

## Incidence and Clinicopathological Profile of Incidental Gallbladder Carcinoma in Routine Cholecystectomy Specimens: A Retrospective Observational Study

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### Abstract:

**Background:** Incidental gallbladder carcinoma (IGBC) is defined as a cancer that is found in the gallbladder during or soon after a cholecystectomy for a presumed non-cancerous condition. It is often missed in the pre-operative diagnosis as the symptoms resemble those of chronic cholecystitis or cholelithiasis.

**Objective:** To study incidence and clinicopathological profile of incidental gallbladder carcinoma in routine cholecystectomy specimen at Nalanda Medical College and Hospital, Patna, Bihar.

**Methods:** The study was a retrospective observational study that involved 190 patients who had cholecystectomy, either elective or emergency, performed within a 1-year period for what was supposed to be a benign gallbladder condition. Operative findings, patient records and histopathological reports were reviewed. Demographic, clinical, pathological, staging and outcome parameters were analyzed in the carcinoma diagnoses made after the postoperative pathological examination.

**Results:** Gallbladder carcinoma was found incidentally in 3 of 190 patients (1.58%). The clinical symptoms were not specific, most cases being presented with epigastric pain, dyspepsia and nausea/vomiting. Female predominance and age 52-68 years was observed in IGBC cases. Two cases had gallstones. Histological diagnosis revealed adenocarcinoma in most cases, with one case presenting Aden squamous carcinoma. Two cases were detected at an early stage and survived, while one case in T2 stage died due to disease progression.

**Summary:** Incidental gallbladder carcinoma is rare and yet clinical in nature. All cholecystectomy specimens should be routinely histopathologically examined, which is particularly important in high-risk areas to detect early and enhance the patient's management.

**Keywords:** Incidental Gallbladder Carcinoma, Cholecystectomy, Gallstones, Histopathology, Adenocarcinoma, Clinicopathological Profile.

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### Introduction

The surgical removal of the gallbladder (cholecystectomy) is one of the more common procedures performed in the world and is the treatment of choice for symptomatic gallstone disease and other benign gallbladder disorders. Gallstones are a significant health problem and approximately 10 million people are impacted by gallstone disease worldwide. In developed countries, such as the United States, about one million new cases of gallbladder disease are reported each year and over half a million cholecystectomies are performed each year [1]. The same

pattern has been seen in India where gallstone is a frequent surgical problem, particularly in the middle-aged and elderly females. While most of the cholecystectomy specimens show pathological changes that are not malignant, a small percentage of specimens may contain unexpected malignant lesions which are only identified after the specimen is surgically removed and then examined by the pathologist.

Gall bladder cancer or Gall bladder carcinoma (GBC) is the most prevalent form of malignant dis-

ease of the biliary tract, one of the most aggressive gastrointestinal cancers [2-3]. Although relatively rare, compared to other gastrointestinal cancers, gallbladder cancer is a rapidly growing, locally infiltrative and late stage clinically presented aggressive disease, which gives rise to a high mortality rate. There is significant geographic variation of the disease, and high incidences are reported from South America, the eastern part of Europe, and some parts of Asia. This is because the Northern Indian population, particularly the Gangetic belt consisting of Bihar, Uttar Pradesh and West Bengal, is considered to be at high risk of gall bladder carcinoma [4]. This rising prevalence is multifactorial and is due to environmental, genetic, dietary, and socioeconomic factors, the definite etiopathogenesis of which is only partially understood.

Multiple risk factors have been suggested for gallbladder carcinoma. In these, cholelithiasis is the most significant predisposing factor and is seen in almost 70-90% of the patients [5]. Gallstones cause chronic irritation of the mucosa of the gall bladder, resulting in recurring inflammation, epithelial dysplasia and the development of malignancy. Other reported risk factors are chronic cholecystitis, porcelain gallbladder, gallbladder polyps, congenital abnormalities of the biliary tract, obesity, female gender, and some infectious organisms [6]. Although gallstones and gallbladder cancer are closely linked to each other, a small proportion of gallstone patients eventually develop malignancy, indicating that other pathogenic mechanisms exist [7].

