose stool were less commonly associated symptoms in our study. Lump in abdomen and jaundice were also presenting symptom in some cases of gall bladder carcinoma (table 1). Similar results were found by Siddiqui FG

*et al.*9 (2013), Khan S *et al.*3 (2013) and Beena D *et al.* 10 (2017) in which pain in abdomen was common presenting symptom in 92%, 68.2% and 77 % of cases respectively.

Laparoscopic cholecystectomy was most commonly performed surgery for gall bladder diseases in our study. (95% of all cholecystectomy). Open cholecystectomy was performed for only 5 conditions of gall bladder (3- adenocarcinoma of gall bladder, 1- intracystic papillary adenoma, 1- cholelithiasis, choledocholithiasis with empyema gall bladder). Similar findings were seen in study done by Shrinivasan *et al.*11 (2019) in which majority number of cases of cholecystectomy were performed by laparoscopy (83%) and remaining open procedure (17%). Laparoscopic cholecystectomy has become the standard treatment for symptomatic gallbladder diseases. Laparoscopic cholecystectomy for acute and chronic inflammation of the gallbladder is safe and is associated with a significantly shorter postoperative stay compared to open surgery. Conversion to open operation was most frequent for empyema and carcinoma of gall bladder, suggesting that once this diagnosis is made, excessive time should not be spent in laparoscopic trial dissection before converting to an open operation.¹²

In the present study, 98 out of 105 cases (93.33%) were non-neoplastic and 7 out of 105 cases (6.67%) were neoplastic. This is in accordance with study by Bansode I and Baheti M1 (2019) who observed 98.6% cases (148 cases out of 150) to be non-neoplastic and 1.4% cases (2 out of 150) to be neoplastic. Kumbhakar D *et al.*13 (2016) also showed that out of 400 cholecystectomy cases, 395 cases (98.75%) were non-neoplastic and 5 cases (1.25%) were neoplastic. Out of the 3423 cholecystectomy specimens, Benkhadoura M *et al.*14 reported that 3417 (99.73%) cases were non neoplastic and 6 (0.17%) cases were neoplastic.

Chronic cholecystitis is a chronic condition caused by ongoing inflammation of the gallbladder resulting in mechanical or physiological dysfunction. It presents as a smoldering course that can be accompanied by acute exacerbations of increased pain (acute biliary colic), or it can progress to a more severe form of cholecystitis requiring urgent intervention (acute cholecystitis). The two forms of chronic cholecystitis are calculous (occurring in the setting of

cholelithiasis), and acalculous (without gallstones). However, most cases of chronic cholecystitis are commonly associated with cholelithiasis.¹⁵

In the present study, chronic cholecystitis with cholelithiasis was the most common histopathological diagnosis seen in 64.76% cases (68 out of 105). This finding is similar to study by Sharma I and Choudhary D *et al.*⁷ (2015) who showed that chronic calculous cholecystitis was the most frequent pathology seen in 86.2 % of cholecystectomy specimens. A study done by Ahadi M *et al.*⁶ in Iran showed the incidence of chronic calculous cholecystitis to be 61.18%. The second most common histopathological diagnosis in our study was chronic cholecystitis (acalculous) seen in 13.33% (14/105) cases. Ahadi M *et al.*⁶ (2020) reported incidence of chronic acalculous cholecystitis to be 3.72%.

In our study, choledochal cyst was identified as histopathological diagnosis in 5.71% of cases. In a histological evaluation of 400 cholecystectomy specimens by Kumar H *et al.*¹⁶ (2015), choledochal cyst amounted to 0.25% of all cases. In our study, there were 6 cases of choledochal cyst, of which 5 cases were in adults aged 21 to 38 years and 1 case in 17 year old female. All of them presented with the symptom of pain in abdomen. 5 cases were observed in female patients and 1 case was in a male patient (female: male ratio 5:1). A marked female preponderance has been widely recognized in literature too (female: male ratio 3:1).¹⁷ The predominant symptom was abdominal pain occurring in all patients. Choledochal cysts are rare disease, typically a surgical problem of infancy and childhood, but in nearly 20% of the patients the diagnosis is delayed until adulthood. The classical triad of jaundice, right upper quadrant mass, and abdominal pain is present in only a minority of patients (0–17%). It is more commonly seen in children than in adults, and 85% of children have at least two features of the triad at presentation, compared with only 25% of adults.¹⁸ The incidence of choledochal cyst in western population is 1 in 100 000–150 000 live births, whereas in Asian populations it has a higher incidence of 1 in 1000.¹⁹ Surgical excision i.e cholecystectomy is the main treatment modality for choledochal cyst.¹⁸

