

Incidental Gallbladder Carcinoma: An Eastern Indian Experience and Necessity of Routine Histopathological Examination after All Cholecystectomy

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ABSTRACT

Introduction: The carcinoma of gallbladder is the most common malignancy of the biliary tract. The incidence of this carcinoma varies geographically. Incidental gallbladder carcinoma is diagnosed during histopathological examination after cholecystectomy due to other reasons. Histopathological examination of all cholecystectomy specimens are very essential to rule out these incidental gallbladder carcinomas.

Aim: To this study to estimate the frequency of incidental gallbladder carcinoma in patients undergoing routine cholecystectomy and also to evaluate the necessity of routine histopathological examination after all cholecystectomy.

Materials and Methods: A retrospective observational study was conducted in Department of Pathology, Midnapore Medical College and Hospital, West Bengal, India between January 2014 to December 2019 (six years) covering 650 patients who underwent laparoscopic and open cholecystectomy. Patients' demographic data, pathologic results, macroscopic

appearance of the specimen, cancer staging were recorded and frequency of incidental gallbladder carcinoma were calculated.

Result: Total 650 cholecystectomy specimens due to benign gallbladder disease were received in pathology department. Histopathological examination revealed 18 cases of incidental gallbladder carcinoma which comprised 2.8% of all the cholecystectomies. Among them 13 were female and five were in male with male: female ratio of 1:2.6 and the age ranges from 35 to 68 years. Among 18 cases 10 cases showed invasion upto lamina propria (stage T1a), five cases had invasion in muscular layer (stage T1b) and three cases showed perimuscular connective tissue invasion (stage T2a).

Conclusion: The present study observed that the incidence of incidental gallbladder carcinoma in cholecystectomy specimen was little higher range in East Indian population and so routine histopathological examination of all cholecystectomy specimens are recommended.

Keywords: Biliary tract, Laparoscopy, Macroscopic appearance, Malignancy, Specimen

INTRODUCTION

Cholecystectomy is the most common surgical abdominal procedure and the majority of the cases are due to stones and chronic inflammation, but some time incidental finding of gallbladder carcinoma is diagnosed after histopathological examination. As the clinical presentation of gallbladder carcinoma are more or less similar to those associated with cholecystitis or cholelithiasis. The carcinoma of gallbladder is the most common malignancy of the biliary tract [1]. The incidence of this carcinoma varies geographically like north, east and central India have higher rate than south and west India [2]. Delhi and Bhopal have highest incidence rates of 6.6 and 5.2 for female and 1.9 and 2.2 for males per 100,000 respectively [3]. This rate among women has increased from 6.2/100,000 in 2001-2004 to 10.4/100,000 in 2012-2014 [4].

Approx 90% of gallbladder carcinoma have cholelithiasis [5]. The major risk factors for carcinoma of gallbladder are stones and chronic inflammation [6]. As it has overlapping clinical presentation many of the time gallbladder carcinoma diagnosed during histopathological examination after cholecystectomy due to other reasons. This type of gallbladder carcinoma is called incidental gallbladder carcinoma [7]. Different studies revealed different frequency of incidental gallbladder carcinoma all over the world. Overall frequency varies 0.2-3.3% from different areas of world [8]. Most of these incidental gallbladder carcinomas are categorised under stage of pT1 and pT2 [9].

In this scenario routine histopathological examination of all cholecystectomy specimens is very essential to rule out these incidental gallbladder carcinomas. But till now there is

debates regarding routine histopathological examination of all cholecystectomy specimen [10]. The aim of this study was to estimate the incidence of incidental gallbladder carcinoma in patients undergoing routine cholecystectomy in Midnapore Medical College and Hospital, West Bengal, India and also to evaluate the necessity of routine histopathological examination after all cholecystectomy. This study specially focused on the data from eastern India, as many literatures covering the north Indian population are found but Eastern Indian data is limited.

