

## RETROSPECTIVE STUDY OF HISTOPATHOLOGICAL SPECTRUM OF GALLBLADDER DISEASES IN A TERTIARY CARE CENTER

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**Abstract**

**Background:** Gallbladder diseases (GBD) are highly prevalent and often require surgical intervention. There is a range of histopathological patterns, from cholecystitis to gallbladder carcinoma. This study aims to investigate the incidence of different histopathology in gallbladder specimens from a tertiary care hospital in India. **Materials and Methods:** A retrospective analysis was carried out on 1528 gallbladder specimens obtained from cholecystectomy at Ganesh Shankar Vidyarathi Memorial Medical College, Kanpur, Uttar Pradesh, India. The prevalence of various histopathological outcomes was evaluated using SPSS software. **Result:** In this study, 1528 cases were examined, out of which 56.61% were female and 43.39% were male. The highest number of patients fell in the age group of 21-40 years (45.80%) followed by 41-60 years age group (39.60%). The most commonly observed histopathological feature in the study was chronic cholecystitis, accounting for 76.04% of the total patients, while adenocarcinoma of the GB was rare with only 4 cases observed. **Conclusion:** Cholecystectomy is commonly performed due to GBD, which can present with a range of underlying pathologies including chronic cholecystitis, cholesterosis, and acute-on-chronic cholecystitis. Routine histopathological examinations of resected GB specimens are important to identify premalignant or malignant lesions such as intestinal metaplasia and reactive atypia, as failure to detect these can lead to progression of GB adenocarcinoma with a poor prognosis.

## INTRODUCTION

The gallbladder, a pouch shaped like a pear, is connected to the biliary system outside the liver's right lobe. Typically, in adults, it measures approximately 10 cm in length and 3 to 4 cm in diameter, with a wall thickness of around 1 to 2 mm.<sup>[1]</sup> The gallbladder's wall is composed of three layers: the mucosa, muscular, and perimuscular layers. Notably, unlike other parts of the digestive system, the gallbladder does not possess a muscularis mucosa and submucosa. The lamina propria of the gallbladder contains a small number of lymphocytes, plasma cells, and mast cells, while neutrophils and eosinophils are typically absent.<sup>[2]</sup> Gall Bladder Diseases (GBD) is a noteworthy gastrointestinal ailment that is primarily instigated by metabolic anomalies in the hepato-biliary system.<sup>[3]</sup> Figure 1 briefly summarized the various factors responsible for the occurrence of GBD. It is a widely prevalent health concern across the globe; however, its incidence varies from one nation to another. In India, for instance, the prevalence of GBD ranges from 2% to 29%. Furthermore, several

factors such as age, gender, and ethnicity influence the prevalence of GBD.<sup>[4]</sup>

Not only does GBD result in pain in the right upper quadrant and digestive grievances, but it also contributes to the emergence of abnormalities in the cells and tissues of the gallbladder. This, in turn, augments the risk of gallbladder carcinoma (GBC), which is an extremely lethal transformation.<sup>[5]</sup> The gallbladder undergoes hyperplasia and metaplasia, which are precursors to dysplasia. Dysplasia, in and of itself, is a potential precursor to carcinoma. Consequently, the presence of these pre-malignant conditions in the gallbladder significantly heightens the probability of developing GBC.<sup>[6]</sup>

GBC is a malignant form of cancer that is particularly deadly and is ranked as the fifth most prevalent gastrointestinal malignancy in India, following colon, pancreas, stomach, and esophagus cancers.<sup>[7]</sup> The development of GBC is influenced by various factors such as obesity, reproductive factors, genetic factors, lifestyle risk factors (including cigarette smoking and alcohol consumption), chronic gallbladder infections, environmental exposure to specific chemicals, and

