

Incidence of Incidental Gallbladder Carcinoma in Cholecystectomy Patients: A retrospective analysis from a Tertiary Care Center in Northern India

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ABSTRACT

Background

Gallbladder diseases, particularly those involving gallstones, are a widespread health issue globally. Cholecystectomy, often performed to manage gallstone-related conditions, can occasionally reveal incidental gallbladder carcinoma (IGBC) during histopathological evaluation. Identifying the incidence and characteristics of IGBC is critical for enhancing patient outcomes and clinical strategies.

Objectives

This study aimed to assess the frequency, clinical features, and pathological characteristics of IGBC in patients undergoing cholecystectomy at a tertiary care center in northern India.

Materials and methods

The retrospective study analysed 847 consecutive gallbladder specimens received from patients who underwent cholecystectomy over a period of two years. All cholecystectomy specimens during the study period were included, except patients with preoperatively suspected carcinoma and poorly preserved or inadequate specimens. Histopathological examination was performed using Hematoxylin and Eosin staining, and tumour staging was carried out according to the American Joint Committee on Cancer (AJCC) guidelines. Patient demographics, clinical presentation, imaging findings, and histopathological features were also reviewed.

Results

Among the 847 specimens, IGBC was detected in 8 patients (0.94%), all in females, with a mean age of 52.38 years. Most presented with right upper quadrant pain (75%). Ultrasonography commonly showed gallstones (87.5%) and thickened gallbladder walls (75%). Histologically, 7 patients were adenocarcinomas, and 1 was lymphoepithelioma-like carcinoma. Pathological staging revealed 3 patients at pT1, 4 at pT2, and 1 at pT3.

Conclusion

The study highlights an IGBC incidence of 0.94%, emphasizing the need for routine histopathological analysis of gallbladder specimens. This practice aids in detecting early-stage carcinomas, which can significantly improve survival rates and guide appropriate management strategies.

Key words: Oncopathology, Gastrointestinal tract, Incidental, staging, cancer

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INTRODUCTION

Gallbladder diseases, particularly gallstone-related conditions, have emerged as a significant healthcare concern globally. Cholecystectomy, the surgical removal of the gallbladder, is one of the most commonly performed elective surgeries worldwide, aiming to alleviate the distressing symptoms and complications associated with gallstones. While this procedure is generally regarded as safe and effective, it often unveils unexpected findings during surgery, such as incidental carcinoma of the gallbladder. (1)

Incidental gallbladder carcinoma (IGBC) refers to the unexpected detection of gallbladder cancer in patients undergoing cholecystectomy for presumed benign gallbladder diseases such as gallstones. This unforeseen diagnosis poses a challenging clinical scenario, as it necessitates a shift from routine gallstone surgery to a more comprehensive and aggressive approach, including radical resection and staging for malignancy. (2)

The incidence of IGBC varies significantly across geographical regions and populations, with some areas showing higher prevalence than others. (3) According to the Indian cancer registry data, the incidence of gallbladder carcinoma (GBC) in India ranges from 0.8–1%, with the highest incidence reported from New Delhi and Bhopal, while Chennai shows the lowest incidence. Northern India has a higher burden of gallstone disease, maybe due to dietary, environmental, and socioeconomic factors that may contribute to the increased incidence of GBC in this region. These factors make Northern India an important area for studying IGBC in patients undergoing cholecystectomy (4).

Risk factors of gall bladder cancer include cholelithiasis, calcified gallbladder wall, adenomatous polyp, obesity, increased levels of estrogen, choledochal cyst and chemical carcinogens. Of these, gallstones are most common risk factor associated with the development of GBCs contributing to 75%–90% of patients. (5) Selective approach for sending these specimens to the laboratory results in missing discrete pathologies like premalignant benign lesions such as porcelain gallbladder, carcinoma-in-situ and early carcinomas. (6) The Royal College of Pathologists suggests a histopathological examination of all

cholecystectomy specimens as IGBC can be easily missed out. However, few authors are of the view that histopathological examination (HPE) is not needed for all surgically resected benign gallbladders as the incidence of IGBC is low and many of the patients present at an early stage with simple cholecystectomy being the optimal treatment. (5)

The 5-year overall survival rate is 5% compared with a 79% survival rate when the disease is detected in its early stages. (7) In this original research article, we present the findings of a comprehensive study conducted at a tertiary care centre in northern India, aimed at examining the incidence of incidental carcinoma of the gallbladder in patients undergoing cholecystectomy.