MATERIALS AND METHODS

This retrospective observational study was conducted in Department of Pathology, Midnapore Medical College, West Bengal, India, between January 2014 to December 2019 (six years). A total of 650 patients who underwent laparoscopic and open cholecystectomy at Midnapore Medical College and Hospital were included in the study. This study was approved by Institutional Ethical Committee (IEC) (Approval number: IEC/2019/08). Consent was obtained from all the participants involved in the study.

Inclusion criteria: Patients with previously diagnosed benign gallbladder disease were included in the study.

Exclusion criteria: Patients with imaging findings of preoperative gallbladder cancer and patients with poorly preserved demographic data, radiological findings, histopathological results were excluded from the study.

Patient data were obtained retrospectively from record files. Patients' demographic data, radiological findings, histopathological

results, macroscopic appearance of the specimens, and cancer staging were recorded. The distribution and frequency of incidental gallbladder carcinoma were evaluated. Pathological findings were compared in terms of age groups and gender relations. Staging of gallbladder tumours was performed according to the American Joint Committee on Cancer TNM system.

STATISTICAL ANALYSIS

In this study Microsoft Excel was use for statistical calculations. The data was entered in Microsoft excel and results were expressed in terms of frequency and percentage.

RESULTS

During the time period of January 2014 to December 2019, 650 open or laparoscopic cholecystectomy specimens were received Amongst them 422 (65%) were females and 228 (35%) were males and the age range of the patient was 31 to 68 years [Table/Fig-1].

Parameters	No. of cases	Percentage
Sex		
Male	228	35
Female	422	65
Age (yrs)		
31-41	76	11.6
42-51	138	21.2
52-61	185	28.46
>61	251	38.61

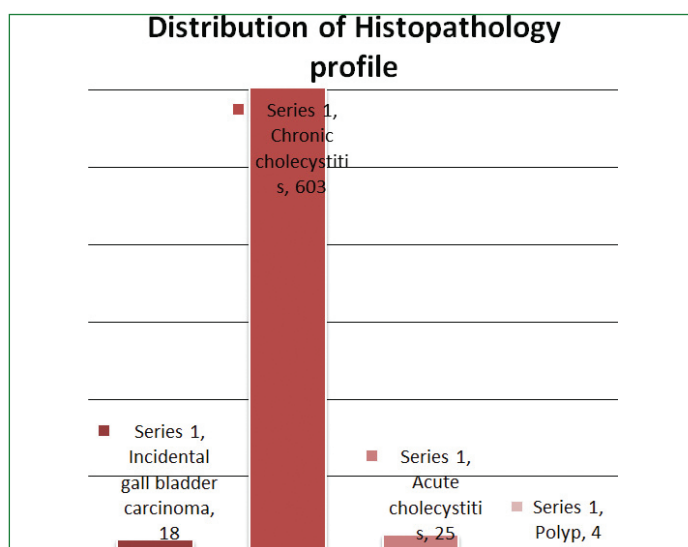
[Table/Fig-1]: Distribution of sex and age of all cholecystectomy specimens.

The clinical and histopathological details of the 18 cases of incidental gallbladder carcinoma has been described in [Table/Fig-2]. Histopathological examination of all the gallbladder specimen revealed 18 cases of incidental gallbladder carcinoma which comprised 2.8% of all the cholecystectomies and the diagnosis of chronic cholecystitis were 603 (92.8%), acute cholecystitis were 25 (3.8%) and polyp were 4 (0.6%) [Table/Fig-3]. Among 18 cases of incidental gallbladder carcinoma 13 were females and five were male, so male: female ratio was 1:2.6 and the age ranges from 35 to 68 years with mean age being 61.33 years [Table/Fig-4].

