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Original Research Article

# Incidentally Discovered Gall Bladder Carcinomas on Routine Histopathology Following Laparoscopic Cholecystectomy

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**Conflict of interest: Nil**

**Abstract:**

**Background:** Gall bladder carcinoma accounts for 98% of all the gall bladder malignancies and it is the fifth most common malignancy of the gastrointestinal tract worldwide. Most incidental gall bladder cancers are detected only after pathological examination of the excised surgical specimens. This study was aimed at detecting the incidence of gall bladder carcinomas which were diagnosed incidentally on histopathological examination of gall bladders which were sent for gall stone disease and cholecystitis in our center and the need for routine versus selective histopathological examination of cholecystectomy specimens.

**Material & Methods:** We retrospectively reviewed 1709 cholecystectomy specimens sent for histopathology in the pathology department after cholecystectomy in the study period from March 2015 to October 2021. Clinical details including clinical presentation, preoperative ultrasound (USG) findings, laboratory data, and surgical procedures as well as outcome and macroscopic features were retrieved.

**Results:** We identified 16 cases of incidental gall bladder cancer (IGBC), consisting of 12 women and 4 men ranging in age from 34 to 75 (60.5 ± 13.2, years with female preponderance) after pathological study of 1709 resected gall bladders. Mean gallbladder thickness in these cases was 0.8±0.5 cm, and 96% cases of IGBC were associated with cholelithiasis. No correlation was seen between the age of patient and gallbladder thickness. Final diagnosis of IGBC was made on microscopical examination of gall bladder with tumor cells infiltrating the lamina propria in two cases (pT1a), muscularis propria in 10 cases (pT1b), and serosa in the remaining 4cases (pT2).

**Conclusions:** The rate of incidental gallbladder carcinoma in our study was 1.06%. This strategy of increased early intervention adds to the advantage of higher chances of gallbladder cancer detection in early stages, and thus better prognosis. IGBC is a clinical disguise which often escapes the radiological diagnosis and comes as pathological surprise. Histopathological examination of cholecystectomy specimens remains the gold standard for the detection of this occult, yet rigorous malignancy and assessment of the depth of invasion in IGBC and further management.

**Keywords:** Incidental Gall Bladder Cancer (IGBC), Gallbladder cancer (GBC), American Joint Committee recommendations for cancer staging (AJCC).



## Introduction

Incidental gallbladder cancer is relatively rare, with an incidence ranging between 0.19 and 5.5% of all the cholecystectomies for benign disease, and carries a poor prognosis. Currently, in the literature, there appears to be some controversy about whether all gallbladder specimens should be sent for routine histopathology. The aim of this study was to find the incidence of incidental gallbladder cancer in cholecystectomies specimen for early management and better prognosis and to investigate the need for either routine or selective histopathological evaluation of all gallbladder specimens following cholecystectomy in our institution. Gallbladder cancer (GBC) is the fifth most common cancer of the gastrointestinal tract and the most common cancer of the biliary tract. GBC has been associated with a poor prognosis [1]. According to the Indian cancer registry data, incidence of GBC is 0.8%–1%. While New Delhi and Bhopal are the leading cities, lowest incidence is seen in Chennai.[2] Risk factors include cholelithiasis, calcified gallbladder wall, adenomatous polyp, obesity, estrogen, choledochal cyst, and chemical carcinogens.[3] Of these, gallstones are a well-established risk factor associated with the development of GBCs in 75%–90% of cases.[4] In this era of laparoscopic cholecystectomy (LC), increased rate of incidental gall bladder cancer detection in early stages is resulting in better prognosis[5] . Rate of Incidental Gallbladder Cancer (IGBC) after LC ranges from 0.5% to 2.1% [6]. However, only 0.5–3% of patients with cholelithiasis will develop GBC [7].

