

# Incidence of incidental carcinoma gall bladder in cases of routine cholecystectomy

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## ABSTRACT

### Background

Carcinoma of gall bladder is the most common malignancy of the biliary tract. Most of the cases are diagnosed as an incidental case among patients undergoing cholecystectomy.

### Objectives

To establish the rate of incidental carcinoma of gall bladder in patients undergoing routine cholecystectomy to study the demographic profile and prognosis of these patients.

### Methods

A retrospective study was carried out in Fishtail Hospital and Research Center, Pokhara during 1998-2009. The surgical notes, hospital records and histopathology reports of 783 patients undergoing routine cholecystectomy were studied.

### Results

Out of 783 cases, gall bladder cancer was detected in 10(1.28%) of cases and was more common in females (M:F ratio 1:2.3) and the mean age of occurrence was 63.8 years. Most of the cases diagnosed were at their early stages and none of them were in T3 and T4 stages. Six of these patients have survived till a mean follow up duration of 23.7 months.

### Conclusion

The rate of incidental carcinoma of gall bladder is 1.28%.

## KEY WORDS

*carcinoma gallbladder, cholecystectomy, incidental*

## INTRODUCTION

Cholecystectomy is the most common major abdominal procedure performed worldwide. In US, annual incidence of gall bladder disease is estimated around 1 million amongst which 500-600 thousand cases are operated annually.<sup>1</sup> Carcinoma of gallbladder is the 5th most common cancer of digestive tract and the most common malignancy of the biliary tract.<sup>2,3</sup> The clinical manifestations of gall bladder carcinoma are generally indistinguishable from those associated with cholecystitis or cholelithiasis. Around 90% of GB (Gall bladder) carcinoma have accompanying stone.<sup>4</sup> Stones and chronic inflammation are the risk factors for carcinoma of gallbladder. However, only 0.5-3% of patients with cholelithiasis will develop gallbladder cancer.<sup>5</sup>

Most of the cases of GB carcinoma are diagnosed during or after surgery performed for stones or benign biliary diseases.<sup>6</sup> Despite advancements in various diagnostic procedures, preoperative diagnosis of GB carcinoma is an exception rather than the rule, occurring in fewer than 20.0% of patients.<sup>7</sup> Advanced stage of the disease because of delayed diagnosis leads to its poor prognosis except when diagnosed at early stages incidentally during routine cholecystectomies. Thus some of the surgeons recommend surgery even for the patient with asymptomatic gall bladder stones because of its likelihood to harbour occult malignancy.<sup>8</sup> Role of histopathology of gall bladder specimen after routine cholecystectomy has

also been challenged by various investigators stating that macroscopic features are always present in cases of GB carcinoma which can be used to selectively send specimens for histopathology.<sup>9,10,11</sup>

The aim is to study the frequency of incidental carcinoma of gall bladder in patients undergoing routine cholecystectomy and to study the demographic profile and prognosis of these patients.

**METHODS**

A retrospective study was done on all routine cholecystectomy cases (n=783) performed from 1998-2009 in Fishtail Hospital and Research Center, Pokhara, Nepal. The surgical case notes including the preoperative entry, the operating notes and all clinical information and the histopathological reports of the patients and their follow up were evaluated. The incidence and clinicopathological factors (presenting symptoms, demographics, histopathology, staging and follow up) of gallbladder carcinoma that were detected incidentally during routine cholecystectomy were reviewed and analysis was done using SPSS11.5 software. The results were tabulated and a through review of literature was done. All the cases in which cholecystectomy was done but had any suspicion of malignancy during preoperative evaluation was excluded from the study. The study was ethically approved by the ethical committee of our hospital.

**RESULTS**

A total of 783 cholecystectomies were performed during the study period. Most of the cases (99.23%) were acute or chronic calculus cholecystitis. Six patients were operated for gall bladder polyp. Out of the 777 cases having cholecystitis; 33 patients also had associated choledocholithiasis, 2 patients had Mirrizi syndrome Type II and 5 patients had cholecystoduodenal fistula. Most

common presentation were pain in epigastric region (70.11%), dyspepsia (62.84%), nausea or vomiting (56.96%) and anorexia (44.57%) (Table 1).

**Table 1. Signs and symptoms of patient undergoing cholecystectomy .**

Symptoms/Signs	Frequency
Pain in epigastric region	549 (70.11%)
Dyspepsia	492 (62.84%)
Nausea/Vomiting	446(56.96%)
Anorexia	349 (44.57%)
Rt upper quadrant pain	219 (27.97%)
Fever	132 (16.86%)
Murphy's sign positive	53 (6.77%)
Jaundice	35 (4.47%)

There were 147 males and 636 females with female: male ratio being 4.33:1. The age of the patients ranged from 8 years to 89 years old.

A total of 10 patients (1.28%), 3 male and 7 female were diagnosed to have carcinoma GB on histopathological examination of the GB specimen. The female: male ratio was 2.33:1. The age ranged between 42 to 83 years with mean age being 63.8 years.

