Section: Pathology

Original Research Article

INCIDENTAL CARCINOMA OF GALLBLADDER IN CHOLECYSTECTOMY SPECIMENS: A HISTOPATHOLOGICAL AUDIT FROM A TERTIARY CARE HOSPITAL IN NORTH INDIA

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ABSTRACT

Background: Gallbladder carcinoma is a highly aggressive malignancy with marked geographic variation, particularly prevalent in Northern India. A subset of cases are diagnosed incidentally following cholecystectomy for benign conditions. Careful histopathological examination of all cholecystectomy specimens is therefore essential for early detection, staging, and guiding further management.

Materials and Methods: A retrospective audit of 55 consecutive cholecystectomy specimens received in the Department of Pathology at a tertiary care hospital in North India was conducted. Specimens were grossed and sampled according to institutional protocols. Histopathological evaluation included tumor type, grade, T stage (AJCC), LVI, PNI, and cystic duct margin status. Data were analyzed using descriptive statistics, and results were compared with published literature.

Results: The majority of specimens showed benign pathology, most commonly chronic cholecystitis (72.7%). Incidental gallbladder carcinoma was identified in 2 cases (3.6%), both in females with gallstone disease. Histologically, both were adenocarcinomas: one well-differentiated (pT1b) and one moderately differentiated (pT2a). Dysplasia/carcinoma in situ was present in one case. One case showed positive cystic duct margin, LVI, and PNI, indicating adverse prognostic features.

Conclusion: Although uncommon, incidental gallbladder carcinoma remains a clinically significant finding in routine cholecystectomy specimens. Meticulous grossing, thorough sampling, and detailed reporting of tumor site, grade, invasion, and margin status are crucial for appropriate staging and to guide surgical decision-making. Close surgeon–pathologist collaboration is essential to ensure timely recognition and management of these cases.

Keywords: Gallbladder carcinoma; Incidental gallbladder cancer; Cholecystectomy; Histopathology; Cystic duct margin; Lymphovascular invasion; Perineural invasion; North India.

INTRODUCTION

India is one of the high endemic areas for Gallbladder cancer (GBC) and contributes to 10% of global GBC burden. Higher incidence is seen in north, north east, central and eastern states of India. It is an aggressive malignancy of the biliary tract that demonstrates a substantial geographical variation in incidence. Chronic gallstones, environmental exposure, infectious factors (as Salmonella typhi, Helicobacter spp.) socioeconomic status and age also are involved in its etiology.[1]

A portion of GBCs is incidentally detected in the cholecystectomy specimens performed for benign causes—an entity known as "Incidental Gallbladder Carcinoma (IGBC)". This is particularly relevant given that these can usually not be preoperatively diagnosed and risk of understaging (i.e. missing perineural or lymphovascular invasion, deep wall invasion) and undertreatment (i.e. absence of additional hepatic resection or lymphadenectomy when indicated) should always be taken into account in oncologic surgery. Research indicates that accurate determination of factors such as depth of tumor, grade and margin status including the cystic duct margin are important in selecting appropriate therapy and improving outcomes.[2,3]

Pathologically, grossing, sampling adequacy (including any suspicious lesions, wall thickening and/or mucosal abnormality), as well as the submission of relevant margins—particularly the cystic duct margin—are critical. Invasion patterns such as LVI, PNI, histologic subtype and grade, and distance to margins reported are factors that can affect re-resection or adjuvant treatment. However, there are also wide variations in institutional protocols as to the number of sections taken from each gallbladder, or indeed how much is actually sampled or what is evaluated at endpoints.[2,4]

Despite its clinical importance, region-specific audits of IGBC are limited, especially from tertiary care centres in Northern India. Many published series emphasize either surgical management or imaging, with fewer studies focusing in detail on histopathologic audit—incidence, stage distribution, margin positivity, and predictors of advanced disease.

MATERIALS AND METHODS

This study was a retrospective cross-sectional histopathological audit carried out in the Department of Pathology at a tertiary care teaching hospital located in North India, for duration from July 2024 to June 2025. A total of fifty-five consecutive cholecystectomy specimens received in the department over this period entered analysis. The cases diagnosed pre- or intra-operatively as gallbladder carcinoma, re-resection specimens and those with insufficient tissue material other than that with incomplete data were excluded. Age, sex and the indication for surgery were recorded from request forms and/or operation notes if requested.