In our study, adenomyomatosis was observed in 3.81% cases. This is similar to a study by Benkhadoura M *et al.*¹⁴ (2019) who reported adenomyomatosis to be present in 2% of all cholecystectomy specimens. Study by Shah B and Degloorkar S *et al.*²⁰ (2018) showed that adenomyomatosis was present in 0.12% cases. Symptomatic adenomyomatosis is an indication for cholecystectomy, which results in complete disappearance of symptoms. A study of 360 cases by Khan S *et al.*³ at a teaching hospital in South Delhi showed 0.5% cases of adenomyomatosis. Asymptomatic adenomyomatosis is not an indication for surgery, but the radiological diagnosis must be beyond any doubt. If there is any diagnostic doubt about the possibility of gallbladder cancer, a cholecystectomy is justified.²¹

The present study demonstrated xanthogranulomatous cholecystitis to be present in 3.81 % of cases. This finding is similar to study by Khan S *et al.*³ (2013) who reported 3.6% cases of xanthogranulomatous cholecystitis. Also, in a retrospective study of 732 cholecystectomy cases by Awasthi N *et al.*²², 13 cases (1.8%) were diagnosed as xanthogranulomatous cholecystitis. The importance of recognizing this variant lies in the fact that they usually present with increased wall thickness and can mimic carcinoma on gross examination.²³ The incidence is slightly higher as compared to studies by Kumar H *et al.*¹⁶ (2015), Benkhadoura M *et al.*¹⁴ (2019) and Ahadi M *et al.*⁶ (2020) who showed xanthogranulomatous cholecystitis to be present in 0.5%, 0.1% and 0.4% respectively. This could be due to the underreporting by the pathologists as heavy lymphoid hyperplasia in the gallbladder wall is usually reported as chronic cholecystitis.³

Empyema was seen only in 1 case (0.95%). It was associated with cholelithiasis and choledocholithiasis. Multiple conglomerated stones were seen within the lumen of gall bladder. Frequently empyema of the gallbladder is associated with calculus cholecystitis, where there is an obstructed cystic duct and stasis of bile.²⁴ The statistics corresponds to most of the studies. In a retrospective study of 732 cholecystectomy cases by Awasthi N *et al.*²², 2 cases (0.3%) were reported to be of empyema. Similarly, Ahadi M *et al.*⁶ (2020) also reported empyema in 0.2% cases. Khan S *et al.*³ (2013) reported 0.5% in

their study, whereas Benkhadoura M et al.¹⁴ (2019) reported 1.4% cases of empyema in their study.

Out of 105 cases, mucocele was seen only in 1 case amounting to 0.95%. On histopathological analysis of 400 cholecystectomy specimens by Kumbhakar D et al.¹³, 2 cases (0.5%) were diagnosed as mucocele. Similar study by Kumar H et al.¹⁶ also showed mucocele to be present in 0.25% (1 out of 400) cases. Mucocele is most often not identified before surgery but is an incidental finding at the time of either laparoscopic or open cholecystectomy. This diagnosis is made when the gallbladder is surgically decompressed, and clear mucus-like fluid has replaced the green or brown bile.¹⁵

Out of 105 cases, adenoma was seen only in 1 case amounting to 0.95%. This is similar to study by Bansode I and Baheti M¹ (2019) who observed benign tumour adenoma to be present only in 1 case (0.7%) out of the 150 cholecystectomy specimens. Also, studies by Benkhadoura M et al.¹⁴ (2019) and Akbulut S et al.²⁵ (2020) where adenoma was reported in 0.1% and 0.05% of cases, respectively. Gallbladder adenoma is a relatively rare benign tumour with a potential for malignant transformation if found to be greater than 1 cm in size.²⁶