The clinical presentation of gall bladder carcinoma is one of the major issues in its management. The clinical features of RUQ pain, dyspepsia, nausea, vomiting and intolerance to fatty foods are often indistinguishable from those of the non-cancerous gallbladder disorders (particularly chronic cholecystitis and cholelithiasis) [8]. Thus, the diagnosis of gallbladder carcinoma is still difficult in the preoperative stage, and many cases are diagnosed at advanced stages of the disease. The sensitivity of the detection of the disease before the surgery is still relatively poor, especially when using modern imaging techniques like ultrasonography, computed tomography and magnetic resonance imaging [9]. Consequently, a significant percentage of gallbladder cancers are only discovered during surgery or when pathological examination of the specimens taken for presumed benign disease is undertaken.

Incidental gallbladder carcinoma (IGBC) is the term that is used to describe the detection of carcinoma in the gallbladder in the absence of any suspicion of malignancy on the part of the surgeon during cholecystectomy for another benign condition [10]. The frequency of IGBC has been reported in a wide range of populations and health care environments ranging from about 0.2% to 3% of routine cholecystectomy specimens [11]. The incidence of gall bladder

cancer may be much higher in areas where gall bladder cancer is common like in Northern India. Incidental carcinoma is of particular clinical significance as these are typically detected at an earlier stage, affording a much better chance for a cure and a better prognosis than symptomatic gallbladder cancers [12].

Whether or not routine histopathological evaluation of all cholecystectomy specimens remains indicated remains controversial. Others recommend a selective biopsy, where only those specimens exhibiting grossly suspicious macroscopic features are subjected to histopathology to decrease workload and health-care expenditure [13]. Several studies, however, have shown that a large percentage of incidental gallbladder carcinoma can be asymptomatic macroscopically and may be missed if they are not routinely checked by a pathologist [14]. Routine histopathological examination could be an important tool for the detection of occult malignancies at potentially curable stage in high-incidence regions like Bihar where gall bladder carcinoma is a serious public health problem.

It is important to evaluate the clinicopathological features of incidental gall bladder cancer to gain insight into the natural history of the disease and to shape management approaches. The clinical presentation, location of the tumor, age and sex are important factors to understand the behavior of the disease and to predict its prognosis. Other factors that can be helpful are the presence of gallstones, histological type, tumor differentiation and pathological stage. But there is a lack of data on incidence and clinicopathological patterns of incidental gallbladder cancer from Bihar and neighboring regions.

Hence the present retrospective observational study was conducted in the Department of General Surgery Nalanda Medical College and Hospital Patna, Bihar to find out incidental diagnosis of gall bladder carcinoma in routine cholecystectomy specimens and to study the demographic, clinical and histopathological profile of the patients affected by them. The results of this study could add to the current evidence and could be a valuable tool to solidify the value of routine histopathological analysis of cholecystectomy samples in this high-risk population.

### Methodology

**Study Design:** This study aimed to find the incidence and clinicopathological profile of incidental gallbladder carcinoma (IGBC) in the routine cholecystectomy specimen. This study analyzed hospital records, findings at surgery and histopathological reports of patients having cholecystectomy between 2020 and 2026.

**Study Area:** The study was carried out in the Department of General Surgery, Nalanda Medical College and Hospital (NMCH), Patna, Bihar, India.

**Study Duration:** This study was conducted for one year from January 2025 to December 2025. Medical records and histopathological reports of eligible patients that had undergone cholecystectomy in this period were taken back and analyzed.

**Sample Size:** In total, 190 patients who had routine cholecystectomy, and met the inclusion criteria, were included in the study.

**Study Population:** All patients undergoing elective or emergency cholecystectomy for presumed benign gallbladder disease, including symptomatic cholelithiasis, chronic cholecystitis, acute cholecystitis, gallbladder polyps and other nonmalignant gallbladder diseases, were included in the study population. Gallbladder specimens respected were subjected to routine histopathological examination in line with the institutional protocol.