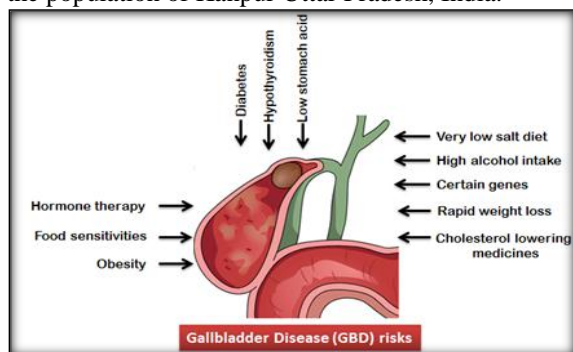
the existence of gallstones. Gallstones, in particular, are thought to have a substantial impact on the occurrence of GBC.<sup>[8]</sup>

Research has revealed that the size of gallstones and the length of chronic gallbladder disease are significant risk factors for the development of GBC. People with large gallstones and a long history of chronic gallbladder disease are reported to be four to seven times more likely to develop GBC.<sup>[9]</sup>

The geographical distribution of GBC in India exhibits considerable variation, with North India demonstrating higher incidence rates in contrast to South India.<sup>[10]</sup> The prevalence of GBC among patients afflicted with GBD varies between 0.3% and 12% across India and other nations. Evidently, a concealed GBC is apparent in approximately 0.5% to 1.1% of all elective cholecystectomies associated with cholelithiasis (gallstones). Contrarily, gallstones are identified in 74% to 92% of GBC patients in India.<sup>[11]</sup>

A significant proportion of patients afflicted with GBD remains unaware of their condition and exhibit no symptoms for a prolonged duration. Only a small minority of individuals present symptoms that necessitate prompt medical intervention.<sup>[12]</sup> Despite the fact that the precise etiology of GBC remains speculative, untreated chronic GBD is generally linked to persistent inflammation of the gallbladder, which may potentially contribute to the development of cancer.<sup>[13]</sup>

Addressing GBD and its impact on gallbladder tissues is of paramount importance, particularly in rural and underserved areas where untreated chronic GBD is prevalent. However, a comprehensive understanding of the histopathological spectrum of gallbladder abnormalities resulting from GBD in rural India remains unclear. Knowledge of the prevalence and distribution of these abnormalities is crucial for preventing GBC and plays a significant role in the management of GBD patients and the formulation of GBC prevention policies.<sup>[14]</sup> Moreover, it is imperative to investigate the association between GBD and GBC to gain a better comprehension of the disease.<sup>[12]</sup> Therefore, the goal of this study is to provide valuable insights into the range of histopathological findings in cholecystectomy specimens from GBD patients in the population of Kanpur Uttar Pradesh, India.



**Figure 1: Various factors responsible for increasing the risk of gallbladder disease**

## MATERIALS AND METHODS

A retrospective study was conducted at Department Pathology, Ganesh Shankar Vidyarthi Memorial Medical College, Kanpur, Uttar Pradesh, India. Histopathological sample of 1528 patients were examined from 16th July 2022 to 17th July 2023. Patient's detail including name, age sex, chief complaint, procedure performed and investigations were taken in pathology requisition form.

### Inclusion Criteria

All cases that underwent cholecystectomy with a diagnosis of cholecystitis, empyema, polyp, premalignant and malignant gall bladder diseases.

### Exclusion Criteria

Secondary gall bladder carcinoma (metastasis), postchemotherapy, post radiotherapy gall bladder malignancy.

### Histopathological Examinations

The specimens of cholecystectomy that originated from the Surgery Department were transferred to the Pathology Department of this establishment for the purpose of histopathological analysis. In order to proceed with the examination, parts from the fundus, body, and neck of the gall bladder were sectioned, along with additional sections from mucosa that appeared abnormal. These samples were then subjected to standard hematoxylin and eosin staining for microscopic analysis [Figure 2&3]. The department's proficient faculty members performed all the histopathology diagnoses. The pre-malignant (PM) and malignant (M) cases were collectively referred to as 'PM-M conditions,' wherein hyperplasia, metaplasia, and dysplasia were recognized as pre-malignant conditions.<sup>[15]</sup>

### Statistical Analysis

All research data was collected and analysis was done by using SPSS software.