Adenocarcinoma was the only malignant tumour seen in 5.71% (6 out of 105) cases. Histologically, the most common carcinoma is adenocarcinoma NOS (80%) followed by papillary adenocarcinoma (4.5%). Other uncommon variants include intestinal type, mucinous, clear cell, signet ring, adenosquamous, squamous cell, small cell and undifferentiated carcinomas.¹⁶ The incidence of adenocarcinoma in our study is higher compared to studies by Bansode I and Baheti M¹ (2019), Kumbhakar et al.¹³, Khan S et al.³ and Siddiqui FG et al.⁹ who have reported incidence of adenocarcinoma as 0.7%, 1.25%, 2.2% and 2.8% respectively. All the 6 cases in our study were pre-operatively diagnosed as cancer or suspected to be cancer. No case of malignancy was diagnosed incidentally on histopathological examination. The gallbladder carcinoma is 5th most common gastrointestinal malignancy, detected in later stage of disease and has witnessed a high mortality due to high propensity for metastasis and poor efficacy of available interventions options. Gallbladder carcinoma has been found to be common in Indian population similar to the prevalence of gall

stone disease however it is reported to be rare in Western nations.²⁰ The incidence rate of gall bladder carcinoma in western countries is low (0.7 per 100 000) compared to the high rates in Asia (8.1 per 100 000). This geographic differences in tumour incidence are likely related to differences in genetic predisposition, environmental exposures to specific chemicals and regional intrinsic risk of carcinogenic factors that predispose to the cancer.²⁷ Northern part of India has witnessed more gall bladder stones and it is the most common gastrointestinal cancer in women. Surgery is the treatment of choice for patients with gallbladder cancer.²⁰

In the present study, the most common type of stone were pigment stones seen in 58.9% cases (43 out of 73) followed by cholesterol stones in 24.66% cases (18 out of 73), mixed stones in 16.43% cases (12 out of 73). This finding is in accordance with Srinivasan G et al.¹¹ who observed that the most common type of stones were pigment stones were 83.87% (26 out of 31) followed by mixed stones 9.67% (3 out of 31) and cholesterol stones 6.45% (2 out of 31). However, in contrast Ahadi M et al.⁶ observed that cholesterol stones (58.36%) are most common, followed by pigment stones (39.03%) then mixed stones (2.6%). Also, Mohan H et al.²⁸ reported that 62.3%, 17.3%, 14.1% and 3.2% were mixed, cholesterol, combined and pigment stones respectively.

In our study, normal wall thickness (< 3 mm) was seen in 79 cases (75.24%). Increased wall thickness (> 3 mm) was evident in 26 cases (24.76%). All 4 cases of xanthogranulomatous cholecystitis and all 4 cases of adenomyomatosis showed a thickened wall. Also, 1 case of adenocarcinoma, 2 cases of chronic cholecystitis and 15 cases of chronic cholecystitis with cholelithiasis showed thickened gall bladder wall. These findings are similar to that of Awasthi N et al.²² who also reported normal wall thickness (< 3 mm) in 72.8% (533 out of 732) cases and increased wall thickness (> 3 mm) in 27.2% (199 out of 732) cases. In contrast, Ahadi M et al.⁶ showed that the gall bladder thickness was normal in only 17.14 % of the cases, whereas 82.86% cases showed increased gall bladder thickness (> 3 mm)

Conclusion

The histopathological spectrum of gallbladder disease after cholecystectomy was found to be quite diverse. The most common histopathological diagnosis in

gallstone disease was chronic cholecystitis, which was associated with cholelithiasis.

Our study strongly recommends routine histopathological examination of all cholecystectomy specimens for detection of various gall bladder lesions and also gallbladder cancer which helps in their treatment and prognosis. Therefore, care must be taken to ensure adequate and immediate fixation of specimen accompanied by meticulous macroscopic and microscopic evaluation by the pathologist.

Histopathology not only establishes a tissue diagnosis in gallstone disease, but also contributes towards understanding its etiopathogenesis and can help in planning the future treatment modality.

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