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# **Original Research Article**

# Study of histopathological spectrum of lesions of gall bladder with clinico radiological correlation

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#### ABSTRACT

**Background:** The gallbladder is frequently affected by a spectrum of diseases, ranging from benign inflammatory conditions to aggressive malignancies. Histopathological examination is the cornerstone of diagnosing gallbladder diseases, providing detailed insights into the cellular and tissue-level changes that occur in various conditions. However, the diagnostic process is significantly enhanced when histopathological findings are correlated with clinical and radiological data. Such a multidisciplinary approach not only improves diagnostic accuracy but also improves treatment strategies, leading to better patient outcomes.

This study aims to investigate the histopathological spectrum of gallbladder lesions and to establish correlations with clinic-radiological findings, thereby advancing the understanding of gallbladder pathology and its management.

Aim and Objectives: To study the histopathological spectrum of lesions of gall bladder with clinic radiological correlation

**Result:** The most common histopathological diagnosis was chronic non specific cholecystitis with cholelithiasis seen in 48 cases out of 100 cases (48%). Total 70 cases out of 100 (70%) were calculous out of which 65.71% cases were of chronic cholecystitis, 24.28% cases were of acute cholecystitis and 10% cases were of gall bladder carcinoma with n=70. Out of 100 cases, 90% cases had mixed stones, 7.15% cases had cholesterol stones and 2.85% cases had pigment stones.

There were 7 cases (7%) of gall bladder carcinoma amongst 100 cases. All 7 cases were of adenocarcinoma of the gall bladder out of which 2 cases showed serosal invasion and infiltration.

**Conclusion:** Multidisciplinary approach is required in the diagnosis and management of gall bladder diseases, integrating clinical, radiological and histopathological findings to ensure accurate diagnosis. Each and every cholecystectomy specimen must be sent for histopathological examination and studied meticulously, as some unusual findings bearing implications on treatment and prognosis may be seen, regardless of the reason for which cholecystectomy is performed.

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### 1. Introduction

The gall bladder is a foregut organ affected by a wide range of pathological diseases, including cholelithiasis, inflammatory lesions, pre-malignant lesions and malignant lesions. <sup>1</sup>

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Cholelithiasis is the predominant condition, constituting over 95% of all gallbladder diseases. Gall Bladder Carcinoma (GBC) exhibits regional disparities within the country. The cancer data of studies from northern India showed GBC accounting for 9.6% of all cancers in females and was the third leading site of cancer whereas studies from eastern India recorded gall bladder cancer between 5.8% to 6.0% of all cancers. <sup>2</sup>

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Histopathological examination has traditionally been a cornerstone of diagnostic procedures, alongside the increasingly recognized value of clinical and radiological correlation being valuable diagnostic tools. Various imaging techniques are utilized to evaluate the gallbladder diseases. Ultrasound has traditionally been the preferred initial method for suspected gallbladder issues, with computed tomography increasingly employed. Magnetic resonance imaging serves as a problem-solving tool. Advancements like contrast-enhanced ultrasound and advanced MRI sequences enhance diagnostic accuracy, aiding in distinguishing between benign and malignant gallbladder conditions. <sup>3</sup>

Laboratory workup such as complete blood count, liverfunction testing, serum cholesterol levels, random blood sugar levels etc should be included to help distinguish the etiology of gall bladder diseases and identify associated complications.<sup>4</sup>

For accurate diagnosis of gallbladder diseases, histopathological examination is considered the gold standard method. Histopathological studies influence treatment decisions, prognosis, and patient outcomes. Thereby, using both traditional and modern diagnostic procedures, medical practitioners can perform appropriate surgical procedures to improve patient survival rates and prognosis of the patients.

## 2. Aim and Objectives

To study the histopathological spectrum of lesions of gall bladder with clinicoradiological correlation

## 3. Material and Methods

### 3.1. Source of data

This was a cross sectional study carried out a tertiary care hospital, conducted over a period of 24 months from July, 2022 to June, 2024. Thus, it included 100 cholecystectomy specimens.

## 3.2. Inclusion criteria

All surgically resected gall bladder specimens that were received in the histopathology section of the Department of Pathology from July, 2022 to June, 2024 were included.

## 3.3. Exclusion criteria

There were no exclusion criteria in this study

## 3.4. Method of data collection

The specimens were collected in 10% formalin following scrutiny and confirmation of patient details and identity. Overnight fixation in formalin was carried out. Gross examination of the specimens were done. Bits from one

representative full thickness section from the fundus, one through the body, one through neck of the gall bladder and one cross section of the cystic duct margin were taken. Additional sections were taken when focal lesions were present. They were followed by routine paraffin processing.