## RESULTS

The current investigation was conducted on a sample of 1528 cases, consisting of 865 female and 663 male patients. The proportion of male and female patients was found to be 43.39% and 56.61%, respectively. As shown in [Table 1], the percentage of male patients is higher than that of female patients. [Table 2] showed the age-wise distribution of patients, with the highest number of patients falling in the age group of 21-40 years (45.80%), followed by the age group of 41-60 years with 39.60% of patients.

The study revealed that chronic cholecystitis was the most common histopathological feature, accounting for 76.04% of the total patients. Our study population also demonstrated a high incidence of cholesterolosis and acute-on-chronic cholecystitis. However, only 4 cases of adenocarcinoma of the GB were identified. The frequencies of the various

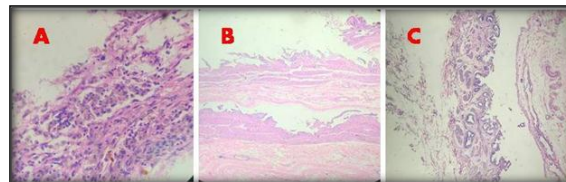
histopathological features and their distribution with respect to gender are delineated in [Table 3].

It is noteworthy that the findings of this study are consistent with previous research, which has also highlighted the prevalence of chronic cholecystitis in patients with gallbladder disease. The high incidence of cholesterosis in our study population is also in line with previous studies that have reported a strong association between gallbladder disease and cholesterol metabolism. Additionally, the low incidence of adenocarcinoma of the GB is consistent with the relatively low prevalence of this disease in the general population.

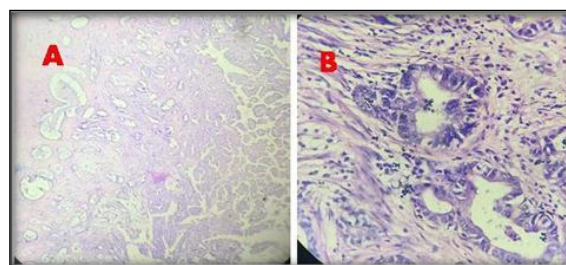
The results of this study have important implications for the diagnosis and treatment of gallbladder disease. The high prevalence of chronic cholecystitis underscores the need for accurate and timely diagnosis of this condition, as well as effective management strategies. The association between cholesterosis and gallbladder disease highlights the importance of dietary interventions in the prevention and management of this condition. Furthermore, the low incidence of adenocarcinoma of the GB suggests that routine screening may not be necessary in the absence of other risk factors.<sup>[16]</sup>

Outcomes of this study provide valuable insights into the prevalence and distribution of histopathological features in patients with gallbladder disease. The high incidence of chronic cholecystitis and cholesterosis highlights the need for effective management strategies, including

accurate diagnosis and dietary interventions. The low incidence of adenocarcinoma of the GB suggests that routine screening may not be necessary in the absence of other risk factors. Further research is needed to explore the underlying mechanisms of gallbladder disease and to develop more effective prevention and treatment strategies.<sup>[17]</sup>



**Figure 2: (A) Xanthogranulomatous Cholecystitis, (B) Chronic cholecystitis, (C) Chronic cholecystitis with pyloric metaplasia.**



**Figure 3: (A) Gall bladder adenocarcinoma (H & E , 10 X) (B) Gall bladder adenocarcinoma with glands showing pleomorphism and high nucleo-cytoplasmic ratio (H & E , 40 X)**