## Materials and Methods

**Study design:** Observational study

**Study area:** Department of Pathology, FH Medical College, Etmadpur, Agra

**Study period:** March 2015 to October 2021

**Study population:** Cholecystectomy specimens were sent in Department of Pathology.

**Inclusion Criteria:**

1. Patients with ASA Grading I and II
2. Patients between 18-80 years of age.

**Exclusion Criteria:**

1. Patients with ASA Grading III, IV and V.
2. Patients below 18 years and above 80 years of age.
3. Pregnant patients.
4. Patient with a cardiovascular abnormality.
5. Patient refusal to give written consent for the study.
6. Poor performance status

**Methodology:** During 7 years a total of 1709 cholecystectomy specimens were sent in our department of pathology. The patients were 607 men and 1102 women with the mean ± SD age of 58 ± 12 range (25-79) years. Of them, 16 patients were diagnosed as having gallbladder adenocarcinoma after pathological studies of the surgical specimens.

**Diagnostic criteria** Diagnosis of IGBC was made on formalin-fixed, paraffin embedded, hematoxylin and eosin-stained sections and pathological staging of carcinoma was done according to American Joint Committee recommendations for cancer staging (AJCC).

The gallbladder wall was said to be thickened if it was found to be >3 mm on preoperative imaging or histopathological examination. The normal thickness of the gallbladder wall is reported to be 1-2 mm.

There were two more cases with the preoperative diagnosis of cancer, which were not included in this study. It means that more than 89% of the gall bladder cancers in our center were incidentally detected. Both gall bladder cancers with preoperative diagnosis (non-incidental cases) were in advanced stages with liver metastasis at the time of operation. Patients demographic variables (age, sex), preoperative radiographic diagnosis (stone, polyp), laboratory findings, histopathological staging (early: Tis, T1a, late: T1b, T2-4) according to AJCC 8th edition, overall survival and mortality were documented.

**Observation Table**

**Table no: 1 Distribution of study participants by Gender and Age (n=1709)**

| Distribution of study participants by Gender and Age (n=1709) | | | | |
|---|---|---|---|---|
| **Age group** | **Male [607]** | | **Female [1102]** | |
| | **n** | **%** | **n** | **%** |
| **<=30** | 58 | 21.74 | 105 | 78.26 |
| **31-40** | 192 | 25.0 | 464 | 75.00 |
| **41-50** | 177 | 41.67 | 345 | 58.33 |
| **51-60** | 109 | 37.5 | 186 | 62.5 |
| **>60** | 71 | 43.48 | 82 | 56.52 |
| **Mean Age** | **45.25** | | **48.44** | |

**Table 2: Gall Bladder Adenocarcinoma after Pathological Study of the Surgical Specimens**

| | **Cholilitiasis** | **Adenocarcinoma** | **Percentage** |
|---|---|---|---|
| **Female** | **1090** | **12** | **1.10** |
| **Male** | **603** | **04** | **.66** |
| **Total** | **1709** | **16** | **1.06** |

**Results:**

Total 1709 specimens of gallbladder were obtained from cholecystectomy done for clinically and radiologically established benign gallbladder disease. In all these cases, there was no suspicion of any kind of gallbladder malignancy after complete clinical and radiological evaluation of the patient. We performed gross and microscopic examination of all these cases and observed that among all specimens 16 cases (1.06%) were incidentally diagnosed as having gall bladder adenocarcinoma after pathological study of the surgical specimens. They were 12 female and 4 male patients. Age of them was from 34 to 75 (60.5 ± 13.2) years. Patients presented with right upper quadrant abdominal pain, jaundice, anorexia or weight loss. After pathological study and diagnosis, all of them were diagnosed as being moderately differentiated adenocarcinoma. (Fig 1&2).