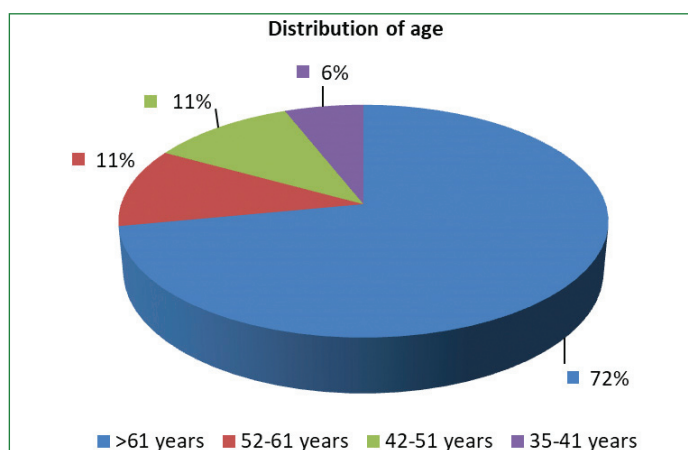
Sl. no.	Age (Years)	Sex	Clinical features	Provisional diagnosis	Stone	Type of tumour	Stage (T)
1	62	F	Epigastric pain, dyspepsia	Chronic calculus cholecystitis	Yes	Adenocarcinoma	T1b
2	58	F	Vomiting, epigastric pain, anorexia	Chronic calculus cholecystitis	Yes	Adenocarcinoma	T1a
3	50	F	Nausea, epigastric pain, dyspepsia	Chronic calculus cholecystitis	Yes	Adenocarcinoma	T1a
4	67	M	Epigastric pain, dyspepsia	Chronic calculus cholecystitis	Yes	Adenocarcinoma	T1a
5	66	F	Vomiting, epigastric pain, dyspepsia	Chronic calculus cholecystitis	Yes	Adenocarcinoma	T1a
6	65	F	Epigastric pain, anorexia	Chronic calculus cholecystitis	Yes	Adenocarcinoma	T1b
7	57	M	Epigastric pain, anorexia	Chronic calculus cholecystitis	Yes	Adenocarcinoma	T1b
8	48	F	Vomiting, epigastric pain, anorexia, fever	Chronic cholecystitis	No	Adenocarcinoma	T1a

9	40	F	Epigastric pain, dyspepsia, fever	Chronic cholecystitis	No	Adenocarcinoma	T1a
10	66	M	Nausea, epigastric pain, anorexia	Chronic calculus cholecystitis	Yes	Adenocarcinoma	T1a
11	68	F	Vomiting, epigastric pain, anorexia	Chronic calculus cholecystitis	Yes	Adenocarcinoma	T2a
12	65	M	Epigastric pain, dyspepsia	Chronic calculus cholecystitis	Yes	Adenocarcinoma	T1b
13	66	F	Nausea, epigastric pain, anorexia	Chronic calculus cholecystitis	Yes	Adenocarcinoma	T1a
14	67	F	Fever, vomiting, epigastric pain, anorexia	Chronic calculus cholecystitis	Yes	Adenocarcinoma	T2a
15	67	M	Epigastric pain, dyspepsia	Chronic calculus cholecystitis	Yes	Adenocarcinoma	T2a
16	65	F	vomiting, epigastric pain, anorexia	Chronic calculus cholecystitis	Yes	Adenocarcinoma	T1b
17	63	F	Epigastric pain, dyspepsia	Chronic calculus cholecystitis	Yes	Adenocarcinoma	T1a
18	64	F	Nausea, epigastric pain, anorexia	Chronic calculus cholecystitis	Yes	Adenocarcinoma	T1a

[Table/Fig-2]: Clinical and histopathological finding of incidental gallbladder carcinomas.

