

# Evaluation of Routine Cholecystectomy Specimens for Incidental Precancerous and Malignant Lesions

Rabia Nazir Wasil<sup>1</sup>, Nawaf Khurshid Sheikh<sup>2</sup>, Aneeta Singh Malhotra<sup>3</sup>, Arvind Khajuria<sup>4</sup>

## ABSTRACT

**Introduction:** Chronic cholecystitis is the most frequent premalignant lesion in India and around the world, with calculi accounting for 78-90 % of cases.<sup>34,23</sup> In this study, we analyzed the clinicopathological features of precancerous and malignant gallbladder lesions in routine cholecystectomy specimens as well as the importance of grossing and histological evaluation of every cholecystectomy specimen in order to diagnose incidental precancerous and malignant gallbladder lesions.

**Material and methods:** A three-year retrospective examination of cholecystectomy tissues was conducted from May 2018 to May 2021. 452 Cholecystectomy specimens were obtained, and each one was examined histopathologically.

**Results:** The most common age group was 21-40 years old (59.29%), followed by 41-60 years old 118 (26.11 %). 302 (66.81 %) females account for gall bladder lesions, with an M: F ratio of 1:2. Chronic cholecystitis was the most frequent lesion, accounting for 226 cases (50%), followed by Cholesterolosis (98 instances) (21.68 %). Acute cholecystitis accounts for 28 instances (6.19%), while metaplasia accounts for 42 cases (9.29 %).

**Conclusions:** Cholecystectomy is the treatment for gall bladder diseases. All cholecystectomy specimens were sent for histopathologic evaluation to detect precancerous and premalignant lesions.

**Keywords:** Cholecystectomy, Cholesterolosis, Gallbladder Cancer, Metaplasia, Malignant Lesions

## INTRODUCTION

The gallbladder is a pear-shaped muscular sac linked to the right lobe of the liver's posterior portion.<sup>1,2</sup> It contracts during and after a fatty meal to assist digestion by delivering bile through the bile ducts into the intestine.<sup>3</sup> Congenital abnormalities, acute and chronic inflammation, cholelithiasis, benign and premalignant diseases, and cancer can all occur in the gallbladder.<sup>4,5</sup>

Cholecystectomy, a surgery that removes the gallbladder, is recommended in cases of gallbladder damage, malignancy, gallstones, and acute cholecystitis. Only 30% of gallbladder carcinomas are suspected before surgery, with the remaining 70% being discovered by chance during or after surgery by pathological testing.<sup>8</sup> Gallbladder dysplasia (GBD) and adenoma are premalignant lesions that can proceed to cancer via many paths. Gallstones and persistent cholecystitis are both significant risk factors for gallbladder malignancies. Gall bladder lesions are infrequent, and they might be difficult to diagnose. Over the last few decades, there has been a link between primary gall bladder cancer and other epithelial alterations such as hyperplasia, dysplasia, and

metaplasia.<sup>1</sup>

Dysplasia and adenomas have been hypothesized in the evolution of gall bladder cancers at different carcinogenic pathways. Gallbladder adenomas are tiny, asymptomatic malignancies found by chance in cholecystectomy specimens.<sup>3,7</sup> Pyloric, intestinal, and biliary adenomas are the histological classifications.<sup>3,7</sup> Carcinoma is frequently associated with single adenomas measuring more than 1 cm in diameter.<sup>7</sup> According to Nakajo et al.<sup>24</sup>, adenocarcinomas can develop from adenomas of either the metaplastic or non-metaplastic form. Metaplasia is described as the change of one distinct epithelium into another, and it is linked to tissue injury and chronic inflammation.<sup>32</sup> Gallstone-related gallbladder carcinogenesis is primarily mediated by the metaplasia-dysplasia-carcinoma pathway, rather than the transformation of a pre-existing benign tumor lesion.<sup>18</sup>

The histopathological examination of gallbladder specimens is a critical step in confirming clinical and radiological diagnoses,<sup>17</sup> and might be useful in court.<sup>18</sup> As a result, most surgical units consider this examination to be standard.<sup>19</sup> Saving pathology departments' time and resources also aid in determining the need for routine review.<sup>17,19-21</sup>

Rarely, routine histopathologic examination reveals incidental low- or high-grade dysplasia without any clinical, radiographic, or gross abnormality. In this present study, routine cholecystectomy specimens were evaluated for precancerous and malignant GB lesions.

## MATERIAL AND METHODS

The present study was conducted for a period of 3 years from May 2018 to May 2021. This study included all individuals who underwent cholecystectomy for presumed benign gallbladder disorders. Gross specimens of GB were processed in our laboratory according to the standard protocol which includes the opening of the specimen, fixation, and extension on paraffin blocks, and thorough examination of suspicious lesions. Clinical and radiological details of

<sup>1</sup>Post Graduate, Department of Pathology, ASCOMS, Jammu,

<sup>2</sup>Assistant Professor, Department of Pathology, ASCOMS Jammu,

<sup>3</sup>Professor, Department of Pathology, ASCOMS, Jammu, <sup>4</sup>Professor, Department of Pathology, ASCOMS, Jammu

**Corresponding author:** Dr Nawaf Khurshid Sheikh, Near Hashmi Masjid, Satellite Colony, Bathindi, Jammu

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all gallbladder specimens were taken and specimens were analyzed and studied for precancerous and malignant lesions.

## RESULTS

Four hundred and fifty-two patients treated with cholecystectomy during the research period were enrolled. There were 150 men and 302 females with a male to female ratio of 1:2. The majority of the patients were between the ages of 21 and 40 (268 out of 452 cases, or 59.29%). The vast majority of patients (94.69 percent) complained of upper abdominal pain of various intensities and duration. Table II shows further signs and symptoms.