All specimens were placed in 10% buffered formalin, grossed as per institution protocol and inspected for mucosal abnormalities, wall thickening, masses and suspect areas. From each case, representative tissue blocks were sampled from the fundus, body, neck, and cystic duct margin. In all cases additional blocks were taken from any lesion or plaque or area of induration. Sections stained with hematoxylin and eosin were reviewed for incidental gallbladder carcinoma (IGBC) and other pathological findings. Information on tumor site, size, histologic type and grade, depth of invasion (pT stage), presence of lymphovascular invasion (LVI) or perineural invasion (PNI) and status of cystic duct margin were collected for IGBC patients. Staging was determined according to the American Joint Committee on Cancer (AJCC) TNM classification, most recent version and advanced until then.

Observations were recorded and entered into a predesigned proforma and analyzed by descriptive statistics. Categorical variables were expressed as frequencies and percentages, whereas continuous variables were reported as mean (SD). The incidence of IGBC was the primary end point in 55 cases. Secondary endpoints included the distribution of histopathologic characteristics, margin status, and LVI/PNI. A chi-square test was used to determine the associations between specific clinicopathological parameters and an advanced stage of disease (≥p, T2), with $p < 0.05$ considered statistically significant. This audit was conducted with the approval of Institutional Ethical Committee and confidentiality of patient detail was retained at all times.

RESULTS

Table 1: Baseline characteristics of patients undergoing cholecystectomy (N = 55)

Variable	Category	n (%)
Age (years)	Mean ± SD	47.3 ± 12.1
Age groups	<40	16 (29.1)
	40–59	28 (50.9)
	≥60	11 (20.0)
Sex	Female	37 (67.3)
	Male	18 (32.7)
Indication for surgery	Symptomatic cholelithiasis	36 (65.5)
	Acute cholecystitis	9 (16.4)
	Biliary colic	6 (10.9)
	Polyp on imaging	2 (3.6)
	Other (e.g., dyspepsia)	2 (3.6)
Gallstones present	Yes	47 (85.5)
Operative approach	Laparoscopic	52 (94.5)
	Open	3 (5.5)

A total of 55 cholecystectomy patients, with a mean age of 47.3 ± 12.1 years, were enrolled in the study. More than half of the patients (50.9%) were aged 40–59 years, and 29.1% were younger than 40 years; only 20% were older than 60 years. A substantial female preponderance occurred, 67.3% being females versus 32.7% males. Most indications for surgery were symptomatic cholelithiasis (65.5%), acute cholecystitis (16.4%) and biliary colic (10.9%). Less common indications were imaging-detected polyps (3.6%) and other causes of nonspecific dyspepsia (3.6%). Gallstones were found in 85.5% reflecting the high correlation between gallstone disease and gallbladder pathology. Regarding the surgical method, most of the participants (94.5%) had undergone laparoscopic cholecystectomy and only a minority underwent open cholecystectomy.

Table 2: Histopathological spectrum of cholecystectomy specimens (N = 55)

Diagnosis	n (%)
Chronic cholecystitis	40 (72.7)
Acute cholecystitis	6 (10.9)
Chronic cholecystitis with cholesterolosis	3 (5.5)
Xanthogranulomatous cholecystitis	2 (3.6)
Adenomyomatosis	1 (1.8)
Polyp (non-neoplastic)	1 (1.8)
Incidental gallbladder carcinoma (IGBC)	2 (3.6)
Total	55 (100)

Histopathological analysis of 55 cholecystectomy specimens showed that chronic cholecystitis was the commonest diagnosis at 72.7% followed by acute cholecystitis in 10.9%. Chronic cholecystitis and cholesterolosis was detected in 5.5%, whereas xanthogranulomatous cholecystitis occurred in 3.6%. Other incidental findings were adenomyomatosis (1.8%) and non-neoplastic polyps (1.8%). Incidental gallbladder carcinoma (IGBC) was detected in two cases (3.6%) being significant for routine histopathological examination of all cholecystectomy specimens.