### 4. Result

The study included a total of 100 prospective cases of cholecystectomy specimens of two years from July 2022 to June 2024. Out of 100 cholecystectomies, 82 were performed laparoscopically (82%), while 18 cases (18%) underwent open laparotomy cholecystectomies.

Maximum number of patients were in the age group of 61-70 years of age (25%) followed by 51-60 years of age (19%). Maximum patients were females comprising a total of 54 cases out of 100 (54%) and remaining 46 cases were male (46%). Females were common in the age group of 31-40 years of age (21.82%). Males were common in the age group of 61-70 years of age (33.33%).

Mean age of patient was 54 years. Oldest patient was 81 years old and youngest patient was 15 years old.

In the present study, 62 cases (62%) were non-vegetarian, 37 cases (37%) were vegetarian and 1 case (1%) was eggetarian.

The most common clinical presentation in cholecystectomy cases was abdominal pain noted in 87 cases out of total 100 cases (87%). The most prevalent weight category was between 51-60 kg, accounting for 35% of the total cases. Mean body weight was 61 kg. Minimum weight was 39 kg. Maximum weight was 88 kg. Average BMI of patients in study was 25.22 kg/m² and was higher which was statistically significant with Odds Ratio of 1.21.

Random blood sugar was performed in all 100 patients, out of which diabetic patients constituted 20 cases (20%). Diabetes proved to be an important risk factor for development of gall bladder diseases with statistically significant Odds Ratio (2.49). TLC was performed in all 100 cases. Higher values of Total Leucocyte count were noted in 67/100 cases (67%). Serum cholesterol levels were performed in all 100 cases. Higher values of serum cholesterol levels were noted in 5 cases (5%). Serum bilirubin levels were performed in all 100 cases. Higher values of serum bilirubin were noted in a total of 12 cases (12%). Amongst 12 cases, 10 cases (83.33%) with elevated serum bilirubin levels showed gall stones whereas 2 cases (16.66%) did not reveal the presence of gall stones. Serum Alkaline Phosphatase levels were performed in 27 cases only out of 100 and was raised in 14 out of 27 cases (51.85%).

Out of total 100 cases, 42 patients (42%) were chronic alcoholics. Amongst the 42 cases of alcohol consuming patients, 35 patients were male (83.33%) and 7 patients were female (16.66%). Amongst the 42 cases of alcohol consuming patients, 5 patients had deranged liver function

test values (11.90%). Positive association of gall stones with history of chronic alcohol consumption was noted in cholecystectomy patients with Odds Ratio of 3.11.

Chronic non-specific cholecystitis with cholelithiasis was the most common histopathological diagnosis condition with 48 cases out of 100 (48%).

Majority cases showed the presence of mixed gall stones. Ultrasonography successfully detected cases of chronic cholecystitis and acute cholecystitis but out of a total of 7 cases of gall bladder carcinoma, ultrasonography diagnosed neoplastic etiology in only 6 cases and 1 case was diagnosed incidentally on histopathological examination. Carcinoma of the gall bladder comprised a total of 7 cases (7%) in the present study. All 7 cases (100%) were of adenocarcinoma of the gall bladder. Amongst the 7 cases of adenocarcinoma of the gall bladder, 2 cases (28.57%).

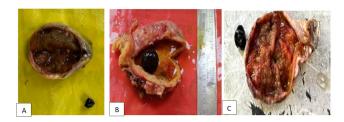


Figure 1: A-C): Shrunken, contracted gall bladders with chronic calculous cholecystitis with mixed stone



Figure 2: A, B): Chronic cholecystitis with cholelithiasis with cholesterol stone

Table 1 showed Chronic non-specific cholecystitis with cholelithiasis, the most common condition with 48 cases followed by Acute Acalculous cholecystitis, constituting 23 cases. Carcinoma of the gall bladder comprised a total of 7 cases.

Out of 100 cases, 7 cases (7%) were of gall bladder carcinoma.

- 1. Youngest patient was 37 years old and oldest patient was 75 years old.
- 2. On ultrasonography, case 6 was diagnosed as Chronic Calculous Cholecystitis, pointing towards inflammatory etiology of the gall bladder.

