

## Original Research Paper

## Study of histopathological spectrum of gallbladder diseases

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**ABSTRACT:**

Introduction: Gallbladder diseases are one of the most common surgical problems encountered on a routine basis. The spectrum of gallbladder histopathology is diverse ranging from acute or chronic inflammation to metaplasia and even malignancies. The aim of this study was to analyse the histopathological spectrum of gallbladder diseases at a tertiary care hospital in Navi Mumbai. Materials and Methods: This is a retrospective study of 471 cholecystectomy specimens received in histopathology section of Department of Pathology over a period of 5 years from January 2016 to December 2020 at MGM Medical College and Hospital, Navi Mumbai. Clinical details of the patient including age and sex along with other relevant clinical findings were taken from the requisition forms received with the surgically resected cholecystectomy specimens. Results: There were total 471 cases consisting of 280 (59%) females and 191 (41%) males. Maximum number of patients were in the 3<sup>rd</sup> and 4<sup>th</sup> decades of life (52.6%). Most common pathology noted in our study was Chronic calculous cholecystitis seen in 280 cases (59.4%). Other benign lesions that were reported were chronic acalculous cholecystitis (33.1%), acute on chronic cholecystitis (4%), xanthogranulomatous cholecystitis (0.6%) and acute cholecystitis (0.4%). One case each of follicular cholecystitis, acute suppurative cholecystitis, subacute cholecystitis, eosinophilic cholecystitis and acute gangrenous cholecystitis were also noted. Three cases of choledochal cysts were observed along with 2 cases of intestinal metaplasia and one case of adenocarcinoma of gallbladder. Conclusion: Almost all of the gallbladder lesions were inflammatory in origin with Chronic Calculous Cholecystitis being the most common. However, a small percentage of patients had congenital defects, pre-malignant and malignant lesions. Hence, thorough and detailed histopathological examination of all cholecystectomy specimens is of utmost importance.

**Keywords:** gallbladder disease, cholecystectomy, histopathology

**INTRODUCTION:**

The gallbladder is a pear shaped sac that lies in a shallow depression on the inferior surface of right hepatic lobe. Gallstone diseases are prevalent worldwide and present with a diverse clinical and histopathological spectrum. Gallbladder is one of the most frequently received specimens in any histopathology laboratory and its diseases may present with a varied spectrum ranging from congenital anomalies, cholelithiasis, inflammatory and non-inflammatory lesions to non-invasive and invasive neoplasms. Cholelithiasis is one of the most common gastrointestinal diseases affecting 10-20% of adult population. The incidence is 2-4 times higher in females than in males. The risk of gallstones is associated with increased body weight, childbearing and oestrogen. Laparoscopic cholecystectomy is the treatment of choice done routinely for gallstone disease. Most common diagnosis in a cholecystectomy specimen is chronic cholecystitis. Other benign changes seen are acute inflammation, cholesterosis, metaplasia and hyperplasia. Gallbladder carcinoma is a rare malignancy with overall poor prognosis especially

if diagnosed late in the course of the disease, hence, detailed histopathological examination of every cholecystectomy specimen is of utmost importance. The purpose of this study was to determine the histopathological spectrum of gallbladder lesions in cholecystectomy specimens at a tertiary care hospital in Navi Mumbai.

**MATERIAL AND METHODS:**

This was a five year retrospective study conducted at Central Laboratory, MGM Hospital, Navi Mumbai during the period of January 2016 to December 2020. Patients of all ages were considered in the study. Clinical details of the patient including age and sex along with other relevant clinical findings were obtained from the requisition forms received at histopathology section of the Central Laboratory. Gallbladder specimens were received in 10% buffered formalin and processed under routine histopathology techniques. All specimens were subjected to gross and microscopic examination. Three full thickness sections from the fundus, body and neck of gallbladder were studied for each case. Additional sections were cut

from the paraffin blocks and then stained with Haematoxylin and Eosin stain and examined microscopically.

**RESULTS:**

Total 471 cholecystectomy specimens were included in the present study. The age of patients ranged from 2 to 80 years, with the maximum number of patients being in the range of 31 to 50 years (52.6%) (Table 1). There were 192 (41%) males and 279 (59%) females with a M:F ratio of 1:1.4 (Chart / Fig 1).