Our study encompasses a diverse patient population and employs rigorous diagnostic and histopathological evaluation to shed light on the prevalence of this unexpected malignancy in this specific geographical and clinical context. Understanding the incidence and associated factors of IGBC in northern India is not only crucial for guiding clinical decision-making but also contributes to the broader knowledge of gallbladder diseases, with potential implications for healthcare strategies and preventive measures in this region. Through this study, we hope to provide significant insight into the landscape of gallbladder pathology in northern India, contributing to the enhancement of patient care, early detection, and ultimately, improved outcomes for individuals undergoing cholecystectomy.

MATERIALS AND METHODS

Study Design and Setting:

The present study was a single-centre, retrospective record-based study conducted over a period of two years after obtaining approval from the Institutional Ethics Committee. The study was carried out in the Departments of Pathology and surgery of a tertiary care hospital.

Study Population:

The study included consecutive hospitalized patients who underwent cholecystectomy during the study period, including both elective and emergency procedures. Most patients



underwent laparoscopic cholecystectomy. All gallbladder specimens received for HPE were included in the study. Patients with preoperative suspicion of gallbladder carcinoma and autolysed or inadequate specimens were excluded.

Data Sources:

Demographic details, presenting clinical features, operative findings, discharge summaries, and preoperative ultrasonography (USG) findings were retrieved from hospital medical records, operative notes, and pathology archives. Patients with incomplete records were excluded from detailed clinicopathological analysis.

Histopathological-Examination:

All gallbladder specimens were fixed in 10% formalin and routinely processed. Gross examination included sampling from the fundus, body, neck, and any suspicious areas identified macroscopically. A minimum of three sections were taken from the gallbladder wall.

Histopathological diagnosis of incidental gallbladder carcinoma (IGBC) was confirmed on paraffin-embedded Hematoxylin and Eosin (H&E) stained sections. Pathological staging was performed according to the American Joint Committee on Cancer (AJCC) TNM staging system, 8th edition.(8)

Statistical Analysis:

Data were entered and analysed using appropriate statistical software. Descriptive statistics were used for demographic and clinicopathological variables. Statistical significance was considered at a p-value of <0.05.

RESULTS

A total of 847 cholecystectomies were included in the present study.

Majority of the patients were in third decade of life (n=291, 34.3%) followed by fourth decade (n=248, 29.3%) (Table 1).

Table 1: Age distribution of cholecystectomy procedure

AGE GROUP	NUMBER OF PATIENTS (n=847)	PERCENTAGE
Less than 20	08	0.9
21-30	291	34.3
31-40	248	29.3
41-50	166	19.6
51-60	85	10.0
61-70	43	5.1
71-80	4	4.7
More than 80	2	0.2

Age of patients undergoing cholecystectomy ranged from 12 to 87 years. Most of the patients were females (n=709, 83.7%) with female to male ratio being 5.14:1. Gall stones were present in 798 patients (94.2%) and were multiple in a number of patients (n= 614, 76.94%). Chronic cholecystitis (CC) (n= 791, 93.4 %) was the most

common histopathological diagnosis followed by Xanthogranulomatous Cholecystitis (n= 25, 2.9%), acute cholecystitis (n= 08, 0.9%), Mucocele (n=06, 0.7%), Eosinophilic Cholecystitis (n=03, 0.3%), empyema gall bladder (n= 02, 0.2%), dysplasia (n=04,0.5%) and IGBC (n=08, 0.9%) (Table 2).