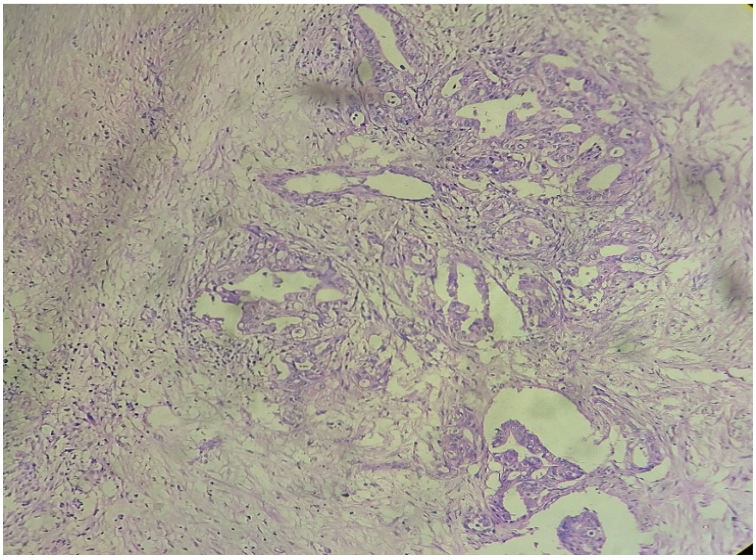

**Figure 1: Incidental adenocarcinoma of gall bladder infiltrating muscular layer**

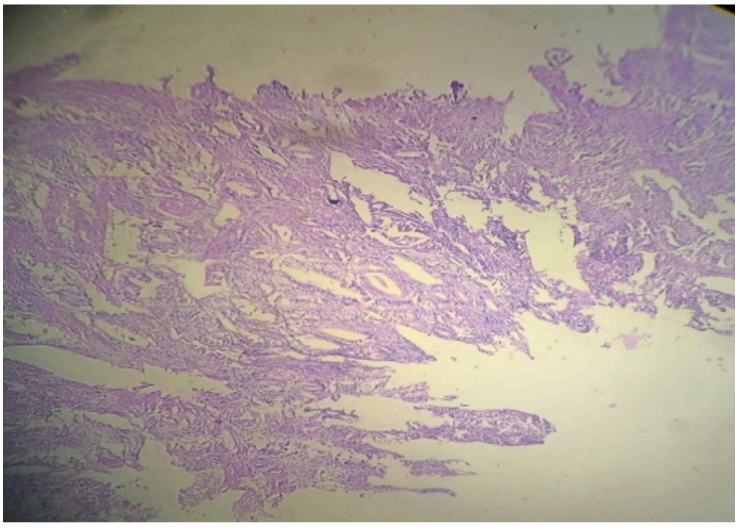

**Figure 2: Incidenatal adenocarcinoma of gall bladder at high power(40X)**

After that, staging was done, which showed T1 in 12 patients and T2 in other 4 patients. No significant association was found with age of the patient and thickness of gall bladder with pathological stage of the tumour, p value 0.064 and 0.034 respectively.

**Discussion**

Gall bladder adenocarcinoma is the most common malignancy of the biliary tract. Increasing laparoscopic cholecystectomies as the gold standard procedure have caused more and more detection of incidental gall bladder cancers. The incidence of IGBC is reported to be 0.2% to 3.3% of all cholecystectomies specimens of benign gallbladder disease [8-11]. In our study, IGBC was found to be 1.06% and our results are similar to some studies from India and Nepal [9,10].

Laparoscopic cholecystectomy is considered to be gold standard for symptomatic gall stones. As a routine every specimen is sent for histopathological examination postoperatively. Incidentally finding gall bladder cancers in those specimens is around 0.5–1.1%. The aim of the study by Talreja V et al is to identify those preoperative and intraoperative factors in patients with incidental gall bladder cancer to reduce unnecessary work load on pathologist and cost of investigation particularly in a developing world.

Gallbladder carcinoma was incidentally found in 11 cases. Macroscopic abnormalities of the gallbladder were found in all those 11 patients. In patients with a macroscopically normal gallbladder, there were no cases of gallbladder carcinoma. So, to conclude, preoperative and operative findings play a pivotal role in determining incidental chances of gall bladder malignancy.[12]

Emmett CD et al compared routine versus selective histological examination after cholecystectomy to exclude incidental gallbladder carcinoma. They concluded that the incidence of incidental gallbladder carcinoma (IGBC) is low and it has

therefore been suggested that macroscopic inspection of the gallbladder by the surgeon, followed by selective histological examination of abnormal specimens, may be safe and cost saving.[13]

Similar study by Alabi A et al who also studied routine versus selective histological examination of incidental gallbladder cancer after cholecystectomy. The records of all patients who underwent a cholecystectomy (laparoscopic and open) for gallstone disease over a 5-year period were reviewed retrospectively in a single university teaching hospital. The incidence rate was 0.14%. All patients with incidental gallbladder cancer had macroscopically abnormal specimens. A selective rather than routine approach to histological evaluation of gallbladder specimens especially in those with macroscopic abnormalities should be employed. This will reduce the burden on the pathology department with potential cost savings.[14]