**Table 1:** Distribution of cholecystectomy specimens according to histopathological diagnosis

| Type of pathology   | No. of cases | Percentage |
|---|--------------|------------|
| Chronic non-specific cholecystitis with cholelithiasis          | 48           | 48%        |
| Chronic non-specific cholecystitis                              | 6            | 6%         |
| Acute on chronic non-specific cholecystitis with cholelithiasis | 4            | 4%         |
| Acute acalculous cholecystitis                                  | 23           | 23%        |
| Adenocarcinoma of the gall bladder                              | 7            | 7%         |
| Gangrenous cholecystitis with peritonitis                       | 7            | 7%         |
| Adenomatous hyperplasia of gall bladder                         | 1            | 1%         |
| Xanthogranulomatous cholecystitis                               | 1            | 1%         |
| Gall bladder adenoma  | 1            | 1%         |
| Eosinophilic cholecystitis                                      | 1            | 1%         |
| Cholecystitis Follicularis                                      | 1            | 1%         |
| Total   | 100          | 100%       |

**Table 2:** Comparison of radiological diagnosis with histopathological diagnosis

# Radiological Histopathological diagnosis diagnosis

Ultrasonography; features suggestive of cholecystitis – 87/100 cases 86/100 cases could correlate with radiological and histopathological diagnosis of Cholecystitis. This included acute and chronic calculous as well as acalculous cholecystitis. However, histopathological examination could detect 1 case of Incidental Gall Bladder Carcinoma (Moderately differentiated adenocarcinoma of gall bladder – Biliary type) in a patient radiologically diagnosed as Cholecystitis.

Ultrasonography; Wall thickening, heterogenous lesion, suggestive of neoplastic etiology – 6/100 cases All 6 cases could correlate with radiological and histopathological diagnosis of Neoplastic etiology viz Carcinoma of the gall bladder. A single case missed by Ultrasonography and diagnosed radiologically as Cholecystitis was detected by Histopathological examination as Incidental Gall bladder carcinoma (Moderately differentiated adenocarcinoma of gall bladder – Biliary type)

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| Case 7 37 female ce Weight loss and loss of apetite since 1 year    | USG – thinned out mural wall, heterogenous lesion, suggestive of neoplastic etiology. Evidence of calculi, sludge, pericholecystic fluid.    | TLC 3500/ cumm, Random BSL 110 , mg/dl, Serum rol cholesterol 120 mg/dl,Total serum bilirubin 0.8 mg/dl                                | ar Perforated area at body all of gall bladder, numerous mixed pigment stones, grey white mass at fundus region of gall bladder. | 1  | Deceased        |
|---|--|--|--|--|-----------------|
| Case 6 75 female Weight loss since 3 months                         | USG - F/S/O<br>Cholecystitis   | TLC 23000/<br>cumm, Random<br>BSL 110 mg/di,<br>Serum cholesterol<br>120 mg/di, Total<br>serum bilirubin<br>0.8 mg/dl                  | Diffuse, irregular<br>thickening of wall<br>at the fundic<br>region of the gall<br>bladder.                                      | Moderately differentiated adenocarcinoma Biliary type, tumor was seen infiltrating upto serosa | Improved        |
| Case 5 37 female Weight loss since 1 year                           | USG – Cholecystiis with wall thickening of gall bladder, suggestive of neoplastic etiology   | TLC 21540/<br>cumm, Random<br>BSL 107 mg/di,<br>Serum cholesterol<br>156 mg/dl, Total<br>serum bilirubin<br>0.8 mg/dl                  | Grey white nodular mass in fundus of gall bladder, notable thickening of wall of sall bladder.                                   | Well<br>differentiated<br>adenocarcinoma   | Improved        |
| Case 4 65 female Loss of weight and loss of apetite since 2 months. | USG- Heterogenous lesion with wall thickening, suggestive of neoplastic etiology. Evidence of small calculi and sludge in lumen, wall edema. | TLC 11250/<br>cumm, Total<br>serum bilirubin<br>0.6 mg/dl,<br>Random 110<br>mg/dl, Serum<br>cholesterol 220<br>mg/dl                   | Irregular grey<br>white tumor on<br>cut section.   | Moderately<br>differentiated<br>adenocarcinoma<br>- Biliary type                               | Improved        |
| Case 3 45 female Weight loss since 3 months.                        | USG - Wall<br>thickening of gall<br>bladder, shows<br>exophytic mass,<br>along with<br>cholecystitis   | TLC 11200/ cumm, Total serum bilirubin 1.1 mg/dl, Serum cholesterol 176 mg/dl, Random BSL 111 mg/dl, ALP 49/ IU/L                      | Exophytic growth<br>arising from<br>fundus of gall<br>bladder  | Moderately<br>differentiated<br>adenocarcinoma -<br>Biliary type                               | Improved        |
| Case 2 50 female Weight loss since 4 months.                        | USG- Cholecystits with intramural growths in gall bladder in fundus and body region, suggestive of carcinoma.                                | TLC 11000/<br>cumm, BSL 105<br>mg/dl, Total<br>serum bilirubin<br>1.3 mg/dl, Serum<br>cholesterol 167<br>mg/ dl, ALP 250/<br>IU/L      | Diffuse, nodular growth arising from fundus of gall bladder.   | Biliary type -<br>Moderately<br>differentiated<br>adenocarcinoma                               | Improved        |
| Case 1 56 male Weight loss since 2 months.                          | USG – Cholecystitis with wall thickening of gall bladder, suggestive of neoplastic etiology.   | TLC 10280/<br>cumm, Total<br>serum bilirubin 1.2<br>mg/dl, Random<br>BSL 110 mg/dl,<br>Serum cholesterol<br>181 mg/dl, ALP<br>50/ IU/L | Infiltrating,<br>irregular grey<br>white tumor,<br>evidence of wall<br>thickening.   | Clear cell<br>adenocarcinoma -   | Improved        |
| Age and sex<br>Clinical presentation                                | Radiological findings  | Lab findings   | Gross appearance   | Histopathological<br>diagnosis   | Patient outcome |