Age group (years)	Male	Female	Total
<10	0	3	3
10-20	5	8	13
21-30	23	47	70
31-40	41	83	124
41-50	53	71	124
51-60	32	39	71
61-70	30	22	52
71-80	7	7	14
	191	280	471

Table 1: Age and sex distribution of patients with gallbladder diseases

**GENDER DISTRIBUTION**

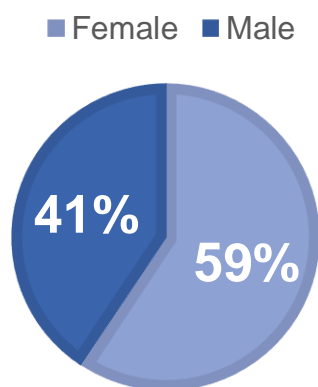


Chart / Fig. 1: Pie chart showing gender distribution (n=471)

Histopathologically the most common diagnosis was chronic calculous cholecystitis (280/471; 59.4%) followed by chronic acalculous cholecystitis (156/471; 33.1%) (Table 2). 19 specimens (4%) were diagnosed with acute on chronic cholecystitis and 3 specimens (0.6%) each of xanthogranulomatous cholecystitis and choledochal cyst. 2 specimens (0.4%) were diagnosed

as cholecystitis with metaplastic changes and 2 specimens (0.4%) as acute cholecystitis. One case each of chronic follicular cholecystitis, acute suppurative cholecystitis, subacute cholecystitis, acute gangrenous cholecystitis and eosinophilic cholecystitis was reported. One specimen (0.2%) was diagnosed as adenocarcinoma of gallbladder. None of the patients

had pre-operative diagnosis of malignancy. Out of the 471 cases we studied, non-neoplastic lesions constituted 468 cases (99.4%), pre-malignant lesions were reported in 2 cases(0.4%) and neoplastic lesion

constituted 1 case (0.2%). The most common gallbladder pathology observed was Chronic Calculous Cholecystitis (59.4%) followed by acalculous cholecystitis (33.1%).

Histopathologic Diagnosis	No. of cases	Percentage
Chronic calculous cholecystitis	280	59.4
Acalculous cholecystitis	156	33.1
Acute on chronic cholecystitis	19	4
Xanthogranulomatous cholecystitis	3	0.6
Choledochal cyst	3	0.6
Acute cholecystitis	2	0.4
Metaplasia (Pre-malignant lesion)	2	0.4
Chronic follicular cholecystitis	1	0.2
Acute suppurative cholecystitis	1	0.2
Subacute cholecystitis	1	0.2
Acute gangrenous cholecystitis	1	0.2
Eosinophilic cholecystitis	1	0.2
Adenocarcinoma	1	0.2

**Table 2 : Histopathology findings in Cholecystectomy specimens ( n=471).**

## DISCUSSION:

Gallbladder is an organ which has a wide spectrum of diseases afflicting it, which can be congenital anomalies, inflammatory and non-inflammatory lesions and neoplasia<sup>1</sup>. Hence, detailed analysis and histopathological examination of gallbladder lesions is important to differentiate between non-neoplastic and neoplastic disease entities. The estimated prevalence of gallstone disease in India is reported between 2% and 29% among which inflammatory conditions of the gallbladder are noted to be more common than other gallbladder pathologies. The prevalence of gallbladder carcinoma is less in general population, it still accounts for 80% of all biliary tract cancers and is the 5<sup>th</sup> most common gastrointestinal malignancy in India following colon, pancreas, stomach and esophagus<sup>2</sup>. Due to its silent course and late presentation, it has a poor prognosis and decreased five-year survival rate. Some of the risk factors for development of gallbladder diseases and carcinoma are obesity, reproductive factors, genetic factors, life style risk factors (smoking, alcohol consumption), chronic infections of the gallbladder, gallstones, exposure to certain chemicals and environmental factors<sup>3,4</sup>. Hence, histopathological examination of all gallbladder

specimens is of utmost necessity in order to rule out pre-malignant and malignant conditions. In the present study, a female predominance amongst the patients suffering from gallbladder disease was observed with a male to female ratio of 1:1.4. This is in accordance with similar studies carried out in different regions of the country namely; Mushtaq et al<sup>5</sup> reported a M:F ratio of 1:2.8, Khan et al<sup>6</sup> 1:4.7, Beena et al<sup>7</sup> 0.86:1 and Kotasthane et al<sup>8</sup> 1:4. Another study conducted in the neighbouring country of Pakistan by Almas et al<sup>9</sup> reported similar findings with a male to female ratio of 1:3. Out of 471 cases included in this study, 468 were inflammatory (non-neoplastic lesions), 2 were pre-malignant lesions and one was reported as malignancy. 280 cases were reported as chronic calculous cholecystitis which account for 59.4% of the total sample size. Other non-neoplastic lesions were chronic acalculous cholecystitis (33.1%), acute on chronic cholecystitis (4%), xanthogranulomatous cholecystitis and acute cholecystitis (0.4%). 3 cases were reported as choledochal cyst (0.6%) which is a congenital anomaly. There was one case each of chronic follicular cholecystitis, acute suppurative cholecystitis, acute gangrenous cholecystitis, subacute cholecystitis and eosinophilic cholecystitis. 2 cases (0.4%) were



reported to have pre-malignant lesions in the form of intestinal metaplasia. One case of adenocarcinoma of

gallbladder was reported in our study.

