

A retrospective audit of gall bladder histopathology following cholecystectomy

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Abstract

Gall bladder carcinoma is one of the common cancer of biliary tree which have rapid progression and high mortality rate. It is difficult to differentiate early stage of gall bladder carcinoma from chronic cholecystitis as it is mostly asymptomatic. It is well accepted that good prognosis and prolonged survival can be achieved only with detection at an early stage. Gall bladder specimens removed for clinically benign conditions for histopathological examination has been topic of debate. The reference retrospective study was carried out at tertiary care hospital for period of 6 years with objective to identify the incidence of unsuspected gallbladder carcinoma. These cholecystectomy specimens received by our histopathology laboratory to analyze their clinico-pathological features. Incidentally detected gallbladder malignancy cases comprised 0.87% from a total of 803 case records. Most patients were found to be in early, surgically resectable stage of their disease. We recommend that in India and other countries with relatively high incidences of gall bladder carcinoma, all cholecystectomy specimens should be submitted to histopathology laboratory, which is in support with current literature. It could help us to treat cases at potentially curable stage if detected early.

Keywords: Malignant Gall bladder carcinoma, Cholecystectomy.

Introduction

The gall bladder carcinoma is 5TH most common gastrointestinal malignancy. It is difficult to differentiate early stage of gall bladder carcinoma from chronic cholecystitis as it is mostly asymptomatic. Literature has documented that gall bladder cancer incidences varies by geographic region, race and ethnic group. Indians, Pakistanis, Chileans, Bolivians, Central Europeans, Israelis, and Americans of Mexican origin has witnessed highest incidences^{1, 2} India being populated country and major fraction of population within lower socioeconomic status, early stage malignancy detection is difficult leading to poor survival as many of them are not able access to proper health facilities. Literature showed gall bladder malignancy as one of the most common malignancy (nearly 80-90%) in the biliary tree.³ Early detection is key in prognosis of such highly aggressive cancer.⁴ Wang *et al* correlated early diagnosis and timely radical surgery with the prognosis of the patients.⁵ cholecystectomy specimens has been reported in 0.3-2% incident rate in all cholecystectomy performed for benign conditions.⁶ Considering the available literature the present study was aimed to identify the incidence of gall bladder carcinoma in cholecystectomy specimens received in histopathology laboratory and correlate it with the clinical pathological variables of incidentally detected gall bladder carcinoma cases.

Methods

The study was commenced after obtaining approval from the Bhaktivedanta Hospital Ethics Committee. Being retrospective study, a waiver for informed consent was granted for this study.

Retrospective audit of hospital records available with general surgery department of all patients who were operated for cholecystectomy due to gallstone disease from April 2010 to June 2015 was carried out. The histopathological reports of these patients were reviewed. Descriptive statistics was used to represent various categorical variables in proportions and numerical variables in mean (SD) format.

Results

Demographic Details: A total of 803 patients [224 (27.9%) males and 579 (72.1%) females] underwent cholecystectomy for symptomatic gallstones during the 6 year period. Mean (SD) age of the study participants was 44 (15) years.

Diagnoses: Chronic cholecystitis was the most common diagnosed in 565/803 (70.4%) patients followed by 2nd most common diagnosis chronic cholecystitis with cholesterosis (70/803, 8.7%). Details of other diagnoses in the isolated specimens are described in Table 1.

Table 1: Histopathological analysis of cholecystectomy specimens (N=803)

Histopathological type	Total number (%) of patients
<i>Cholecystitis</i>	
Chronic cholecystitis	565 (70.36)
Chronic cholecystitis with cholesterosis	70 (8.7)
Chronic lympho eosinophilic cholecystitis or Eosinophilic cholecystitis	6 (0.7)
Chronic cholecystitis adenomatous and	1 (0.12)

Adenomyomatous polyp	
Xanthogranulomatous cholecystitis	4 (0.49)
Chronic cholecystitis with hyperplastic polyp	1 (0.12)
Cholesterosis	9 (1.12)
Cholesterol polyp	2 (0.24)
Acute cholecystitis	30 (3.73)
Acute on chronic cholecystitis	69 (8.59)
Acute on chronic cholecystitis with gangrene	16 (1.99)
Cholelithiasis	18 (2.24)
<i>Benign lesions</i>	
Benign adenomatous polyp in the fundus of gall bladder	5 (0.6)
<i>Gall bladder carcinoma</i>	7 (0.87)

Gall bladder Carcinoma Incidences: As per expectation, most of specimen had benign origin

expected. Out of the total 803 specimens, carcinoma gall of bladder incident rate was 0.87% (n=7). The peak age group was sixth decade and the mean (range) age of patients with gall bladder carcinoma incidental was 56 in range of 40-68 years. All were associated with multiple gall stones. A female preponderance was observed (6/7, 85.75%). The histopathological diagnoses of these patients include the following: Adenocarcinoma – 5 (71.4%); Papillary adenocarcinoma – 1 (14.3%) and adenosquamous carcinoma – 1(14.3%). Table 2 describe clinical and pathological details of 7 carcinoma gall of bladder cases. The pre-operative diagnoses in all were symptomatic gall stone disease and have undergone laparoscopic cholecystectomy and none of these patients had been suspected to have had gall bladder cancer pre-operatively.