Table 2: Distribution of patients based on histopathological diagnosis

HISTOPATHOLOGICAL DIAGNOSIS	NUMBER OF PATIENTS (n=847)	PERCENTAGE
Chronic Cholecystitis	791	93.4
Acute Cholecystitis	08	0.9
Xanthogranulomatous Cholecystitis	25	2.9

Eosinophilic Cholecystitis	03	0.3
Empyema	02	0.2
Mucocele	06	0.7
Dysplasia	04	0.5
IGBC	08	0.9

Other histopathological findings seen include cholesterosis were seen in 232 patients (21.1%), papillary hyperplasia in 102 patients (9.3%), pyloric metaplasia in 245 patients (22.3%) and intestinal metaplasia in 16 patients (1.4%). IGBC was diagnosed in 08 (0.9%) out of 847 cholecystectomy specimens. All 8 patients were females. Mean age of patients of IGBC was 52.38%. Most of the patients were in sixth decade of life (n= 4.5%). The most common presenting complaint was pain in right upper quadrant (RUQ) (n=06, 75.0%) followed by nausea, vomiting and dyspepsia (n=02, 25.0%). Additionally, one patient had history of jaundice (Table 3). Preoperative USG was performed in all

the patients. Most common finding was presence of multiple stones (n=07, 87.5%) followed by thickened wall (n=06, 75.0%). Common bile duct was dilated in one patient but there was no calculus. None of the patients had any mass or polyp in gall bladder on USG. Laparoscopic cholecystectomy was performed in all patients but in one case it was converted to open cholecystectomy due to dense adhesions. On gross examination wall thickness was more than 3mm in 6 patients and measurement varied from 3mm to 1cm. One case had perforated wall; internal adhesions were seen in one case (Table 3).

Table 3: Clinical presentation, histopathological diagnosis, pathological stage of IGBC(n=8)

Age/ gender	Clinical presentation	Wall thickness	Gall stones	Operative finding	Histopathological diagnosis	Pathological stage
51/F	Pain in RUQ x 15 days	3mm-1cm	Multiple stones	Lap cholecystectomy Thick-walled gall bladder	Moderately Differentiated Adenocarcinoma	pT2a
52/F	nausea, vomiting & Dyspepsia x 2 month	3 to 6mm	Multiple stones	Lap cholecystectomy Perforation is present Thick-walled gall bladder	Moderately Differentiated Adenocarcinoma	pT1b
50/F	Pain in RUQ since 6 months	6mm	Multiple stones	Lap cholecystectomy Thick-walled gall bladder	Moderately Differentiated Adenocarcinoma	pT2a

50/F	Pain in RUQ since 10 months	6mm	Multiple stones	Lap cholecystectomy Thick-walled gall bladder Internally adhesion present	Lymphoepithelioma like carcinoma with adjoining focus of undifferentiated carcinoma	pT1a
65/F	nausea, vomiting & Dyspepsia x 1 month	4mm	Multiple stones	Lap cholecystectomy Thick-walled gall bladder	Moderately Differentiated Adenocarcinoma	pT2a
52/F	Pain in RUQ since 1 month	2mm	Multiple stones	Lap cholecystectomy Smooth gall bladder wall	Well Differentiated Adenocarcinoma	pT1a
60/F	Pain in RUQ since 20 days	8mm	Multiple stones	Lap cholecystectomy Thick-walled gall bladder and hardening at fundus of gall bladder	Mucinous Adenocarcinoma	pT2a
40/F	Jaundice since 1 month Pain in RUQ since 3 months	3mm	No stone	Lap cholecystectomy Smooth walled gall bladder	Well Differentiated Adenocarcinoma	pT3

On microscopic examination, seven of IGBC patients were diagnosed as Adenocarcinomas whereas one case was given a diagnosis of

Lymphoepithelioma like carcinoma with adjoining focus of undifferentiated carcinoma (**Figure 1**).