The histopathological diagnoses of the 55 specimens of cholecystectomy are portrayed in Fig.1. The most common diagnosis was chronic cholecystitis (72.7%), and the second one was acute cholecystitis (10.9%). Chronic cholecystitis with cholesterolosis was 5.5% and xanthogranulomatous cholecystitis in 3.6%. Adenomyomatosis (1.8%) and non-neoplastic polyps (1.8%) were rarer lesions. Two specimens (3.6%) demonstrated incidental gallbladder carcinoma (IGBC), hence stressed the need for histopathological examination of all cholecystectomy specimens.

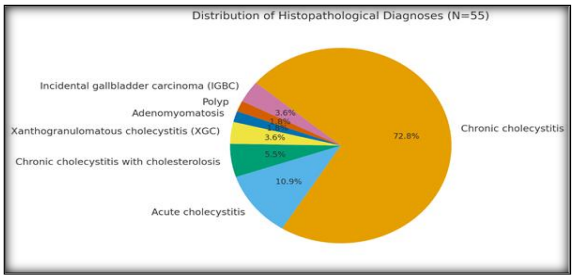

Figure 1: Distribution of histopathological diagnoses in cholecystectomy specimens (N = 55).

Table 3: Clinicopathological features of IGBC cases (N = 2)

Variable	Case 1	Case 2
Age/Sex	62/F	58/F
Indication	Symptomatic cholelithiasis	Symptomatic cholelithiasis
Gallstones	Present	Present
Approach	Laparoscopic	Laparoscopic
Tumor site	Fundus	Neck
Tumor size (cm)	1.8 × 1.5 × 1.2	2.6 × 2.2 × 1.8
Wall thickness (mm)	5	7
Distance to cystic duct margin (cm)	2.3	0.6

Of the two incidental gallbladder carcinoma cases, both patients were female aged late fifties to early sixties and had laparoscopic cholecystectomy for symptomatic cholelithiasis. Both were found to have gallstones. Location of the tumor differed: one originated from the fundus and another encompassed the neck of the gallbladder. The size of the tumors was 1.8 × 1.5 × 1.2 cm and 2.6 × 2.2 × 1.8 cm with the associated wall thickening as 5 mm and 7 mm respectively. The tumor was 2.3 cm away from the cystic duct margin and near the fundal lesion, while for the neck lesion it was closer (only a 0.6 cm distance from the cystic duct margin), demonstrating surgical relevance in this case.

Table 4: Histopathological profile of IGBC (N = 2)

Feature	Category	n
Histologic type	Adenocarcinoma, NOS	2
Tumor grade	Well differentiated	1
	Moderately differentiated	1
Dysplasia/CIS	Present	1
Pathologic T stage (AJCC)	T1b	1
	T2a	1

Histopathology of those two gallbladder cancer cases showed that all of them were adenocarcinoma, no specific type. In relation to tumor differentiation, one was well-differentiated and the other had moderate differentiation.

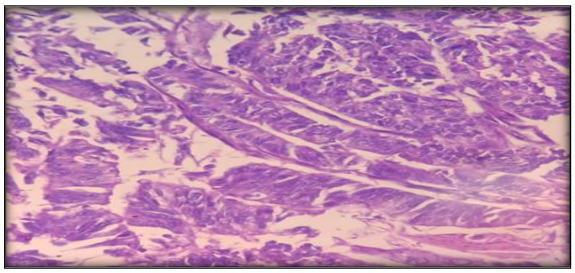

Figure 2: High-power image of Carcinoma gall bladder

An associated intraepithelial dysplasia/cis (CIS) focus was recognized in one of the cases. One case was classified as pT1b (invasive to muscularis propria), and the other as pT2a (invading serosa on peritoneal aspect without penetration through peritumoral tissue). This underlines the fact that these incidental carcinomas can be at an early as well as a relatively advanced stage, thereby emphasizing the necessity of inspection and microscopic evaluation of all material in question.