The work of Hasan A et al aims to study the incidence and the clinical significance of detecting unusual gallbladder findings upon the RHPE of the referred cholecystectomy specimens to a histopathology laboratory section at a referral hospital in Saudi Arabia during one year period. The results of histopathological examination of gallbladder specimens showed that 0.7% cases of incidental carcinomas and other three cases (0.7%) of dysplasia. Eosinophilic carcinomas were detected in two cases (0.45%), gallbladder complete septum was found in one case, and one case of Phrygian cap anomaly. RHPE of cholecystectomy materials are required to confirm the final diagnosis and document any other pathology. Failure to detect incidental occult carcinoma may be catastrophic, given the poor prognosis ,so they advocate histopathology of all specimens is a must.[15]

Siddiqui FG et al also advocate that selective approach for sending cholecystectomy specimens for histopathology results in missing discrete pathologies such as premalignant benign lesions such as porcelain gallbladder, carcinoma-in-situ, and early carcinomas. To avoid such blunders therefore, every cholecystectomy specimen should be routinely examined histologically. All gallbladder specimens were sent for histopathology, irrespective of their gross appearance.[16]

Jha V et al also evaluated the utility of all histopathological evaluation of routine cholecystectomy specimens and findings were similar as found in our study.[17]

Radiological and clinical features of benign gall bladder disease can mask gall bladder adenocarcinoma, which causes mistaken diagnosis of cholelithiasis and cholecystitis instead of gall bladder cancer. The clinical features are very similar in early stages of cancer and benign diseases. The most common ultrasonographic finding in gall bladder cancer is wall thickening and it is very rare for gall bladder cancer to create a definite mass.[18,19]. In our study only four cases out of the 16 incidental gall bladder cancers showed mild gall bladder wall thickening and in all the others, there was just cholelithiasis or completely normal gall bladder, which makes it impossible to diagnose a cancer based on sonographic findings before surgery. [20,21]

In the literature, there has been debate on routine versus selective histological assessment of benign gallbladder specimens after cholecystectomy. Most of the studies in the literature recommend that the routine histopathological examination of all post-cholecystectomy specimens is the safest approach to increase detection of IGBC.

The diagnosis of gall bladder cancer by computed tomography (CT) is accurate and reliable; however the ability to identify early-stage cancer on CT is still not promising and its accuracy is about 85%.[22] Most of the incidental gall bladder cancers are early stage and in our cases also all of the incidental gall bladder adenocarcinomas were either T1 or T2. According to the recent consensus, simple or laparoscopic cholecystectomy is an adequate procedure for T1 stage. Radical surgery is necessary for T2 and higher stages using segmental hepatectomy as well as hilar lymphadenectomy. [22-25]

## Conclusions

IGBC is diagnosed for the first time by the pathologist while doing routine histopathological examination of benign gallbladder specimens and presents as a surprise to histopathologist on microscopic examination. There is no definitely identifiable symptom and sign for prediction of this disease in the cases operated on with the impression of benign gall bladder diseases especially cholelithiasis and cholecystitis. Radiological findings including ultrasonography and CT would not add much information before surgery, in early stages of gall bladder cancer. The most important predictor of prognosis in incidental gall bladder cancer is the stage of the tumor. T1 cases have better prognosis even with simple or laparoscopic cholecystectomy.

## Declarations:

**Availability of data and material**: Department of Pathology, FH Medical College, Etmadpur, Agra

**Code availability**: Not applicable

**Consent to participate**: Consent taken

**Ethical Consideration**: There are no ethical conflicts related to this study.

**What This Study Add to Existing Knowledge**

The histopathological spectrum of gallbladder is extremely variable. Incidental diagnosis of carcinoma gall bladder is not rare; if the protocol of routine histopathology of all gallbladder specimens is not followed, subclinical malignancies would fail to be identified with disastrous results. We strongly recommend routine histopathology of all cholecystectomy specimens.

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