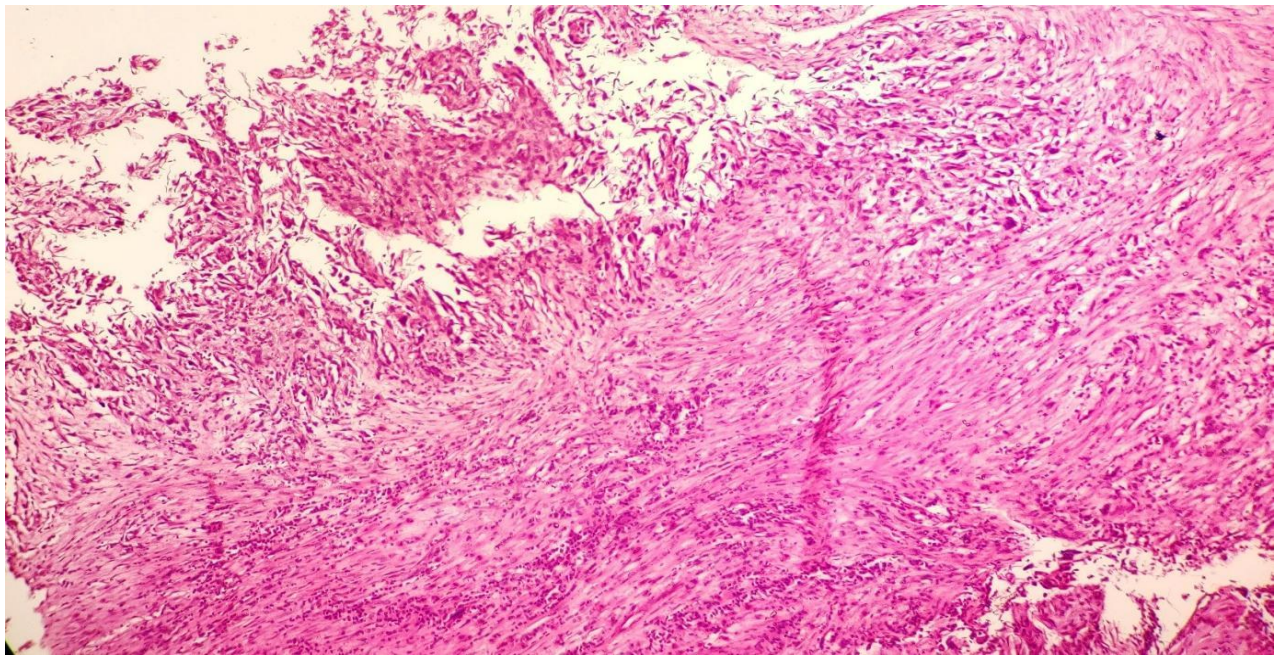


Figure 01: HPE (40X) showing Lymphoepithelioma like carcinoma with adjoining focus of undifferentiated carcinoma

Out of seven patients of Adenocarcinoma, four were moderately differentiated, two were well differentiated (**Figure 2**) and one was Mucinous Adenocarcinoma (**Figure 3**). Pyloric gland metaplasia was seen in four patients & cholesterosis in five patients. Majority of patients

(n=04,50.0%) were stage pT2a, two stage pT1a, one each stage pT1b and stage pT3. Lympho-vascular emboli were documented in one case. Perineural invasion was not seen in any of the eight patients of IGBC (Table 3).