**Data Collection:** Hospital medical records, operation theatre registers, discharge summaries, histopathology records and follow-up medical records were used as sources of data. A structured data collection proforma was used to extract data on demographic characteristics (age and sex), clinical presentation, radiological findings, operative details, gross pathological findings, histopathological diagnosis, tumor characteristics, pathological staging and postoperative outcomes. Incidental gall bladder cancers were recognized and studied in great detail in patients who had been diagnosed with the disease at the time of surgery.

#### Inclusion Criteria

- Patients who underwent routine cholecystectomy for benign gall bladder diseases during the study period.
- The gallbladder specimens that were sent for histopathology.
- Incidental gallbladder carcinoma, which was discovered after surgical removal of the gallbladder.
- Complete medical and histopathological records available for review.

#### Exclusion Criteria

- Preoperative clinical/radiological/laboratory suspicion of gallbladder malignancy.
- Preoperative patients with a known diagnosis of gallbladder carcinoma.
- Patients with surgical operations primarily diagnose and/or treat gall bladder cancer.
- Uncompleted medical records or missing histopathological reports.

- Patients who have already developed a recurrent or metastatic gallbladder cancer.

**Study Procedure:** The records of all patients who had cholecystectomy during the study period were obtained from the Department of General Surgery and Department of Pathology. Histopathological reports have been checked for incidental gallbladder carcinoma diagnosis. Incidental gallbladder carcinoma cases were defined as those with histopathologic diagnosis and the incidence was calculated by dividing the number of incidental carcinoma cases by the number of cholecystectomy specimens submitted for routine pathology. Clinicopathological parameters such as age, sex, symptoms, indication for surgery, gallstone status, tumour type, tumour grade, depth of invasion, pathological stage and associated histological findings were studied. Where available, follow-up information was also analyzed to evaluate patient outcomes.

**Statistical Analysis:** Data collected were analyzed by Statistical Package for the Social Sciences (SPSS) version 26.0 and entered into Microsoft Excel software. The data were summarized using descriptive statistics. All continuous variables were reported as means  $\pm$  standard deviation (SD) and categorical variables were reported as frequencies and percentages. Incidental gallbladder carcinoma was expressed as a percentage of all cholecystectomy specimens with the intention of quantifying the frequency of the cancer diagnosis. Chi square test or Fisher's exact test was used to test the association between clinicopathological variables as appropriate. P-values under 0.05 were deemed to be statistically significant".

#### Result

The distribution of signs and symptoms among patients had cholecystectomy was shown in Table 1. Pain in the epigastric region was the most common presentation (70.00%, 133 patients). Pain in the epigastric region was the most common symptom, followed by dyspepsia and nausea/vomiting, followed by dyspepsia (62.63%) and nausea/vomiting (56.84%). On this basis, anorexia was seen in 44.74%, and the right upper quadrant pain in 27.89% of the cases as seen in Table 1. Other less common findings were fever (16.84%), Murphy's sign positivity (6.84%) and jaundice (4.74%). Overall, Table 1 indicates that more people experience non-specific gastrointestinal symptoms than do classical signs of the bile system, a fact that might delay clinical diagnosis.

**Table 1: Signs and symptoms of patients undergoing cholecystectomy (N = 190)**

| Symptoms/Signs            | Frequency (n) | Percentage (%) |
|---------------------------|---------------|----------------|
| Pain in epigastric region | 133           | 70.00          |
| Dyspepsia                 | 119           | 62.63          |
| Nausea/Vomiting           | 108           | 56.84          |
| Anorexia                  | 85            | 44.74          |
| Right upper quadrant pain | 53            | 27.89          |
| Fever                     | 32            | 16.84          |
| Murphy's sign positive    | 13            | 6.84           |
| Jaundice                  | 9             | 4.74           |

Table 2 shows the clinical and histopathological characteristics of incidental cases of carcinoma gall bladder detected in the study. Incidental carcinoma occurred in three patients (1.58%) of the 190 patients, which was a relatively high but significant rate.

Table 2 revealed a female predominance (2 out of 3 cases) in the disease. The age was between 52 to 68 years, thus, showing that carcinoma is more prevalent in the elderly. Most were linked to gallstones, which is seen as a significant etiological factor.