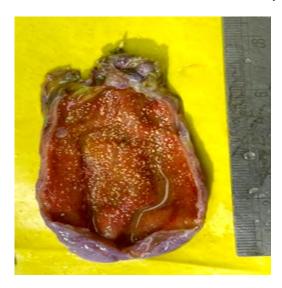


Figure 3: Strawberry gall bladder

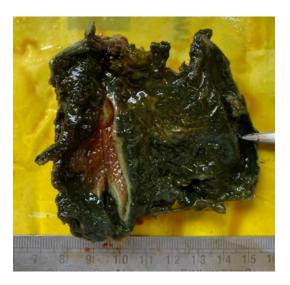


Figure 4: Gangrenous gall bladder

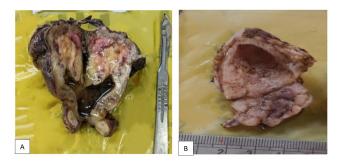
3. Case 6 on gross examination of the specimen of gall bladder revealed a diffuse, irregular thickening at the fundic region of the gall bladder. Microscopically, it showed Moderately differentiated adenocarcinoma – Biliary type, tumor was seen infiltrating upto serosa thus highlighting the importance of histopathological examination for all routine cholecystectomy specimens.

## 5. Discussion

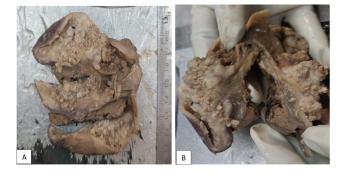
Findings of age and gender distribution were in concordance with studies of Mondal B et al,<sup>6</sup> Dattal DS et al.,<sup>7</sup> Agrawal R et al.,<sup>8</sup> Almas T et al.,<sup>9</sup> with having female preponderance amongst gall bladder diseases.



**Figure 5:** Clinically and radiologically diagnosed as a case of Chronic cholecystitis showing diffuse thickening at fundic region of gall bladder. Gall bladder carcinoma was diagnosed incidentally on histopathological examination, thus highlighting the importance of microscopic examination for all routine cholecystectomy specimens



**Figure 6:** Gall bladder carcinoma specimens with diffuse gall bladder wall thickening and grey white tumor on cut section

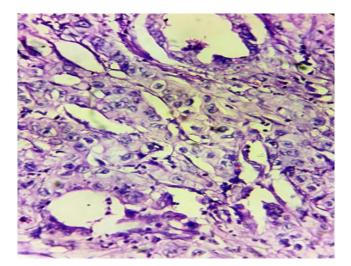


**Figure 7: A, B**): Gall bladder carcinoma specimen with ulceroinfiltrative growth replacing body and neck of gall bladder and infiltrating serosa

Cholecystitis Follicularis

| Type of pathology   | Kotasthane et al, <sup>2</sup> 2020 | Savanur et al, <sup>5</sup> 2022 | Present study, 2024 |
|---|-------------------------------------|----------------------------------|---------------------|
| Chronic non-specific cholecystitis with cholelithiasis          | 63.26%                              | 55%                              | 48%                 |
| Chronic non-specific cholecystitis                              | 10%                                 | 4.4%                             | 6%                  |
| Acute on chronic non-specific cholecystitis with cholelithiasis | 1.16%                               | 4%                               | 4%                  |
| Acute acalculous cholecystitis                                  | 13.95%                              | 33%                              | 23%                 |
| Adenocarcinoma of the gall bladder                              | 2.33%                               | 0.2%                             | 7%                  |
| Gangrenous cholecystitis with peritonitis                       | 1.16%                               | 0.2%                             | 7%                  |
| Adenomatous hyperplasia of gall bladder                         | -                                   | 0.4%                             | 1%                  |
| Xanthogranulomatous cholecystitis                               | 2.33%                               | 0.6%                             | 1%                  |
| Gall bladder adenoma  | -                                   | 0.6%                             | 1%                  |
| Eosinophilic Cholecystitis                                      | -                                   | 0.2%                             | 1%                  |