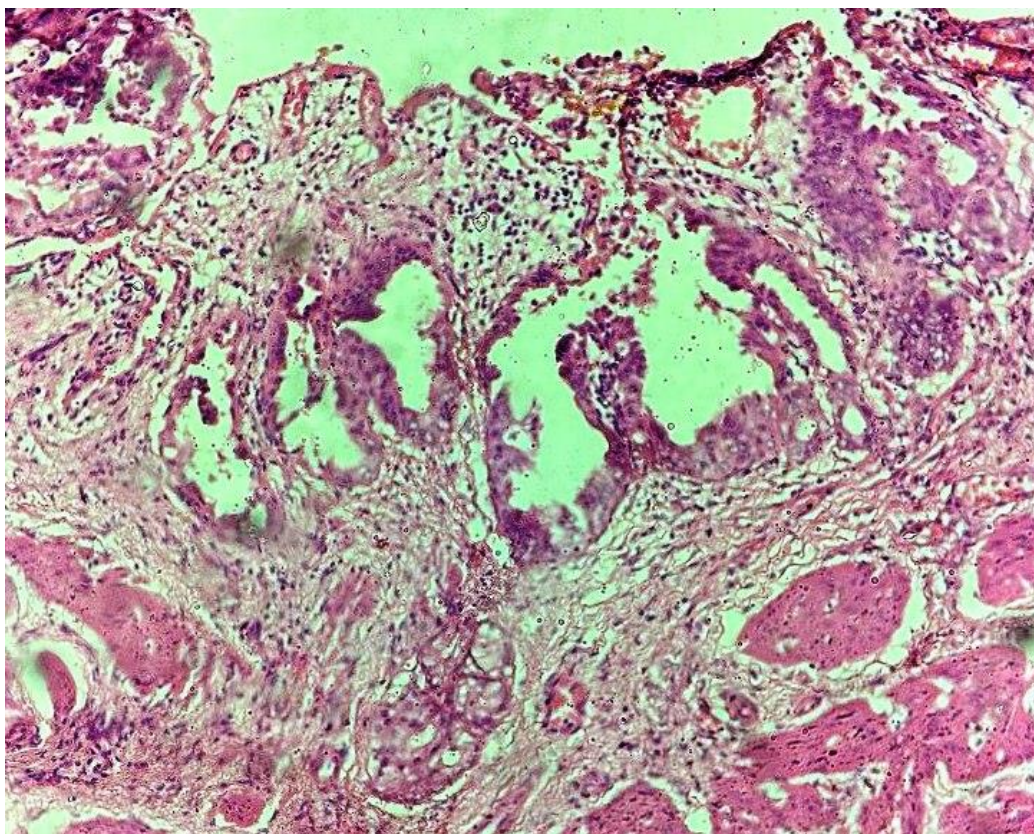


Figure 02: HPE (40X) showing well Differentiated carcinoma

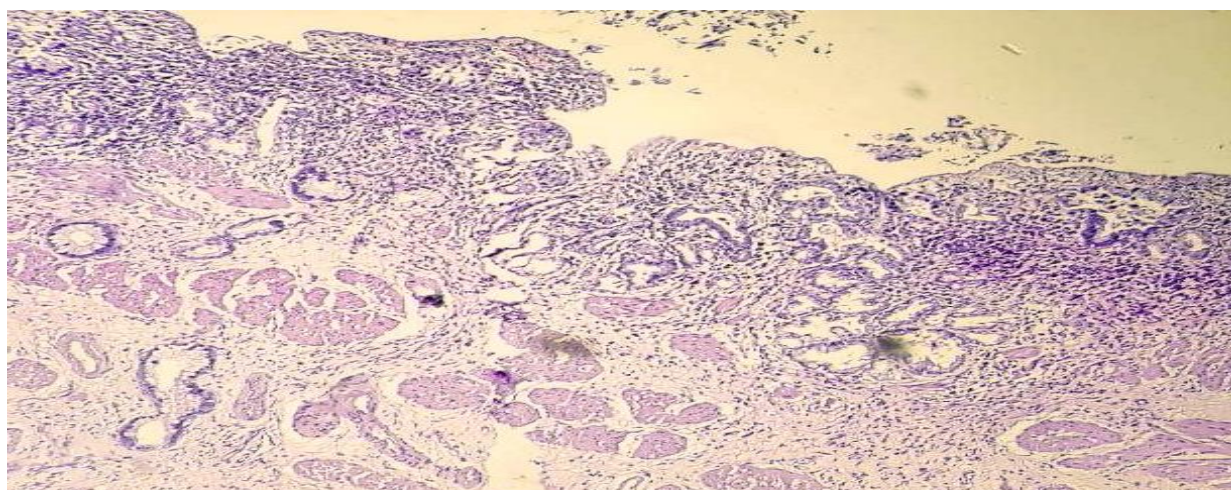


Figure 03: HPE (40X) showing mucinous carcinoma of gall bladder

DISCUSSION

The most common site of carcinoma in biliary tract is gall bladder and it is the fifth most common site of cancer in gastrointestinal tract. (9) In our study the incidence of IGBC was 0.9%

and our results are in the agreement with some studies from India, Nepal and Turkey (5, 11-18) (Table 4).