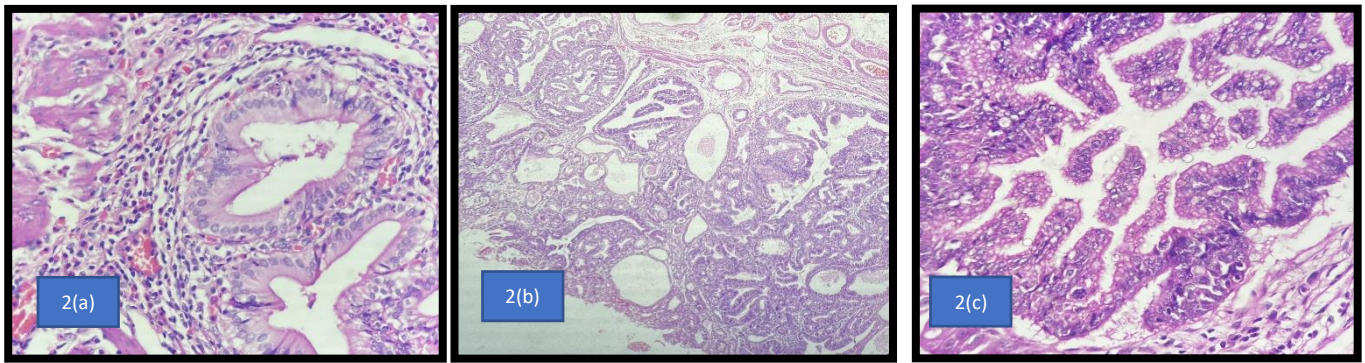


Fig 2: (a) Eosinophilic cholecystitis (b) &(c) Adenocarcinoma of gallbladder, low and high power view.

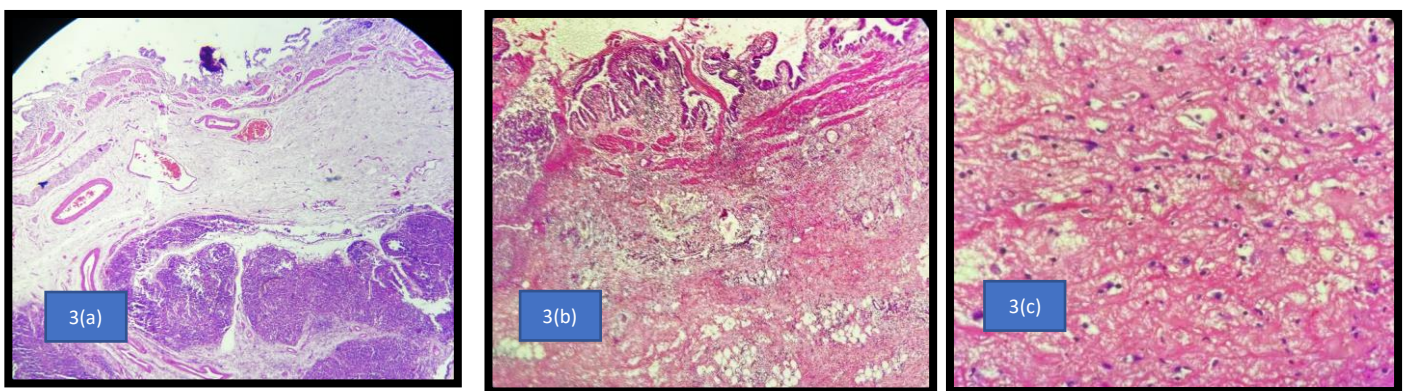


Fig 3: 3(a) Follicular Cholecystitis. Low power view showing diffuse involvement of gallbladder wall by lymphoid aggregates with reactive germinal centers. 3(b) and (c) Xanthogranulomatous cholecystitis (b) Low power view showing transmurial inflammation comprising of lymphocytes, plasma cells and neutrophils along with proliferative fibrosis (c) Lipid laden foamy macrophages on a background of chronic inflammation, High power view.

