

## Incidence of Incidental Gall Bladder Malignancy in S.P.M.C and A.G Hospitals Bikaner

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### Abstract:

#### Background

1. To study the incidence of incidental carcinoma of gall bladder in patients undergoing routine cholecystectomy.

2. To study the demographic profile and management of these patients.

**Material And Method:** A retrospective plus prospective study was conducted from January 2016 to August 2018.

A total of 2371 patients were included in this study. All patients who have undergone cholecystectomy for cholelithiasis were included in this study.

**Results:** A total of 2371 patients, who underwent cholecystectomy for cholelithiasis, were included in the study. There were 868 males (36.6%) and 1503 females (63.4%). Mean age in malignant patients was 51.96 with SD  $\pm 2.09$  and the mean age in benign patients was 42.48 with SD  $\pm 2.28$ . The mean age of IGBCs patients was significantly higher.

Laparoscopic cholecystectomy was performed in 1458 patients out of 2371. All gallbladder specimens were sent for HPE and twenty eight were reported as adenocarcinoma of the gallbladder.

In our study out of 28 IGBC patients, 10 underwent radical cholecystectomy (pT1b), 3 patients underwent extended radical cholecystectomy (pT2), 5 patients never followed up and 7 patients followed up late with locoregional recurrence. 3 patients were managed with only simple cholecystectomy since the pathological staging showed pT1a.

Incidental gallbladder cancer was thus found in 1.18% of patients undergoing cholecystectomy for cholelithiasis.

**Conclusion:** To conclude, this study from a centre in the northern part of India has found that IGBC is present in 1.18%.

**Keywords:** Gallbladder, Incidental carcinoma.

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### I. Introduction

Gall bladder carcinoma (GBC) is the sixth most common cancer involving the gastrointestinal tract but it is the most common malignant tumour of the biliary tract worldwide. GBC is a rare entity, and diagnosed in 0.3-1.5% of all cholecystectomies.<sup>[1-4]</sup> Life expectancy of GBC varies greatly with clinical stage at the time of detection.

Incidental gall bladder carcinoma (IGBC) is defined as carcinoma of gall bladder suspected for the first time during cholecystectomy or accidentally found on histological examination of gall bladder.<sup>[2,4]</sup>

Women are 2-6 times more commonly affected and the incidence steadily increases with age<sup>[5]</sup>. There are also marked geographical and racial differences in the frequency of the disease with high incidence rate have been reported from Japan, South American countries, Central and Eastern European nations and it is rare in the western world including the USA, UK, CANADA, AUSTRALIA and NEWZEALAND<sup>[6]</sup>.

Incidence of gall bladder carcinoma varies greatly within India, with highest rates from Northern and Central parts of India i.e. as high as 6.6-5.2 per 100000 populations and lowest in Chennai and Bangalore in Southern India i.e. between 0.6-0.8 per 100000 populations<sup>[7,8]</sup>.

Carcinoma gallbladder is an aggressive malignancy that occurs predominantly in the elderly and apart from incidentally diagnosed cancer, the prognosis is poor with 5 years' survival rate ranging from 05-40%. The poor prognosis relates to difficulty in early diagnosis of the disease due to absence of specific signs and symptoms.

Most of the patients have systemic disease at the time of presentation.

The interest in the incidental finding of gall bladder carcinoma arises from an excellent outcome associated with it when compared in terms of survival and out come with that of Gall bladder carcinoma.

## II. Material And Methods

A retrospective plus prospective study was conducted from January 2016 to August 2018. A total of 2371 patients were included in this study. All patients who have undergone cholecystectomy for cholelithiasis were included in this study.

Ultrasound scan of the abdomen was done for all patients and was the first-line imaging modality. The number of calculi and thickness of the gall bladder wall and its type, i.e. localized or diffused, were recorded. A contrast-enhanced CT scan was done for the cases that had abnormal gallbladder wall thickness or had a suspicion of malignancy on an ultrasound scan of the abdomen. MRI/magnetic resonance cholangiopancreatography (MRCP) was done selectively for patients who presented with obstructive jaundice. The nature of surgery and HPE diagnosis were recorded.

## III. Results

Incidence of incidental gall bladder carcinoma was 1.18%.

**TABLE NO 1: INCIDENCE OF IGBC**

TOTAL	BENIGN	%	MALIGNANT (IGBC)	%
2371	2343	98.8	28	1.18

In our study majority of the cholelithiasis patients were less than 50 and IGBCs patients were more than 50 years. Mean age in malignant patients was 51.96 with SD  $\pm 2.09$  and the mean age in benign patients was 42.48 with SD  $\pm 2.28$ . The result is significant as p value is  $< 0.05$ .

The mean age of IGBCs patients was significantly higher. Most of the patients with incidental carcinoma GB were females. More than 60% of patients were from rural areas. Abdominal pain was the most common complaint, 2300 patients (97%). Ultrasonography was the first line investigation and was done in all the patients. Ultrasonography abdomen in IGBC patients showed multiple calculi in gall bladder in 20 patients and single calculi in 08 patients.