Table 4: Incidence of IGBC as reported by other studies

S. No.	Study	Place of study	Year	Incidence
1	Present study	Northern India	2023	0.94%
2	Jetley et al ¹¹	Northern India	2012	0.96%
3	Sangwan et al ¹²	Northern India	2015	1.90%
4	Utsami et al ¹³	Japan	2017	2.3%
5	Jha et al ⁵	Northern India	2018	0.41%
6	Poudel et al ¹⁴	Nepal	2020	1.67%
7	Acharyya et al ¹⁵	Eastern India	2021	10.12%
8	Jain et al ¹⁶	Northern India	2021	2.5%
9	Mauro et al ¹⁷	U.K.	2021	0.1%
10	Altioek et al ¹⁸	Turkey	2022	0.3%

Incidence of IGBC was significantly higher in Northern India due to dietary habits and lifestyle. In the present study, IGBC was seen more commonly in women and mean age was 52.4 % which was in agreement with the study by Jha et al, Ahl et al and Munshi et al in which IGBC were more common in female. (5,10,11) Male predominance was, however, seen in the study

by Utsami et al. (14) High incidence of IGBC in females is explained by the fact that estrogen hormones which increases cholesterol saturation in bile and increase the chances of cholelithiasis. Gall bladder stones especially multiple stones is the most prominent risk factor for IGBC. (20) In present study, 85.71% patients of IGBC showed multiple stones which was in concordance with



findings by Rita (93.70) and Altioek et al (100%) (3, 19) Patients of IGBC present with nonspecific symptoms like pain in abdomen, nausea and vomiting associated with common benign disorders of gall bladder (cholecystitis and cholelithiasis). Probability of IGBC is seldom suspected priorly in these patients. (10) Normal thickness of Gall bladder wall is 1-2 mm. Grossly, if wall thickness is >3mm, then it is said to be thickened. Thickened gall bladder wall is seen in a number of conditions like CC, xanthogranulomatous cholecystitis, and gall bladder cancer. (11) In present study thickened gall bladder wall was found in six patients (75%). So, it is very difficult to diagnose gall bladder cancer based on USG and gross findings. (13, 21) It is essential to do HPE of every cholecystectomy specimen which is done for benign reasons. Routine HPE of all cholecystectomy specimens is recommended so as to not miss any patients of IGBC. The same ensures that early carcinomas which have not caused abnormal gross morphology and have been overlooked on USG, can be picked up. Siddiqui, Torres, Nagarajan and Agarwal et al have recommended that routine histopathology of all resected specimens post cholecystectomy is the safest perspective to detect IGBC. (6, 22, 23, 24) However, Darmas and Emmet et al have supported selective histopathological evaluation of cholecystectomy specimens following thorough inspection of gross specimens. (25-27) Ninety-eight percent of

all gall bladder cancer are epithelial in origin, out of which 90% is adenocarcinoma. Grossly gall bladder cancer are diffusely infiltrating mostly whereas others present as intraluminal polypoidal growth. (28) In present study all patients of IGBC showed focal or diffuse wall thickening and seven patients were diagnosed adenocarcinoma. Pathological stage of gall bladder carcinoma determines treatment and prognosis. (15) IGBC patients are usually diagnosed in early stage for which treatment is simple cholecystectomy, no additional surgery is required. Five-year survival for early-stage tumour is approximately 90-100%. In present study three patients were in stage pT1, four were in stage pT2 and one patient was in stage pT3.

CONCLUSION

The present study analysed 847 cholecystectomy specimens over a period of two years, of which 8 cases were diagnosed as IGBC, giving an incidence of 0.9%. The high burden of gallstone disease in North India contributes to the large number of cholecystectomies performed in this region. As there were no definite clinical, USG, or preoperative indicators suggestive of malignancy in these cases, careful gross and microscopic examination becomes essential. Routine HPE of all cholecystectomy specimens is therefore recommended for early detection of IGBC and improved patient outcomes.

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