**Table 1: Distribution of study participants based on their gender**

Gender	Number of Patients	Percentage
Male	663	43.39 %
Female	865	56.61 %

**Table 2: Distribution of study participants on the basis of age**

Age	Percentage of patients
5-20 Years	7.20%
21- 40 Years	45.80%
41-60 Years	39.60%
61-70 Years	5.80%
> 70 Years	1.60%

**Table 3: The histopathological findings observed in the study population in relation to gender**

Histo-pathological features	Males	Females	Total
Chronic cholecystitis	529	633	1162 (76.04%)
Acute cholecystitis	8	12	20 (1.30%)
Acute on chronic cholecystitis	20	37	57 (3.37%)
Chronic cholecystitis with pyloric metaplasia	31	46	77 (5.04%)
Xanthogranulomatous cholecystitis	12	26	38 (2.48%)
Cholecystitis with cholesterosis	58	102	160 (10.47%)
Gall bladder polyp	2	4	6 (0.39%)
Empyema	2	2	4 (0.26%)
Gall bladder adenocarcinoma	1	3	4 (0.26%)
Total	663	865	1528

## DISCUSSION

Cholecystectomy is a commonly performed surgical procedure that is utilized to manage various pathologies, including cholelithiasis, cholecystitis, GB polyps, and GBC. Cholelithiasis is the most

prevalent biliary tract pathology globally, with a prevalence rate of approximately 10%-15%.<sup>[18]</sup> Although gallstones are benign, they are associated with an increased risk of hepatobiliary and GBC. Despite the low incidence of GBC in the general population, it represents 80% of all biliary tract

cancers. GBC is often diagnosed at a late stage, which contributes to a poor prognosis and low five-year survival rates.<sup>[19]</sup>

This research conducted an observation of a patient population and found a predominance of females. This is consistent with a study carried out in India, a neighbouring country. Interestingly, the female gender is considered a risk factor for the development of gallstones. The majority of patients in this study presented with cholelithiasis, which is a condition that can lead to various pathologies, such as acute cholecystitis, chronic cholecystitis, follicular cholecystitis, and cholesterolosis. Chronic cholecystitis, which is the most common pathology within the patient population, was observed in 76.04% of cases.<sup>[20]</sup> A study conducted elsewhere concluded that the prevalence of chronic cholecystitis is 79.8%, which is in line with the findings of this study. Chronic cholecystitis is characterized by thickening of the GB wall and the presence of calcifications, which can eventually lead to a condition known as porcelain GB.<sup>[21]</sup>

Cholesterolosis, on the other hand, results from mucosal villous hypertrophy and the accumulation of cholesterol esters and triglycerides in a diffuse or polypoid form in the macrophages present within the wall of the GB. This study found that cholesterolosis was present in 10.47% of cases.<sup>[22]</sup> In contrast, a study conducted by Mondal et al. reported a prevalence of only 2.9% of the patient population, while Sangwan et al. reported a prevalence of 9.43%. The prevalence of cholesterolosis in this study was therefore significantly higher than the study of Mondal et al., but similar with the study of Sangwan et al.<sup>[23]</sup>

It is important to note that the female gender is a risk factor for the development of gallstones, as observed in this study and others. Cholelithiasis, which was observed in almost all patients in this study, can lead to various pathologies, including chronic cholecystitis, follicular cholecystitis, and cholesterolosis. Chronic cholecystitis, which was the most common pathology observed in this patient population, is characterized by thickening of the GB wall and the presence of calcifications. The prevalence of this condition was found to be similar to that reported in other studies.<sup>[24]</sup>

This study has provided important insights into the prevalence of various pathologies associated with cholelithiasis, including chronic cholecystitis and cholesterolosis. The findings of a female predominance and a high prevalence of cholesterolosis are particularly noteworthy and warrant further investigation. Overall, this study has contributed to our understanding of the risk factors and pathologies associated with gallstones and has important implications for the management of this condition. Further research is needed to build upon these findings and to develop more effective treatments for patients with cholelithiasis and its associated pathologies.<sup>[25]</sup>