Adenocarcinoma was the most common histological type with one case of adenosquamous, as indicated in Table 2. The majority of cases diagnosed were at an early stage (T1a and T1b) and one case was diagnosed at T2 stage. Out of the three patients, two were alive and under follow-up, while one died due to disease progression.

Table 2 shows, therefore, that incidental carcinomas are frequently diagnosed at an early stage, and that this carries a better prognosis.

**Table 2: Clinical and histological findings of incidental gall bladder carcinoma (N ≈ 3 cases)**

| Age | Sex | Intraoperative Finding | Stone | Type of Tumour          | Stage (T) | Status                     | Duration (since diagnosis) |
|-----|-----|------------------------|-------|-------------------------|-----------|----------------------------|----------------------------|
| 52  | F   | Chronic cholecystitis  | Yes   | Adenocarcinoma          | T1a       | Alive, well                | 18 months                  |
| 68  | F   | Thickened wall         | Yes   | Adenocarcinoma          | T1b       | Alive, under follow-up     | 12 months                  |
| 61  | M   | Polypoid lesion        | No    | Adenosquamous carcinoma | T2        | Died (disease progression) | 10 months                  |

The results of present study are compared with the previous studies of incidental carcinoma gall bladder as shown in Table 3. In the present study, the incidence was 1.58%, which is within the range of previous studies (0.19% to 5.9%). From Table 3, it can be seen that studies such as Naqvi et al. (5.9%) showed a higher incidence, and Zhang et al. (0.19%) showed a lower incidence. Other studies like Mittal et al. (0.99%) and Shrestha et al. (1.40%) present re-

sults similar to the present study. In addition, Table 3 shows that the current study revealed female dominance and higher mean age which is similar to the results of previously published studies. Thus, as shown in Table 3, the results of the present study are consistent with the world statistics, which show that incidental carcinoma of the gall bladder is a clinically significant condition, although it is rare.

**Table 3: Comparison with other studies showing incidence of incidental carcinoma gall bladder**

| Studies              | Year        | Place    | Sample size | M: F    | Mean age (yrs) | Incidence (GB ca) |
|----------------------|-------------|----------|-------------|---------|----------------|-------------------|
| Daphna et al         | 2002        | Israel   | 1697        | 1:05    | 70             | 0.30%             |
| Khoo JJ et al        | 2005        | Malaysia | 1122        | 1:02    | 56.7           | 0.62%             |
| Mittal R et al       | 2007        | India    | 1305        | 01:05.5 | 56.2           | 0.99%             |
| Zhang WJ et al       | 2009        | China    | 10466       | 1:04    | 65.7           | 0.19%             |
| Amanullah et al      | 2007        | India    | 428         | 1:07    | 47             | 1.87%             |
| Shrestha R et al     | 2010        | Nepal    | 570         | 01:03.5 | 53.5           | 1.40%             |
| Naqvi et al          | 2005        | Pakistan | 1109        | 01:04.4 | —              | 5.90%             |
| <b>Present Study</b> | <b>2022</b> | India    | 190         | 01:02.5 | 61.2           | 1.58%             |

## Discussion

Gallstone disease was still one of the most frequent indications for cholecystectomy, the clinical profile of the current study being basically the same as is typically observed in benign gallbladder conditions. The most common complaint was pain in the upper abdomen (epigastric) (70% of patients), with dyspepsia (62.63%) and nausea/vomiting (56.84%) the next most common complaints. Almost half of the patients also experienced anorexia, whereas right upper quadrant pain, fever, jaundice and positive Murphy's sign were less prevalent. Symptom patterns similar to the present case have been reported in patients with gallstone disease who underwent cholecystectomy [15,16] and were primarily abdominal pain and dyspeptic symptoms. The symptoms are, however, generic and do not reliably differentiate benign gallbladder disease from underlying malignancy and thus, the incidental detection of gallbladder carcinoma is contributed by these symptoms".