Laparoscopic cholecystectomy was performed in 1506 out of 2371 patients and elective open cholecystectomy was done in 865 out of 2371 patients and 50 patients required conversion from laparoscopic to open cholecystectomy.

**TABLE NO 2: SEX DISTRIBUTION IN IGBC PATIENTS**

SEX	MALE	FEMALE
NO OF PATIENTS	8	20

Out of 28 cases of IGBC, laparoscopic cholecystectomy was done in 14 patients, open in 12 patients and conversion of laparoscopic to open cholecystectomy in 2 patients. All IGBC cases showed adenocarcinoma. 14 patients showed moderate differentiation, 10 patients were well differentiated and 4 were poorly differentiated.

**TABLE NO 3: HISTOPATHOLOGICAL DIAGNOSIS**

HISTOPATHOLOGICAL DIAGNOSIS	NUMBER	%
CHRONIC NON-SPECIFIC CHOLECYSTITIS	1564	65.9
CHRONIC EOSINOPHILIC CHOLECYSTITIS	390	16.4
ACUTE ON CHRONIC CHOLECYSTITIS	263	11
XANTHOGRANULOMATOUS CHOLECYSTITIS	86	3.6
ACUTE CHOLECYSTITIS	40	1.6
ADENOCARCINOMA(IGBC)	28	1.18

Majority of the patients in the study showed chronic non specific cholecystitis changes on HPE 1564(65.9%) followed by chronic eosinophilic cholecystitis in 390 patients (16.4%). Only 28 cases showed adenocarcinoma(IGBC).

According to pathological staging, pT1a staging was present in 3 patients, pT1b in 15 patients and pT2 in 10 patients. In our study out of 28 IGBC patients, 10 underwent radical cholecystectomy (pT1b), 3 patients underwent extended radical cholecystectomy (pT2), 5 patients never followed up and 7 patients followed up late with locoregional recurrence. 3 patients were managed with only simple cholecystectomy since the pathological staging showed pT1a.

**TABLE NO 4: COMPARISON OF INCIDENCE RATE OF IGBC IN OUR STUDY WITH PREVIOUS STUDIES**

Sr. No	Authors (year)	Total no of cholecystectomy cases in the study	Incidental gall bladder carcinoma (IGBC) cases	Rate of incidence (%)
1	Shrestha R et al (2012)	570	9	3.3
2	GENC V et al (2010)	5164	5	0.09
3	Ghimire P et al (2011)	783	10	1.38
4	Weinstein D et al (2002)	1697	6	0.37
5	Malik K H et al (2009)	260	16	6.15
6	Present study	2371	28	1.18

#### IV. Discussion

Incidental gall bladder carcinoma (IGBC) is defined as GBC found in histopathological analysis after removal of gall bladder tissue for symptomatic benign gall bladder disease.

In our study the incidence rate of incidental GB carcinoma in routine post-cholecystectomy cases was 1.18%. Amanullah et al (1.8%)<sup>[24]</sup> and Shrestha R et al (1.4%)<sup>[14]</sup> have found the incidence similar to ours whereas Zhang WJ et al<sup>[12]</sup> have shown its occurrence to be as low as 0.19% and Navqi et al have found its occurrence to be as high as 5.9%. The variation in the incidence may be due to inadequate preoperative evaluation or less number of cholecystectomy used for the study purpose. This is because the incidence of primary carcinoma of the gall bladder is itself low.

A study done by A.Panebianco, et al<sup>[25]</sup> stated that patients with GBC are around 15–20 years older than patients with gallstones, suggesting that the intraepithelial evolution takes over 10 years. In the era of laparoscopic cholecystectomy for treatment of benign diseases, incidental gallbladder carcinoma has dramatically increased and allows to detect cancer at early stages with a better prognosis.

In our study majority of the cholelithiasis patients were less than 50 years and IGBC patients were more than 50 years. By using Mann-Whitney U test the mean age in malignant patients was 51.96 with SD  $\pm 2.09$  and the mean age in benign patients was 42.48 with SD  $\pm 2.28$ . The p value was 0.0041. The result was significant as p value was  $< 0.05$ .

Carcinoma of the gallbladder affects women 2-6 times more frequently than men, although the extent of this bias varies in different geographical regions (Lazcano-Ponce et al, 2001)<sup>[26]</sup>. In our study both benign and malignant cases, female sex was affected more than male.

A cross sectional study done by Shipra Dwivedi et al<sup>[27]</sup> on gall bladder cancer and some epidemiological factors observed that majority of gall bladder cancer patients belonged to upper lower socioeconomic scale. In our study more than 60% of patients were from rural areas.