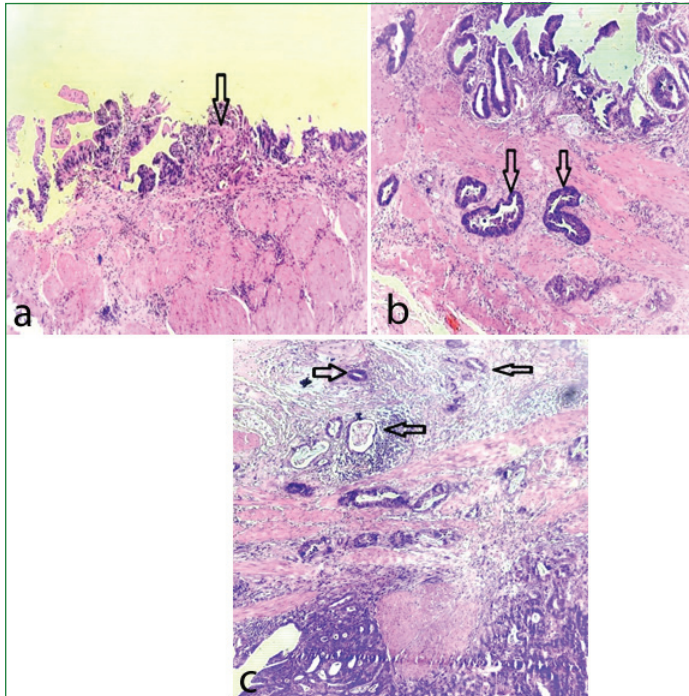


[Table/Fig-3]: Distribution of histopathology profile of received specimens.



[Table/Fig-4]: Distribution of age of all cholecystectomy specimens diagnosed as Incidental gall bladder carcinoma.

In this study all the cases were presented with common clinical features of chronic cholecystitis (nausea, vomiting, epigastric pain, dyspepsia, anorexia) and chronic calculus cholecystitis were found in 16 (88.9%) cases out of the 18 cases of incidental gallbladder carcinoma. Microscopically all incidental gallbladder carcinomas are well to moderately differentiated adenocarcinoma. Among them 10 (55.5%) cases were showing invasion upto lamina propria (stage T1a), 5 (27.8%) cases had invasion in muscular layer (stage T1b) and 3 (16.7%) cases perimuscular connective tissue invasion were present (stage T2a) [Table/Fig-5a-c].



[Table/Fig-5]: Well-differentiated adenocarcinoma (stage T1a). Photomicrograph (10X magnification, H&E stain) shows mucosa lined by epithelium consistent with moderate-grade dysplasia. Below the surface there are malignant glands (arrow) infiltrating the lamina propria. There is a mild infiltrate of chronic inflammatory cells. b) Moderately-differentiated adenocarcinoma (stage T1b). Photomicrograph (10X magnification, H&E stain) shows malignant glands invades the muscle layer (arrows). c) Moderately-differentiated adenocarcinoma (stage T2a). Photomicrograph (10X magnification, H&E stain) shows malignant glands invasion through the muscle layer and into the perimuscular connective tissue (arrows).

DISCUSSION

Gallbladder carcinoma is the most common malignancy of biliary tract and 5th common malignancy of digestive tract [1]. The incidence of it varies geographically. The occurrence of gallbladder carcinoma is more in female than male [11] and it occurs usually in elderly person [10]. Most of the cases in this study were in age group of 51-68 years with a mean age of 61.33 years and among the all cases, 13 were females and five were males with male: female ratio of 1:2.6. According to the Ghimire P et al., [12] study

mean age was 63.8 years and male: female ratio was 1:2.3 which are more or less similar to present study. Chronic cholecystitis is often associated with gallbladder carcinoma, it was found in 54-97% cases of carcinoma [13]. In this study the association is found 88.9% of cases it was little lower than Basak F et al., study result [13]. Most of the cases of gallbladder carcinoma in this study presented with non specific symptoms like epigastric pain, dyspepsia, anorexia, vomiting and also similar USG findings of chronic calculus cholecystitis.

Many of the gallbladder carcinomas are detected in advanced stage with a poor prognosis but if it was diagnosed in early stage then prognosis may be better even up to 90-100% five years survival rate [14].

Many of the cases of incidental gallbladder carcinoma are detected incidentally after cholecystectomy and this group having best prognosis [15]. In present study this incidental finding of gallbladder carcinoma was 2.8% of all cholecystectomy specimens send to Pathology department. Different studies reviled different frequency of incidental gallbladder carcinoma all over the world. Overall frequency varies 0.2-3.3% from different areas of world [8]. Various studies were conducted in India shows different results. The list of various authors with the variety in their observation of incidental gallbladder carcinomas is listed in [Table/Fig-6] [16-20]. These studies were conducted mainly in north Indian populations. Comparison to other studies present result, which covers the Eastern Indian population, is little higher. This is may be due to geographical and ethnic variations.