Table 2: Clinico-pathological profile of patients with incidental gall bladder carcinoma (n=7)

Preoperative and intraoperative data	Patient one	Patient two	Patient three	Patient four	Patient five	Patient six	Patient seven
Age , sex	65 Y, female	68 Y, male	64 Y, female	40 Y, female	66 Y, female	40 Y, female	60 Y, female
Preoperative Diagnosis	Symptomatic gallstone disease	Symptomatic gallstone disease	Dyspepsia	Symptomatic gallstone disease	Symptomatic gall stone disease	Symptomatic gall stone disease	Symptomatic gall stone disease
Preoperative findings from imaging	Few calculi in gallbladder	Multiple calculi	Gallbladder calculi with sludge	Multiple calculi	Gallbladder calculi	Gallbladder calculi	Calculous cholecystitis
Intra-operative findings	Normal anatomy	Mild adhesion in calot triangle	Cholecystitis	Normal anatomy	Normal anatomy	Acute cholecystitis	Chronic Cholecystitis
Histopathology	Well differentiated adenocarcinoma	Moderately differentiated adeno carcinoma and transmural tumour	Large polyp with no stones; Low grade papillary adenocarcinoma stage IB	Adenosquamous carcinoma	High grade adeno carcinoma	Moderately differentiated adenocarcinoma	Predominantly <i>in situ</i> adenocarcinoma with small focus of invasion into muscularis propria and the serosa was not involved
TNM stage	T1N0Mx	T3N0Mx	T1N0Mx	T1N1Mx	T2N1Mx	T3N0Mx	T2N0MX

Table 3: Prevalence of incidental gall bladder carcinoma from various studies

Study	Incidence	Number of cases studied
Tantia <i>et al</i> , 2009 [12]	0.59%	3205
Shreshtha <i>et al</i> , 2010 [13]	3.30%	668
Mitrovic <i>et al</i> , 2010 [14]	0.69%	3007
Mittal <i>et al</i> , 2010 [15]	1.00%	1312
Ghimire <i>et al</i> , 2011 [16]	1.28%	783
Yi X <i>et al</i> , 2013 [17]	0.18%	14073
Kalita <i>et al</i> , 2013 [18]	0.44%	4115
Our study 2015	0.87%	803

Discussion

The present study was carried out to find out the incidence of gall bladder carcinoma in patients who underwent cholecystectomy and analyses their clinic-pathological features. Incident rate of gall bladder cancer is 7/803 (0.87%). Patients with incidental gall bladder cancers were mostly females, in their age range of sixth decade and none of them had been suspected to have cancer pre-operatively. Pathologically, adenocarcinoma was the most predominant type followed by papillary adenocarcinoma and adenosquamous carcinoma.

The gall bladder carcinoma is 5TH most common gastrointestinal malignancy, detected in later stage of diseases and has witnessed a high mortality due to high propensity for metastasis and poor efficacy of available interventions options. Gall bladder carcinoma has been found to be common in Indian population similar to the prevalence of gall stone disease however it is reported to be rare in Western nations.⁷ Northern part of India has witnessed more gall bladder stones and it is the most common gastrointestinal cancer in women.⁸ Surgery is the treatment of choice for patients with gallbladder cancer⁹ and to achieve the R0 resection, early diagnosis of the carcinoma is vital. Simple cholecystectomy is advisable till pT2a stage of the cancer after which radical cholecystectomy is preferred.¹⁰ The prevalence of incidental gall bladder cancer was found to occur around 0.19%¹¹ ranging between 0.18 to 3.3% (Table 3). Few risk factors that have been identified to increase the risk of gall bladder carcinoma are performing or conversion from laparoscopic to open cholecystectomy, older age, Asian or African American, female gender, and elevated alkaline phosphatase level.¹¹ Similar risk factors such as older age, sex and ethnicity have been observed in the present study in addition to the chronic presence of gall stones.

The clinical presentation of early gall bladder carcinoma is non-specific and symptoms are similar to acute or chronic cholecystitis. Cuccinotta *et al* found that the most important factor determining the outcome of incidental gall bladder adenocarcinoma is related to tumor stage rather than the surgical approach.¹⁹ The high incidence (74-92%) of mixed pathology (neoplastic and inflammatory) makes the preoperative diagnosis very difficult.²⁰ There is possibility that an

expert radiologist can detect the presence of early lesions characterized by focal gall bladder wall thickening or lesions of small mass, however all cases of early gall bladder carcinoma does not present with an obvious lesion on abdomen ultrasonography.²¹ Gross examination of the cholecystectomy specimen can pick up some of the small lesions missed on preoperative ultrasound but the histopathological examination of the cholecystectomy specimen help to detect tumors that are not visible even on gross examination of the specimen.²² Hence, histopathological examination of cholecystectomy specimens is traditional practice. Several authors have highlighted that preoperative imaging findings and intraoperative gross examination may not be reliable tool in detection of malignancy.^{15, 23} Roa *et al* from Chile, observed that 37% of primary tumours were macroscopically in-apparent.²³ Lohsiriwat *et al* reported the absence of pre- or intraoperative suspicion in all 24 cases of gall bladder carcinoma diagnosed on histopathological examination of 4317 cholecystectomy specimens examined over a period of 8 years. [24] Recently, a report from Nepal found that pre- and intraoperative examination was accurate in identifying only 55% of all Gall bladder carcinoma cases.¹⁵ All these reports underscore the importance of routine histopathological examination of all cholecystectomy specimens. We also found out that the incidental gall bladder carcinoma were either in T1 or T2 stages and so resectable. In fact, most of the incidentally detected carcinoma were reported to be surgically resectable, with a good survival rate.^{17, 25} Similarly, Histological examination of the tumors revealed findings similar to other studies.⁴

To conclude, we recommend to keep incidental gall bladder carcinoma in mind while treating patients with chronic gall stones. Patients with intra-operative findings suspicious of gall bladder carcinoma should benefit from frozen-section examination of cholecystectomy specimen. In all other patients, the cholecystectomy specimen should be sent for routine histopathological examination so that the detection of early gall bladder carcinoma is not missed in a subgroup of patients who might derive maximum benefit from radical resection.

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