Cholesterolosis (21.68%). Metaplasia (pyloric and intestinal) was detected in 42 patients (9.29%) with a great prevalence. The GB wall was thickened in gross chronic cholecystitis, and histological examination revealed fibrosis and lymphocytic infiltrates. 18 cases with dysplasia were identified. 12 (2.65%) cases exhibited signs of adenocarcinoma of various differentiation. Hyperplastic polyps were seen in 12 (2.65%) cases. Acute cholecystitis and Xantho-granulomatous Cholecystitis account for 28 (6.19%) and 8 (1.77%) instances respectively. Acute suppurative cholecystitis was seen in 4 (0.88%) gallbladders. Biliary atresia and choledochal cyst account for 0.44% of cases each. (as shown in Table III).

Age-group	No. of patients	%
≤20	22	4.87
21-40	268	59.29
41-60	118	26.11
61-80	44	9.73
Total	452	100.00

**Table-1:** Age-wise distribution of gall bladder lesions

Symptoms	No. of patients	Percentage
Intolerance to fatty food	70	15.49 %
Flatulence and/ or dyspepsia	318	70.35 %
Upper abdominal pain	428	94.69 %
Nausea and/ or vomiting	66	14.60 %

**Table-2:** Common presenting symptoms of the patients

Histopathology	No. of cases	No. (%)
Cholesterolosis	98	21.68
Chronic cholecystitis	226	50
Acute cholecystitis	28	6.19
Xanthogranulomatous cholecystitis	8	1.77
Acute suppurative cholecystitis	4	0.88
Adenocarcinomas	12	2.65
Pyloric metaplasia	20	4.42
Intestinal metaplasia	22	4.87
Dysplasia	18	3.98
Biliary atresias	2	0.44
Choledochal cysts	2	0.44
Hyperplastic Polyps	12	2.65
Total	452	100

**Table-3:** Histopathological findings of the cases

## DISCUSSION

The incidence of detection of premalignant lesions of GB in routine histopathological examination of cholecystectomy specimens has been increased. High-grade dysplasia is reported in 1 to 3.5% of cholecystectomies performed and low-grade dysplasia in up to 15% in areas of the world with a high incidence of GBC, whereas adenomas are detected in <1% of cholecystectomies performed. (3)

Gallbladder malignancies have a terrible prognosis unless it is detected early after pathological examination of gallbladder specimens removed for benign diseases (including cholelithiasis). Females are 2–3 times more likely than males to develop it, with a peak incidence in the seventh decade of life.<sup>23,24</sup> Gallbladder cancer affects 0.3–2% of patients who receive a cholecystectomy for benign gallbladder disorders.<sup>20,24-26</sup>

In our study the male to female ratio was 1:2. Similar investigations have also revealed a female majority (Channa et al., 2007).<sup>27</sup> Chronic Cholecystitis was the most common GB lesion in our analysis, accounting for 50%, compared to 85.13% in Vani BR et al's study and 88.8% in Zoysamim De et al's study.<sup>28,29</sup>

The association between gallbladder cancer and chronic inflammation due to gallstones has been mentioned in various studies since 1861.<sup>13–15</sup> Inflammation of the gallbladder wall was also seen in chronic inflammatory conditions and was found usually to be non-specific.<sup>8</sup> chronic cholecystitis was observed in more majority of the gallbladder followed by cholesterolosis. For both advanced and early gallbladder cancer, ultrasound had good diagnostic accuracy. Preoperative ultrasonography failed to detect any of the eight carcinomas in this series. Chronic inflammation, infection, and gall stones are thought to be the conditions that cause the gall bladder epithelium to become malignant.<sup>31</sup> Gallstones and carcinoma gallbladder have a close link.<sup>32</sup> There are two models for carcinogenesis of the gallbladder: the metaplasia–dysplasia–carcinoma sequence and the adenoma–carcinoma sequence.<sup>8</sup> However, It is likely that hyperplasia could also progress to dysplasia via the stage of metaplasia.<sup>25</sup> Metaplastic changes to the gallbladder epithelium are known to cause precancerous lesions.<sup>14,16</sup> In our study we observed metaplasia in 42 cases (22 intestinal and 20 pyloric). Seretis et al. reviewed the histopathology reports of 86 cases with chronic cholecystitis to identify the prevalence of gallbladder metaplasia in the course of chronic cholecystitis. We encountered 4 cases of Congenital anomalies of GB like 2 cases (0.44%) of biliary atresia and 2 cases (0.44%) of Choledochal Cyst. (23) In Biliary atresia GB may be absent or represented by a fibrous cord without a lumen. Choledochal cyst commonly presents with obstructive jaundice in childhood beyond infancy but it may also present in Adulthood. In the present study, 12 (2.65%) cases of Adenocarcinoma of GB were encountered.

## CONCLUSION

In the literature, we characterized the premalignant

conditions in the gallbladder specimens through histopathological examination. There are several ancillary techniques of examining gallbladder specimens, such as trans-abdominal ultrasound, which has a sensitivity of up to 70%, but are ineffective in detecting GB cancer at an early stage. Histopathological diagnosis of GB cancer is still the Gold Standard and superior to clinical and radiographic evaluation. Cholecystectomy, the primary treatment for GBC and other GB lesions linked with Cholelithiasis, results in a better overall prognosis and survival rate. As a result, every Cholecystectomy specimen should be histopathologically examined for incidental precancerous and malignant lesions.

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