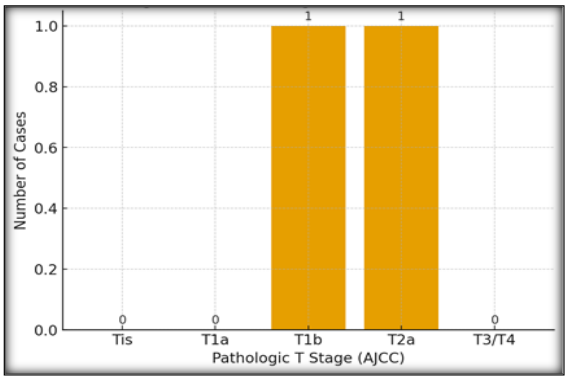

Figure 3: Pathologic T-stage distribution of incidental gallbladder carcinoma cases (N = 2).

The T-stage of incidental gallbladder carcinoma is reported in Figure 3. These were classified as pT1b, signifying invasion of the proper muscle layer, and pT2a, penetrating perimuscular connective tissue outside the peritoneum, respectively. None of the in sitû (Tis), T1a and even advanced T3/T4 cases were detected. This observation shows that despite the rarity, incidental carcinomas may present at both early and intermediate pathological stages justifying a routine histopathological examination for accurate staging and remodeling of subsequent treatment.

Table 5: Prognostic factors and margins in IGBC (N = 2)

Factor	Category	n
Lymphovascular invasion (LVI)	Present	1
Perineural invasion (PNI)	Present	1
Cystic duct margin	Positive	1
	Negative	1
Stage grouping	Early (≤T1b)	1
	Advanced (≥T2)	1

Analysis of prognostic factors in 2 IGBC cases revealed lymphovascular invasion (LVI) and perineural invasion (PNI), one each. The cystic duct margin was positive in the neck GB case, and negative for the fundal lesion. One patient was categorized as early stage (≤T1b) and the other was classified as advanced disease (≥T2). These results emphasize the heterogeneity of IGBC and underscore the significance of detailed data analysis on invasion and margin status, with a direct bearing on prognosis and potential need for re-resection.

Table 6: Comparison of baseline characteristics between benign pathology and IGBC

Variable	Benign (n=53)	IGBC (n=2)	p-value*
Mean age (years)	46.9 ± 11.5	60.0 ± 2.8	0.04†
Female sex (%)	34 (64.2)	2 (100)	0.32‡
Gallstones present (%)	45 (84.9)	2 (100)	1.00‡
Laparoscopic surgery (%)	50 (94.3)	2 (100)	1.00‡

When baseline characteristics of patients with benign pathology (n = 53) were compared to those with incidental gallbladder carcinoma (n = 2), the mean age of patients with IGBC was higher (60.0 ± 2.8 years) than those with benign conditions (46.9 ± 11.5 years), and this difference reached statistical significance (p = 0.04). Although both IGBC cases were female, the association between sex and malignant pathology was not statistically significant (p = 0.32). Similarly, the presence of gallstones was universal in IGBC (100%) compared to 84.9% in benign cases, but this difference was not significant (p = 1.00). Almost all patients in both groups underwent laparoscopic cholecystectomy, with no significant difference in surgical approach (p = 1.00). While interpretation is limited by the small number of IGBC cases, these findings suggest that older age may be a potential risk factor, whereas sex, gallstones, and surgical approach did not show a statistically meaningful difference.

DISCUSSION

In this review of 55 cholecystectomy specimens, we found IGBC in 3.6% (2/55) patients which is slightly higher than other Indian and worldwide reports where

the range of IGBC recurrence lies somewhere between approximately 0.3% to as high as 2.0% of cholecystectomies.[4,5] This higher rate, although based on modest numbers, may potentially represent regional differences as well as referral or selection bias and emphasize that when a routine cholecystectomy is performed, carcinoma might be even more frequent than generally accepted.