**Table 4:** Comparison of distribution of different types of gall bladder pathologies



**Figure 8:** Photomicrograph showing clear cell adenocarcinoma of the gall bladder (400 X H&E)

Gall bladder diseases are more common in non-vegetarian than in vegetarian patients. In the present study, 62% patients were non vegetarian. Findings were in concordance with study of Srinivasan AC et al., <sup>10</sup> wherein patients consuming a mixed diet were predominant.

Average BMI in this study was 27.81 kg/m<sup>2</sup>. Average BMI in study for gall bladder diseases patients was higher than average BMI of normal population which was statistically significant by higher odds ratio. Findings of high BMI in gall bladder diseases patients were in concordance with study of Wegene Borena et al., 2014, <sup>11</sup> Yen Chun Chen et al, 2014 <sup>12</sup> and Dara Jokhi C et al, 2019. <sup>13</sup>

The commonest clinical presentation of patients was abdominal pain followed by associated complaint of vomiting. Most common finding of pain was in concordance with other studies done by Festi D et al., 2008, <sup>14</sup> Pradhan SB et al., 2009, <sup>15</sup> Siddique et al., 2013, <sup>16</sup> Yaser Froutan et al., 2015, <sup>17</sup> Sangma MMB et al, 2016. <sup>18</sup>

Significant number of patients with gall bladder disease had higher total leucocyte count, serum bilirubin levels and serum alkaline phosphatase levels. Levels of serum bilirubin were raised in a total of 12 cases out of 100 (12%).

1%

0.2%

- 1. Amongst the 12 patients who showed raised serum bilirubin values, 10 patients showed the presence of gall stones (83.33%, where n = 12).
- 2. 2 patients with raised serum bilirubin levels did not show the presence of gall stones (16.67%, n = 12).

These findings of present study were in concordance with study conducted by Dara Jokhi C et al., 2019. <sup>13</sup>

Present study noted increased incidence of gall bladder diseases in diabetic patients. Present study findings were in concordance with studies conducted by Festi et al., 2008, <sup>14</sup> Yaser Froutan et al., 2015, <sup>17</sup> Dara Jokhi C et al., 2019. <sup>13</sup>

Present study showed alcohol as a causative factor in occurrence of gall bladder disease and this finding was in concordance with study of Rodriguez, Antonio et al., <sup>19</sup> Study conducted by Byung Hyo Cha et al., <sup>20</sup> showed that there is an increased incidence of gall stone formation if person is a chronic alcoholic. In present study, amongst the 42 cases of alcohol consuming patients, positive association of gall stones with history of chronic alcohol consumption was noted in cholecystectomy patients.

In present study, out of total 100 cases, 70 cases (70%) showed the presence of gall stones. These findings were in concordance with study conducted by Devi Beena et al., 2017.<sup>21</sup>

In present study, out of total 100 cases, 54 cases (54%) were of chronic cholecystitis. Out of 54 cases, 48 were or chronic cholecystitis with cholelithiasis while 6 cases were of chronic non- specific cholecystitis without the presence of gall stones. Findings were in concordance with study conducted by Savanur et al., 2022.<sup>5</sup>

Distribution of various types of pathologies showed chronic cholecystitis with cholelithiasis (48%) as most

common histopathological diagnosis. Findings were in concordance with studies conducted by Kotasthane et al., 2019, <sup>2</sup> Savanur et al., 2022. <sup>5</sup>

In the present study, 100% of the gall bladder carcinoma cases were of adenocarcinoma of the gall bladder. Findings were in concordance with studies conducted by Dara Jokhi C et al., 2019. <sup>13</sup>

### 6. Conclusion

Multidisciplinary approach is required in the diagnosis and management of gall bladder diseases, integrating clinical, radiological and histopathological findings to ensure accurate diagnosis. Each and every cholecystectomy specimen must be sent for histopathological examination and studied meticulously, as some unusual findings bearing implications on treatment and prognosis may be seen, regardless of the reason for which cholecystectomy is performed.

# 7. Ethical Approval

This study was conducted after taking approval from the institute Ethical review board, ref. no. KIMSDU/IEC/07/2022.

## 8. Source of Funding

None.

## 9. Conflict of Interest

None.

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