

## The Evaluation on Incidental Gallbladder Carcinoma in Eastern India

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### Abstract

GBC is the most common cancer of the biliary tract Worldwide. Cholecystectomy is one of the most common abdominal surgeries. Gallbladder malignancy is a lethal disease and is the fifth commonest malignancy in the gastrointestinal tract. A detailed clinical history and thorough physical examination was done in all cases. Routine ultrasonography and blood investigations were done. Both open and laparoscopic techniques were used in surgery. GBC is not an uncommon clinical entity in our Indian scenario, unlike western countries. It is predominantly a disease of females. Incidental gallbladder carcinoma is a nightmare for patients after cholecystectomy. Despite careful preoperative investigations and meticulous gross examination, a significant number of incidental carcinoma cases are still missed.

**Key Words:** gallstone; carcinoma; cholecystectomy

### Introduction:

Cholecystectomy is one of the most commonly performed procedures all over the world. Cholecystectomy is one of the most common abdominal surgeries. In the U.S, the annual incidence of gallbladder diseases is estimated to be about one million and among them approximately 500,000-600,000 undergo surgery.<sup>1</sup> Gallbladder malignancy is a lethal disease and is the fifth commonest malignancy in the gastrointestinal tract.<sup>2</sup> It is a significant health problem affecting 10-15 % of adult population in the Western world.<sup>3</sup> Cholelithiasis is the most common indication of cholecystectomy in Eastern India with prevalence rates varying from 2-29 %.<sup>4,5</sup> It is seven times more common in Eastern India, with female to male ratio of 3.1:1.6.<sup>7</sup> It can lead to chronic cholecystitis, acute cholecystitis, emphysema, mucocele, gangrene of gallbladder, carcinoma and gallbladder perforation.

Histopathological analysis may reveal myriad of disorders including chronic cholecystitis, acute cholecystitis, cholesterolosis, xanthogranuloma- tous cholecystitis, adenomatous hyperplasia, follicular cholecystitis, metaplasia, gallbladder polyp and carcinoma of gallbladder.

Carcinoma of the gallbladder (GBC), although it has a low overall prevalence, is the most common cancer of the biliary tree and one of the most highly malignant tumors

with poor prognosis<sup>8</sup>. Whether routine histopathology of all cholecystectomy specimens should be done or not is a matter of debate. Rarity of incidental gallbladder carcinoma along with high load of cholecystectomy specimens demands a selective approach for histopathological analysis to improve its cost effectiveness. However, aggressive nature of tumor along with unfortunate diagnostic misses in early stage demands routine analysis especially in high risk zones of gallbladder carcinoma. Here, we are presenting the experience of dealing with the clinicopathological aspect of the disease in patients of gallbladder carcinoma. Our aim was to the incidence of gallstones in these patients of gallbladder cancer in this part of India.

### Material and Methods

It is a retrospective study of 1927 patients undergoing cholecystectomy for gallstones from 01.04.2013 to 31.09.2016 in our surgical unit at Panda Medical Centre, Orissa, India. The hospital records of these patients were reviewed. A detailed clinical history and thorough physical examination was done in all cases. Routine ultrasonography and blood investigations were done. Both open and laparoscopic techniques were used in surgery. Only ultrasonographically documented thick walled cholecystectomy specimens were grossly examined after

removal on table. All specimens were routinely sent for histopathological analysis. Patients without a confirmed histological diagnosis and patients with history of any previous malignancy were excluded from the study. The results were analyzed using SPSS 18.

## Results and Discussion

In the present study spanning for three and half- years, a total of 17 patients with gallbladder carcinoma and 1927 patients with gallstone diseases were observed. The age of patients with gallbladder disease ranged from 21yrs to 79 yrs. Out of total 1927 cases, 747 were males while 980 were females. About 2/3rd of the cases were present in 31-60 years of age group. The mean age of patients with gallstones was  $39.04 \pm 6.21$  years. Although all

histopathological conditions showed a female predominance in general but cholesterolosis, follicular cholecystitis and adenomatous hyperplasia were significantly common in females. The mean age of adenomatous hyperplasia, carcinoma, follicular cholecystitis and xanthogranulomatous cholecystitis was significantly higher than rest of the cases. Chronic cholecystitis was the most common variety followed by cholesterolosis, follicular cholecystitis, xanthogranulomatous cholecystitis and carcinoma.

Laparoscopic cholecystectomy is the 'gold standard' procedure for management of gallstones all over the world. Majority (76%) of the cases in this study were also operated by Laparoscopic and rest cases by opencholecystectomy technique.

Age	Female/Male	No. of patients
10-20	-	-
21-30	4/1	-
31-40	7/5	5
41-50	11/3	7
51-60	6/2	3
61-70	3/1	1
70-80	1/1	1
>80	-	-

**Table 1: Age distribution of cases.**

		No. of patients	Percentage (%)
Symptoms	Abdominal pain	12	70.58
	Anorexia	4	23.5
	Dyspepsia	7	41.1
	Weight loss	2	11.7
	Jaundice	5	29.4
	Nausea and vomiting	3	17.64
	Malaise	1	5.8
	Pruritus	1	5.8
Signs	Abdominal mass	13	76.47
	Tenderness	7	41.1
	Icterus	3	17.6
	Ascites	2	11.7
	Cachexia	3	17.6
	Fever	2	11.7

**Table 2: Distribution of Symptoms and Signs**

GBC either remains asymptomatic for a long time or presents with very non-specific symptoms depending on the site of malignancy in the gallbladder. Commonly, symptoms are related to associated gallstones.<sup>13</sup> In our study, abdominal pain (70.58%) followed by abdominal