In this study majority of incidental gallbladder carcinomas were in an early pathological stage like T1a and T1b (83.3%) and carries a good prognosis even up to 90-100% five years survival rate [14]. According Yadav R et al., it was 62.6% in their study [20].

There are many debates regarding routine histopathological examination after each and every cholecystectomy. Some authors suggested selective histopathological examination [21] but there are other studies which recommended that the routine histological examination is crucial for every cholecystectomy to detect the incidental gallbladder carcinoma [22,23]. Even Royal College of Pathologist also advised for histopathological examination of every cholecystectomy [24].

According to Yadav R et al., [20] routine histopathological examination of cholecystectomy specimen is very useful in the areas where incidence is high [20]. Ghimire P et al., also suggest routine histopathological examination, because it can diagnosed gallbladder carcinoma in early stage [12]. At the same time Mittal R et al., [25] and Tayeb M et al., [26] recommended that histopathological examination is required only if there are any macroscopic abnormalities. But Dincel O et al., [27] advised that even absence of any macroscopic abnormalities routine examination is useful for all gallbladder specimens. Elshaer M et al., [28] proposed that age was an indicator for selective histopathological examination [28]. In this context it is very

Studies	Study year	Publication year	Place	Sample size	M:F	Mean age (yrs)	Incidence of incidental gallbladder carcinoma	Stage (T)
Waghmare RS and Kamat RN [16]	June 2010 to July 2011	2014	--	270	--	50	2.59%	T1a- 1.42% T2- 85.71%
Sangwan MK et al., [17]	June 2012 to June 2015	2015	Khanpur Kalan, India	530	1:6.07	44.16±14.64	1.9%	--
Jha V et al., [18]	July 2014 to June 2016	2018	New Delhi	4800	1:4	50.65	0.41%	T1a-15% T1b-75% T2- 10%
Butti et al., [19]	2020	2020	New Delhi	906	--	--	0.77%	--
Yadav R et al., [20]	April 2018 to March 2021	2021	North India	1268	1:7	58.63±9.99	1.26%	T1a-31.3% T1b-31.3% T2-18.8% T3-18.8%
Present study	January 2014 to December 2019	2022	Paschim Midnapur, West Bengal, India	650	1:2.6	61.33	2.7%	T1a-55.5% T1b-27.8% T2-16.7%

[Table/Fig-5]: List of various studies showing incidence of incidental gallbladder carcinomas [16-20].

difficult to decide, selective or routine histopathological examination, which is best.

Limitation(s)

There are some limitations in this study. As this is a retrospective observational study some patient's demographic data, radiological findings and histopathological results were poorly preserved, so these data could not be included in this study. This is an institution based study, the findings are very specific to a particular region. The results in regions with high incidence of gallbladder cancer may differ. Therefore, there is a need for multicentre studies from different regions and countries.

CONCLUSION(S)

Majority of cholecystectomy specimen, received in pathology department, are operated due to symptoms and radiological findings of chronic cholecystitis and /or stone. But histological evidence of incidental gallbladder carcinomas were detected among them, as it was usually radiologically undetectable. Incidental gallbladder carcinoma is an early stage of carcinoma so it carries good prognosis. In spite of many controversies about selective or routine histopathological examination of all cholecystectomy specimens, present study believes in routine examination of all specimens as frequency is little higher in East Indian population.

Acknowledgment

Authors are very much thankful to surgery department of the institution and all staffs of the department.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Feb 09, 2022
- Manual Googling: Apr 07, 2022
- iThenticate Software: May 28, 2022 (12%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Feb 06, 2022**

Date of Peer Review: **Mar 17, 2022**

Date of Acceptance: **Apr 15, 2022**

Date of Publishing: **Oct 01, 2022**