Xanthogranulomatous cholecystitis (XGC), a persistent, focal, or extensive fibro-inflammatory process caused by an intramural buildup of foamy histiocytes, was discovered in 2.48% of the incidents. The preoperative and intraoperative observations of XGC are comparable to those of GBC. XGC is characterized by pericholecystic infiltration, hepatic involvement, and lymphadenopathy, making its diagnosis challenging. If XGC is not diagnosed early, it necessitates more radical surgery than the standard cholecystectomy. Furthermore, its association with GBC has been well established.<sup>[26]</sup>

Empyema of the gallbladder is a complication of acute cholecystitis and has been found to occur in 5%-15% of cases. Clinically, this pathology is manifested as a distended gallbladder filled with pus, with histopathological findings indicating significant edema, inflammation, and fibrinous exudate surrounding the gallbladder wall. In this investigation, empyema of the gallbladder was observed in 0.26% of the cases, which is similar to the prevalence rate reported in another study. The presence of empyema of the gallbladder necessitates prompt medical intervention, as it can lead to life-threatening complications such as sepsis and perforation.<sup>[27]</sup> It is crucial to distinguish between simple and complicated cases of cholecystitis using radiological and laboratory investigations since this can affect the management approach. Early recognition and treatment of these conditions are essential in reducing morbidity and mortality rates. The incidence of these diseases in the population should be investigated further to identify their risk factors and develop preventive measures. The importance of educating the general public on the symptoms and signs of gallbladder diseases cannot be overstated, as it can aid in early detection and management.<sup>[28]</sup>

Chronic cholecystitis with pyloric metaplasia and was observed in a mere 5.04% in the current study. However, even though the prevalence of these premalignant conditions was low, it is important to consider their malignant potential. Both intestinal metaplasia can lead to the development of carcinoma, making it crucial to detect them early. Significantly, most patients who presented with these premalignant afflictions were from older age groups, which implies that an increased age at presentation raises the risk of malignant transformation. Failure to detect these lesions early can orchestrate the pathogenesis underlying the development of GBC.<sup>[29]</sup>

Therefore, it is necessary to evaluate the histopathology of each GB specimen, irrespective of its macroscopic appearance intraoperatively, to aid in the early detection of carcinoma in high-risk patients. This can help curb the risk of progression to advanced disease. GB adenocarcinoma was observed in only 0.26% of cases, which is lower than the prevalence rates reported in various other



studies ranging from 0.5% to 1.05% of the total cases.<sup>[30]</sup>

Despite the advent of modern diagnostic techniques, GBC is still diagnosed at a late stage, leading to poor prognosis. Since GBC often remains clinically silent in its initial stages, it can evade prompt detection. However, histopathological examination, improved imaging techniques, and specific diagnostic markers can assist in yielding a timely diagnosis, thereby improving disease outcomes. It is crucial to detect GBC early to avoid adverse consequences. Thus, it is important to emphasize the relevance of screening high-risk groups, including individuals from regions with a high incidence rate, women, and patients with a history of gallstones or biliary tract disease. Screening could involve ultrasonography, computed tomography, magnetic resonance imaging, and endoscopic retrograde cholangiopancreatography.<sup>[31]</sup>

## CONCLUSION

GB disease continues to be a significant reason for cholecystectomy, with postoperative histopathological analysis of the excised GB specimens revealing a wide range of underlying pathologies. Chronic cholecystitis, cholesterosis, and acute-on-chronic cholecystitis are the most common of these pathologies. Additionally, there is a possibility of an underlying premalignant or malignant lesion, even in the absence of notable macroscopic features. Therefore, it is imperative to conduct routine histopathological examinations of resected GB specimens to exclude premalignant conditions like intestinal metaplasia and reactive atypia. Failure to detect these lesions can result in the progression of GB adenocarcinoma, which is known for its particularly unfavorable prognosis.

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