None of the cases were suspected pre or intra-operatively to have GB carcinoma despite of thorough investigation preoperatively including liver function tests, routine blood tests, USG of abdomen and pelvis in all cases and CT scan abdomen whenever required. Out of the 10 cases of GB carcinoma 8 were adenocarcinoma and 2 were adenosquamous carcinoma. Eight patients had associated stone whereas 2 cases had GB polyp but no stones. None of the cases had metastasis or involvement of the regional lymph nodes histologically. Eight cases were pathologically staged as T1 whereas two were staged as T2. Out of these two cases re-exploration with resection of segment 4a and 5b was done in one case with T2 disease whereas the other case denied further surgery in view of prognosis and the

**Table 2. Clinical and histological findings of incidental carcinoma GB.**

Age	Sex	Intraoperative Finding	Stone	Type of tumour	Stage (T)	Status	Duration(since diagnosis)
47	F	CCC, Mirizzi	yes	Adenocarcinoma	T1a	Alive, Well	33 months
69	F	Thickened wall	yes	Adenocarcinoma	T1b	Alive, Loss of weight and apetite, No metastasis	11 months
63	F	ACC	yes	Adenosquamous carcinoma	T1a	Alive , well	24 months
57	F	Polyploid mass	No	Adenocarcinoma	T1b	Died	17 months (Trauma)
82	F	CCC, CBD stone	yes	Adenosquamous carcinoma	T2	Died, denied further surgery or chemo	8 months
73	M	CCC	yes	Adenocarcinoma	T1b	Alive, well	36 months
49	F	CCC	yes	Adenocarcinoma	T1b	Alive, well	23 months
76	M	Polyploid mass	No	Adenocarcinoma	T2	Alive, well	12 months
42	M	CCC, CBD stone	yes	Adenocarcinoma	T1a	Died	38 months
80	F	CCC	yes	Adenocarcinoma	T1b	Died	13 months (MI)

CCC= Chronic Calculus Cholecystitis; CBD= Common Bile Duct; MI= Myocardial Infarction

**Table 3.** List of various studies showing incidence of incidental carcinoma GB.

Studies	Year	Place	Sample size	M:F	Mean age (yrs)	Incidence (GB ca)
Daphna et al <sup>21</sup>	-	Israel	1697	1:5	70	0.3%
Khoo JJ & Nurul AM <sup>22</sup>	2000-2005	Malaysia	1122	1:2	56.7	0.62%
Mittal R et al <sup>9</sup>	1998-2007	India	1305	1:5.5	56.2	0.99%
Zhang WJ et al <sup>19</sup>	1999-2007	China	10,466	1:4	65.7	0.19%
Amanullah et al <sup>17</sup>	2000-2002	India	428	1:7	47	1.87%
Shrestha R et al <sup>18</sup>	2003-2007	Nepal	570	1:3.5	53.56	1.4%
Naqvi et al <sup>20</sup>	1985-2004	Pakistan	1109	1:4.4	-	5.9%
Present Study	1998-2009	Nepal	783	1:2.3	63.8	1.28%

age of the patient. All the cases were further consulted with oncologist for further adjunctive therapy.

Out of the 10 cases of incidental carcinoma GB, two patients died at 13 and 17 months of diagnosis due to causes unrelated to GB carcinoma; two patients died due to metastatic disease. 6 (60%) of the patient have still survived at a mean follow up duration of 23.17 months. The details of the 10 cases of incidental carcinoma GB has been described in Table 2.

## DISCUSSION

Though Gallstones are very often implicated with gall bladder carcinoma; other factors implicated to increase the risk include porcelain gallbladder, adenomatous polyps of the gallbladder, chronic infection with Salmonella typhi, carcinogen exposure (e.g., miners exposed to radon), and abnormal pancreaticobiliary duct junction (APBDJ).<sup>5</sup> Most of the cases of carcinoma GB are diagnosed at advanced stage and have a poor prognosis having 5 year survival rate of <5%. When detected at early stages prognosis may improve significantly up to 90-100% five years survival rate.<sup>12,13</sup> However these carcinomas are known to have delayed onset of symptoms. They are also usually diagnosed as incidental finding post cholecystectomy and theoretically this group carries the best prognosis.<sup>14</sup> In our series, 60% of our patients with incidental carcinoma had survived till a mean follow up duration of 23.17 months.

In our series the incidence rate of incidental GB carcinoma in routine post-cholecystectomy cases was 1.28%. Amanullah et al (1.8%) and Shrestha R et al (1.4%) have found the incidence similar to ours whereas Zhang WJ et al has shown its occurrence as low as 0.19% and Navqi et al has found its occurrence as high as 5.9%.<sup>15-18</sup> The list of various authors with the variety in their observation of occult carcinoma of GB is listed in Table 3.<sup>9,15-20</sup> The variety 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. Most of the patient with incidental carcinoma GB were female (M:F ratio 1:2.33) and the mean age was 63.8 years. Most of the studies listed in table 3

show similar pattern of findings.

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 have recommended for this routine standard practice.<sup>15,21</sup> 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 polypoid mass and one case had thickened wall whereas rest seven (70%) of the cases of incidental carcinoma GB had no macroscopic intraoperative findings suggesting the need of routine histopathology of all cholecystectomy sample.

There are few limitations of the study which include the retrospective nature of the study. The shorter follow up period for cases of incidental GB carcinoma and no comparison between laparoscopic and open cholecystectomy while studying the incidence and clinicopathological nature of this disease in this study.

## CONCLUSION

The rate of incidental carcinoma of gall bladder in our setting was found to be 1.28%. 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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