With the increasing widespread acceptance of laparoscopic cholecystectomy (LC) and difficulties in diagnosing GBC preoperatively, the number of cases of IGBC during and after LC has increased. In our study laparoscopic cholecystectomy was performed in 1506 patients out of which 375(25%) were male and 1131(75%) were female patients. Elective open cholecystectomy was done in 865 out of 2371 patients, out of which 204(24%) were male and 661(76%) were female patients and 50 patients required conversion from laparoscopic to open cholecystectomy.

It is a standard practice to perform routine histopathological examinations for all cholecystectomy specimens. Various studies including the working report of Royal College of Pathologists<sup>[28]</sup> have recommended for this routine standard practice. Recently few other investigators have challenged this practice. They have suggested that all cases of GB carcinoma have some macroscopic features like thickened fibrotic wall, mucosal ulceration, nodular mucosa or polypoid projections which can be used as a guide for sending for histopathology. In our study we have found that two cases had thickened wall whereas rest 26 (92.8%) of the cases of incidental carcinoma GB had no macroscopic intraoperative findings suggesting the need of routine histopathology of all cholecystectomy sample.

All cholecystectomy specimens were sent for HPE in our study.

Adenocarcinoma is the most common histologic type, accounting for 98% of all gallbladder tumours, two-thirds of which are moderately/poorly differentiated. The remaining common histopathological variants include papillary, mucinous, squamous, and adenosquamous subtypes were noted by R. Hundal and E. A. Shaffer, in their study on "Gallbladder cancer: epidemiology and outcome"<sup>[29]</sup>.

In our study all 28 cases of IGBC showed adenocarcinoma on HPE. Out of 28 patients 14 were well-differentiated, 10 were moderately differentiated and 04 were poorly differentiated.

Ultrasonography is most frequently the initial diagnostic study obtained when gallbladder disease is suspected.

G. Miller and W. R. Jarnagin<sup>[30]</sup>, stated that in advanced gall bladder malignancy disease, sensitivity and specificity of ultrasound imaging is 85% and 80%, respectively; however, in early disease, ultrasound examination often fails to detect any abnormality, particularly when the tumour is flat or sessile and is associated with cholelithiasis.

In our study all patients underwent abdominal ultrasonography as the first-line imaging modality. Shrikhande SV et al in their study on “cholelithiasis in gallbladder cancer: coincidence, cofactor, or cause?”<sup>[31]</sup> Stated that gallstones appear to have a causative role for cancer, the risk increases with increasing size, volume and weight, and number of the stones. In our study only number of stones was taken for study as risk factor. In IGBC cases, multiple gall bladder calculi were present in 20 patients and single calculi were present in 08 patients. Results observed in our study are similar to what observed in above study.

The gallbladder wall thickness was reported to be more than 4 mm in two patients out of 28 IGBC patients. They had focal wall thickening involving the fundus. These two patients were further evaluated with a CECT scan which did not reveal any features suggestive of gallbladder malignancy. MRCP was done for two patients who had choledocholithiasis and they subsequently underwent ERCP for clearance of the CBD.

Ajit Singh et al<sup>[32]</sup> in their study observed that abdominal pain was the most common complaint with which patients had presented and this is similar to what we have observed in our current study i.e. 2300 patients (97%).

The management of IGBC is influenced by the TNM staging. Simple cholecystectomy is an adequate treatment for a pT1a disease provided the margins are negative and there is no evidence of residual disease on imaging. Their outcomes are excellent and are not likely to be improved by radical surgery. Radical surgery is advised in patients with pT1b diseases and above with the aim to resect all possible residual disease and is associated with improved survival compared to that associated with simple cholecystectomy alone.

In our study 10 patients underwent radical cholecystectomy (pT1b), 3 patients underwent extended radical cholecystectomy (pT2), 5 patients never followed up and 7 patients followed up late with locoregional recurrence.

These 7 patients were treated only by chemotherapy as they were diagnosed inoperable at follow up.

3 patients were managed with only simple cholecystectomy since the pathological staging showed pT1a. Major reason for failure to follow up was that the patients were from rural areas.

## V. Conclusion

To conclude, this study from a tertiary care centre in the western part of Rajasthan has found that IGBC is present in 1.18% of patients undergoing cholecystectomy for cholelithiasis.

We have also noted that an age of more than 50 years is significantly associated with IGBC.

Rural population are at a higher risk for gall bladder malignancy because of the late presentation to hospital. Diagnosis of GB carcinoma is difficult at an early stage because of a lack of specific sign and symptoms. Ultrasonography is most frequently the initial diagnostic study obtained when gallbladder disease is suspected. Ultrasonography of cholelithiasis patient showing multiple calculi are at increased risk for gall bladder cancer.

Our study strongly recommends routine histopathological examination in all cholecystectomy specimens as they help in detection of majority of cases of occult carcinoma GB. This study also highlights that although primary carcinoma of gall bladder are known for their late presentation and hence poor survival rates; occult carcinoma GB diagnosed incidentally on histopathological examination of post-cholecystectomy specimen are usually detected at earlier stages and thus have better prognosis.

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