Chronic cholecystitis was most common (≈72.7%), followed by acute (~10.9%); other benign lesions (cholesterolosis, adenomyomatosis, polyps) were less common. The identification of two IGBCs (3.6%) among this mixture demonstrates the importance of standard histopathologic examination; grossly unremarkable gallbladders may conceal neoplasms. This is consistent with those (e.g., Indian audits) where carcinomas were detected in the specimens where there was not much pre-operative suspicion or gross abnormality.[6]

In the malignant cases, their histologic type was adenocarcinoma, NOS in one well differentiated and 1 moderately differentiated case. One case showed high-grade dysplasia / carcinoma in situ in the surrounding mucosa. These results are in line with the data showing that incidental gallbladder cancer is frequently associated with dysplastic changes.[7,8]

The T-stage distribution (one patient T1b; one patient T2a) supports that incidental tumors may range from early to intermediate invasive stages. This trend is consistent with other series in which a significant proportion of incidental GBCs are T1 / T2 at discovery, which has clinical implications because T1a carcinoma can often be managed with simple cholecystectomy and lesions ≥ T1b or T2 may signal the need for more extensive surgery up to margin evaluation.[4,9]

One IGBC case was positive for cystic duct margin; both LVI and PNI were detected in one case. These characteristics have long been known as poor prognostic factors. For example, Vega et al. concluded that positive cystic duct margin at index cholecystectomy is an independent prognostic factor for IGBC.[10] There are clinical implications of margin status: in many centers, a positive cystic duct margin results in resection recommendation or wider surgical clearance.[4]

Both LVI and PNI are common and consistently found to be correlated with more aggressive tumor behavior and worse survival in gallbladder carcinoma.[1,11] In GBC in a more general sense, these features are associated with increased T and N stages of disease, probability of recurrence and poorer overall survival.[1,12] Although our sample size is too small for survival analysis or multivariable modeling, the occurrence of LVI and PNI in one of two malignant cases serves as a reminder that even among incidental tumors not all are "low-risk."

The IGBC incidence has been reported by Indian studies as higher, with an approximation to 0.5-1% in large number of cholecystectomies,[4,6-8] For instance, Butti et al. analyzed 906 cholecystectomies and reported IGBC ~1% of the time.[6] The higher proportion in our review may be explained by the selection of all specimens (some possibly originating from symptomatic gallstone disease) or chance variation because of the small size.

Female preponderance, associated high incidence of gallstones and laparoscopic approach as an operative method are the same trends found in Indian literature.[6,13] Additionally we feel that the tumor size and distance from cystic duct margin in our cases are also following known risk profiles of having higher stage or margin positivity if tumors are closer to cystic duct and larger in size.[10]

The findings of this audit have several important clinical implications. First, effective surgeon–pathologist collaboration is crucial. In one of our cases, the tumor was located close to the cystic duct margin (0.6 cm) and showed both lymphovascular and perineural invasion. Such adverse features highlight the need for meticulous pathology reporting of tumor site, size, grade, depth of invasion, and margin status. Surgeons must be promptly informed when margins are positive or when the disease is staged as ≥T1b, so that timely decisions regarding re-resection can be made. Second, standardized grossing and sampling protocols are essential. Representative sections must be taken from all key regions of the gallbladder—fundus, body, neck—as well as the cystic duct margin, with careful inspection for subtle mucosal abnormalities or wall thickening. Although some authors advocate selective sampling based on gross abnormalities, several studies demonstrate that carcinomas can arise even in macroscopically normal gallbladders, thereby justifying routine and comprehensive sampling.[6] Finally, in terms of management, treatment should be stage-guided. For T1a tumors with negative margins, simple cholecystectomy is generally considered sufficient, whereas patients with T1b, T2a lesions, or positive margins should be evaluated for extended surgical procedures, such as hepatic resection or lymph node dissection, to optimize oncologic outcomes.[4,13,14]

CONCLUSION

In this histopathological audit of 55 cholecystectomy specimens, incidental gallbladder carcinoma (IGBC) was identified in 3.6% of cases, a frequency slightly higher than that reported in most Indian series, reaffirming the need for routine microscopic examination of all specimens. Both IGBC cases occurred in females with gallstone disease and were adenocarcinomas—one well-differentiated (pT1b) and the other moderately differentiated (pT2a)—demonstrating that incidental tumors may present across both early and intermediate stages. Importantly, adverse prognostic factors such as lymphovascular invasion, perineural invasion, and a positive cystic duct margin were observed in one case, highlighting their relevance for surgical decision-making. These findings underscore that meticulous grossing, comprehensive sampling, and detailed histopathological reporting are critical for

accurate staging and guiding further management, while close collaboration between surgeons and pathologists remains essential to optimize patient outcomes.

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