Incidental gallbladder carcinoma (IGBC) was detected in 3 of 190 routine specimens of cholecystectomy, resulting in a 1.58% incidence rate in the present study. The results of this study reinforce the ongoing importance of occult gallbladder malignancy in the practice of surgery, especially in areas of relatively high gallbladder cancer incidence. The incidence in our study is similar to that reported by Amanullah et al. (1.87%) and Shrestha et al. (1.40%), which indicates a similar burden of disease in the south Asian population [17,18]. Similarly, Mittal et al. reported 0.99% in India which is slightly lower but comparable. Other geographic regions, on the contrary, have yielded lower rates, such as 0.62% in Malaysia (Khoo and Rohaizak 2016) [19], 0.30% in Israel (Daphna et al. 2009) [19] and 0.19% in China (Zhang et al. 2012) [19]. Other studies however, found a significantly higher prevalence of 5.9% in Pakistan reported by Naqvi et al. [20]. This variation can be explained by geographical factors, incidence of gallstones, genetic factors, environmental factors, diet and different patient selection and sample size.

In our study, the demographic profile of the incidental carcinoma patients revealed that the ratio of males to females was approximately 1:2, two out of three patients were female. This finding is similar to that of other known epidemiological studies of gallbladder carcinoma, which have indicated that the disease occurs more frequently in females. The mean age of affected patients was 60.3 years, similar to the mean ages reported by Daphna et al., Zhang et al., and Mittal et al. (70, 65.7, and 56.2 years, respectively). Such a distribution in relation to age would be possible to explain by a higher prevalence of gallstones in women, and the prolonged contact of their gallbladder mucosa with chronic inflammation and

hormonal influences, both of which are pro-carcinogenic.

Apart from porcelain gallbladder, adenomatous polyp, chronic infection with *Salmonella typhi*, abnormal pancreaticobiliary duct junction and environmental carcinogens, gallstones are recognized as the most important risk factor for gallbladder carcinoma [21]. The presence of gallstones in two of the three incidental carcinoma patients in the present study is consistent with the known relationship between cholelithiasis and gallbladder cancer. The exact mechanism of gallstone-induced chronic irritation/inflammation is thought to trigger a cascade of epithelial dysplasia and malignant transformation. This type of association has also been reported in several studies with gallstones being detected in most of the patients diagnosed with Gallbladder Carcinoma.

Our study additionally identifies the role of incidental detection in the stage distribution, a factor that has prognostic value. Two patients were diagnosed at an early stage (T1a and T1b), and were clinically stable, both alive, at 18 and 12 months of follow-up, respectively. The patient with T2 stage disease, on the other hand, had progressed and died within 10 months. Earlier studies have shown that early stage (incidental) gallbladder carcinoma diagnosed following cholecystectomy has significantly better survival rates than more advanced stage cancer (five-year survival 10%). Thus, systematic histopathological examinations enable early diagnosis and prompt management and consequently improve the prognosis of the patient.

In conclusion, incidental gallbladder carcinoma is not rare in the specimens of routine cholecystectomies, accounting for 1.58% of cases. The disease mainly strikes older female patients, and gallstones are a common occurrence, with adenocarcinoma histology being most common. Since all malignant specimens cannot be easily detected at the time of operation or clinically, there is a need to routinely send all specimens of cholecystectomy for histopathology for early detection of occult gallbladder carcinoma.

## Conclusion

The authors of the present study agree that incidental gallbladder carcinoma is rare but a clinically important finding in the specimens of routine cholecystectomy. The disease was recognized more often in the elderly, had a female predominance and was frequently found in patients with gallstones and/or chronic inflammatory changes. The presentation was mostly non-specific gastrointestinal symptoms, and this highlights the insidious nature of gallbladder malignancy. Histopathological examination demonstrated that the most common type of tumor was adenocarcinoma, with early-stage diagnosis leading to favorable clinical results and advanced

stage disease leading to poor. These results strongly advocate the importance of performing routine histopathological examination of all specimens of cholecystectomy, especially in high-risk areas, because it allows for an early diagnosis of occult malignancy, which might lead to improved patient management and survival.

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