Mushtaq et al<sup>5</sup> reported that out of 360 specimens studied, 225 specimens (62.5%) showed chronic calculous cholecystitis, 45 (12.5%) showed acute on chronic cholecystitis, 42 (11.6%) showed cholesterolosis, 15 specimens (4.1%) showed empyema, 12 (3.3%) showed follicular cholecystitis, 9 (2.5%) showed xanthogranulomatous cholecystitis, 6 (1.6%) showed eosinophilic cholecystitis and 6 cases (1.6%) showed neoplastic lesions of the gallbladder. Memon et al<sup>10</sup> reported a total of 282 specimens, out of which 183 (64.8%) were reported as chronic cholecystitis, 89 (31.5%) reported as acute calculous cholecystitis, 4 cases (1.4%) of adenocarcinoma and gall bladder polyp each and 2 cases (0.7%) of acute acalculous cholecystitis. Khan et al<sup>11</sup> studied 197 cholecystectomy specimens, out of which 126 (63.9%) showed chronic calculous cholecystitis, 37 cases (18.7%) showed chronic acalculous cholecystitis, 21 cases (10.6%) showed chronic cholecystitis with cholesterolosis, 11 cases (5.5%) showed

xanthogranulomatous cholecystitis and 2 cases (1%) of adenocarcinoma of gallbladder. Mondal et al<sup>12</sup> studied 786 gallstone disease patients and divided the histopathological findings into non-neoplastic, pre-malignant and malignant lesions. They reported that chronic calculous cholecystitis was most prevalent (79.8%) followed by acute on chronic cholecystitis (6.1%), cholesterolosis (2.9%) and xanthogranulomatous cholecystitis (1.7%) among the patients. Beside these, hyperplasia, metaplasia, dysplasia and gallbladder carcinoma were observed in 2.0%, 4.7%, 2.2% and 0.6% of the patients respectively. They concluded that there is an association between gallstone disease and gallbladder carcinoma. In our study, it was observed that 2 cases showed pre-malignant changes in the form of intestinal metaplasia along with chronic calculous cholecystitis.

HP lesions	Present study	Mushtaq et al	Memon et al	Khan et al	Mondal et al
Chronic calculous cholecystitis	59.4%	62.5%	64.8%	63.9%	79.8%
Chronic cholecystitis	33.1%	-	31.5%	18.7%	-
Acute on chronic cholecystitis	4%	12.5%	-	-	6.1%
Xanthogranulomatous cholecystitis	0.6%	2.5%	-	5.5%	1.7%
Chronic cholecystitis with choledochal cyst	0.6%	-	-	-	-
Acute cholecystitis	0.4%	-	0.7%	-	-
Chronic follicular cholecystitis	0.2%	3.3%	-	-	-
Acute suppurative cholecystitis	0.2%	4.16%	-	-	-
Subacute cholecystitis	0.2%	-	-	-	-
Acute gangrenous cholecystitis	0.2%	-	-	-	-
Eosinophilic cholecystitis	0.2%	1.6%	-	-	-
Chronic cholecystitis with intestinal metaplasia	0.4%	-	-	-	4.7%
Adenocarcinoma of gallbladder	0.2%	1.6%	1.4%	1%	0.6%

Table 3: Comparison of histopathological spectrum of lesions

There were three cases of chronic cholecystitis with choledochal cysts all of which were observed in female patients with age ranging from 2 years to 29 years. Choledochal cysts are uncommon congenital anomalies of the bile duct with increased risk of malignancy which increases with age, supposed to be 0.7% in the first decade of life to 14.3% after 20 years of age<sup>13</sup>. Literature reporting cases of choledochal cysts associated with gallbladder disease is scarce. Lien et al<sup>14</sup> reported a case of 7 year old female with choledochal cyst associated with acute perforated acalculous cholecystitis. They postulated that the congenital defect lead to biliary stasis, which in turn induced the acalculous cholecystitis. In our study, we observed female preponderance in gallbladder diseases with majority of cases reported as chronic calculous cholecystitis. Two cases showed metaplastic changes in male patients along with a single case of gallbladder carcinoma. Mondal et al<sup>6</sup> found in their study that proportion of male patients was significantly higher in the development of pre-malignant and malignant conditions. Similar findings were reported by Alvi et al<sup>15</sup> who observed that males were comparatively dominant in gallbladder cancer group of gallstone patients.

#### CONCLUSION:

The histopathological spectrum of gallbladder diseases is vast and varies from inflammatory to infectious to pre-malignant and malignant lesions. The most common histopathological diagnosis is chronic calculous and acalculous cholecystitis and its variants which include xanthogranulomatous, follicular and eosinophilic type. Three cases of congenital defect of choledochal cyst were also noted. Pre-malignant and malignant lesions included intestinal metaplasia and adenocarcinoma respectively. Females are more prone to gallbladder diseases in general but males have higher prevalence of pre-malignant and malignant lesions of gallbladder. Thus, there is a need for routine histopathological examination of all cholecystectomy specimens in order to rule out pre-malignant and incidental malignant lesions.

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