The laboratory investigations in our study revealed anemia (hemoglobin, <10 g/dl) in 8 (47.05%) patients;

mass (76.47%) and jaundice (29.4%) were the most common presenting features. Consistent results were reported in other studies.<sup>9,14</sup> Clinical signs mimic benign gallbladder diseases until the invasion of surrounding structures give clue to correct diagnosis.

hyperbilirubinemia (serum bilirubin, >2 mg/dl) in 5(29.41%) and elevated levels of alkaline phosphatase

(>100 IU/ml) in 7(41.17%) of the patients. Comparable findings were reported in other studies.<sup>12,16</sup> Abnormal serum alkaline phosphatase and gamma

glutamyltransferase may be elevated in the absence of jaundice.<sup>17</sup>

Histopathology	Females/ Males	Total no.of patients	Total Percentage(% )
Acute cholecystitis	1/05	1	5.8
Chronic cholecystiti s	17/4	5	29.4
Follicular cholecystitis	2/0	2	11.7
Xanthogranulomatous cholecystitis	6/2	3	17.6
Adenomatous hyperplasia	2/0	1	5.8
Metaplasia	0/1	-	-
Cholesterolosis	2/0	2	11.7
Carcinoma	2/1	3	17.6
Total	32/13	17	100%

**Table 4: Histopathological diagnosis of cases with mean age and sex distribution**

Gallbladder cancer is the most common cause of death from biliary malignancies.<sup>9</sup> It is usually detected at an advanced stage due to its non-specific symptoms.<sup>10</sup> In India, cancer of gallbladder shows varying geographic distribution, as the incidence is much higher in Eastern India as compared to the other geographical Indian population. Gallbladder cancer ranks among the first five common cancers in females in Delhi, India.<sup>11</sup> In the endemic zone of West Bihar and Eastern Utter Pradesh, it is the third most common malignancy of the alimentary tract.<sup>12</sup>

It was found that increasing numbers of patients were being referred to our hospital in recent past, thus increasing the number of cases per year. This fact may be attributed to the increasing awareness of this disease amongst general physicians and general surgeons working in the peripheral areas and small medical facilities within the city. This is in contrast to the study<sup>18</sup> in which global trends for GBC reveal falling incidence rates, probably as a result of increasing rates of cholecystectomy for gall stone disease and better diagnostic offerings with patient affordability. Some European studies<sup>19</sup> also noted declining rates of GBC incidence and mortality. However, no such inverse relationship was observed in another study.<sup>10</sup> Cholelithiasis can cause histopathological changes in gall bladder mucosa varying from acute cholecystitis, chronic cholecystitis, follicular cholecystitis, xanthogranulomatous cholecystitis, cholesterolosis, adenomatous hyperplasia, metaplasia and carcinoma. Genetic susceptibility for gallstone formation have been studied with a relative risk of 5 times in relatives of gallstone patients.<sup>3,20</sup> Geography and ethnicity also plays an important role in the prevalence of gall stones. North American Indian natives, Mabuchi Indians and Mexican Americans have highest reported incidence of gall stones varying from 49.4% to 64.1%<sup>21,22</sup> Asian population have

intermediate prevalence ratio.<sup>23</sup>

Literature is biased on need of routine histopathology of all gallstones related cholecystectomy specimens. Recently few studies have refuted its usefulness in all cases stating that it not only overburdening our pathologists but also cost ineffective due to low incidence of incidental gallbladder carcinoma.<sup>24-27</sup> Routine histopathological examination of all gallstones related cholecystectomy specimens is a safety link for earliest detection of this carcinoma. High index of suspicion is warranted specially in high risk regions of carcinoma gallbladder like north and eastern India for better prognosis. A high burden of disease even at a significantly young age is an alarming sign in our region. It has been a standard practice over the decades to assess all specimens histopathologically to rule out carcinoma. Moreover, recent studies at apex institutes also strongly justified this recommendation.<sup>28,29</sup> The Royal college of Pathologists have also recommended routine histopathological analysis of all specimens of gallstones related cholecystectomies.<sup>30</sup>

It has been reported by various studies that majority of the cases of gallbladder carcinoma are suspected by either during ultrasonography or on gross examination of the specimen and hence only these suspected cases should be sent for histopathology.<sup>7,26,27</sup> On the contrary, other studies have doubted their claim with evidence of a significant number of missed incidental carcinoma cases in their studies despite standard investigations and specimen examination.<sup>28,31-33</sup>

This observation showed that radiological and peroperative findings were not helpful in raising high index of suspicion in most of the cases of incidental carcinomas. Routine histological examination of all gallbladder specimen is therefore well justified as finding of incidental carcinoma might alter the management and thus the clinical outcome.

## Conclusion

GBC is not an uncommon clinical entity in our Indian scenario, unlike western countries. It is predominantly a disease of females. Incidental gallbladder carcinoma is a nightmare for patients after cholecystectomy. Despite careful preoperative investigations and meticulous gross examination, a significant number of incidental carcinoma cases are still missed. Although a selective approach of histopathology can decrease cost and burden on pathologist to a large extent but it will also result in missing early staged carcinoma and hence preventable mortality if timely offered curative treatment. Therefore a routine histopathology of all cholecystectomy specimens should be considered in all cases especially in high risk zones of carcinoma gallbladder as a token of respect to human life. Education through regular conduction of educational programmes at district levels to all surgeons to send the resected gallbladder specimens to good qualified pathologists with oncology exposure is mandatory.

We strongly advise that all GBs removed for presumed gallstone disease should be opened up by the surgeon in the operating room for a careful gross examination. If changes suspicious of malignancy are seen, the GB should be subjected to a frozen section examination and if it is positive, an extended cholecystectomy should be performed.

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