



## ROUTINE HISTOPATHOLOGY FOR ALL CASES OF ELECTIVE CHOLECYSTECTOMY AND ITS SIGNIFICANCE IN INCIDENTAL MALIGNANCY OF GALLBLADDER

### KEYWORDS

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### ABSTRACT

**Objectives :** All gallbladder removed for presumed benign disease has been sent for histopathological examination (HPE), but this practice has been the subject of controversy. This study was undertaken to observe the significance in detecting the malignancy of gallbladder which was not detected pre operatively.

**Methods :** This study is a retrospective study where 531 patients who underwent cholecystectomy in the department of general surgery were included in the study for the yr 2013-2015. All the patients underwent cholecystectomy for benign pathology and histopathology reports were studied.

**Results :** The incidence of gallbladder malignancy in this study was 6.5% which is a significant value with more in male and patients above the age of 60 years. Out of 531 (35) patients had ca gallbladder which was detected in the histopathology report.

**Conclusion :** All patients undergoing cholecystectomy the specimen should be sent for histopathology to detect inapparent malignancy pre operatively for early treatment and better management.

### Introduction

Gallbladder cancer (GBC) is the most common cancer of the biliary tract worldwide. 1 Surgical resection of the tumour and its loco-regional spread remains the only hope for long-term cure and survival. Incidental GBC (IGBC) refers to GBC that is not suspected before or at operation and even on gross examination of the opened gallbladder specimen by the surgeon, but is detected for the first time on histopathological examination (HPE) of a gallbladder removed for presumed (clinical, ultrasound, operative) diagnosis of gallstone disease (GSD). In practical terms, all GBCs not detected preoperatively and diagnosed during or following surgery are considered as IGBC. The incidence of IGBC has been reported to range from 0.3–1.5% in various series. 2 Although the overall prognosis of GBC is poor, IGBC is associated with better outcomes. 3,4 The literature-based support for a better prognosis in IGBC is based on the fact that tumours detected on HPE usually represent early-stage disease and patients are referred promptly by their treating physicians for definitive surgery. Completion radical cholecystectomy is the standard treatment for IGBC of stage Ib and beyond. 3,5,6 The early-stage tumours for which surgical resection provides the greatest benefit are difficult to diagnose preoperatively and are often missed even after intraoperative examination of the cholecystectomy specimen. 7–9 Hence, it has been standard practice to submit all gallbladders removed for presumed GSD to routine HPE to exclude gallbladder malignancy. 10 In recent years, however, the role of routine HPE of cholecystectomy specimens has been questioned. 11–15 In India, some centres do not send all cholecystectomy specimens for HPE and this centre often manages post-cholecystectomy GBC patients who present late in the course of disease without HPE data and with symptoms of recurrence. This provided an opportunity to study the impact of avoiding routine histopathology of all cholecystectomy specimens. This study was done to observe the significance of the histopathology for detecting gall bladder surgery and the significance in the HPE to detect the ca gallbladder which is not detected pre operatively.

### Methods and materials

This study was a retrospective analysis of prospectively collected GBC data for 531 patients with gallbladder diseases who were diagnosed to have malignancy after

cholecystectomy, who were referred to this centre during the period 2013-2015.

All the patients who were admitted in the JSS hospital during the study period underwent USG abdomen which showed cholelithiasis along with essential pre-operative evaluation for anaesthesia and they were subjected to laparoscopic cholecystectomy without any pre-operative suspicion of gallbladder malignancy. Some cases intraoperatively were suspicious of malignancy however all the specimens were sent to histopathology. All the data was collected in a perform.

### Results

Over a period of two years, five hundred and thirty-one patients with symptomatic gallstones were admitted for cholecystectomy. There were 315 females and 216 males with a male to female ratio of 1:4. The age ranged from 19 to 80 years with the mean age of  $32.3 \pm 5.3$  years (Table 1). Majority of patients (80%) presented with upper abdominal pain of varying duration. Other symptoms are depicted in Table 2.

**Table 1 Age distribution\***

Age of patients(years)	No.of Patients(n=531)	%
19-30	98	24.6
31-40	301	27.8
41-50	90	26.8
51-60	30	15.4
61-70	10	4.5
71-80	02	0.9

Age of patients(years)	No.of Patients(n=531)	%
61-70	10	4.5
71-80	02	0.9

**Table 2 Presenting symptoms**

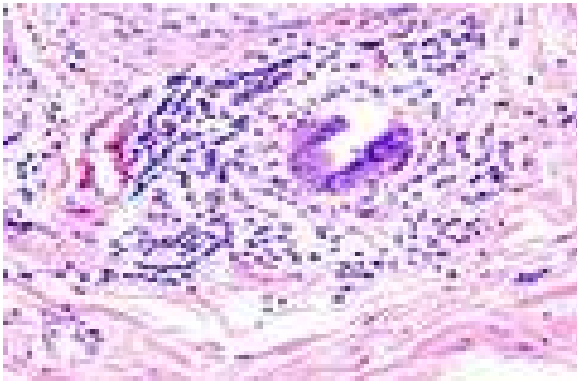
Symptoms	No.of Patients(n=531)	%
Pain in Upper abdomen	201	91.4
Intolerance to fatty food	274	61
Nausea and/or vomiting	51	20
Mass in right hypochondrium	5	2.3

All 220 gallbladders were palpated and were opened per-operatively for any focal or diffuse thickening of the gallbladder wall, a raised mucosal plaque, polypoid growth or an infiltrating grey white mass. The specimens were then sent for histopathology. Two hundred and three of the specimens showed evidence chronic cholecystitis, 7 acute cholecystitis with mucocele, 3 acute cholecystitis with empyema and one incidental associated polyp. Six gallbladders (2.8%) showed evidence of adenocarcinoma of varying differentiation along with cholelithiasis, (Table 3).

**Table 3 Histopathological report (n=531)**

Histopathology	Male	Female	%
Chronic Cholecystitis	100	275	92.3
Acute cholecystitis with mucocele	21	31	3.2
Acute cholecystitis with empyema	15	22	1.3
Polyp	30	20	0.5
Malignancy	15	20	2.7

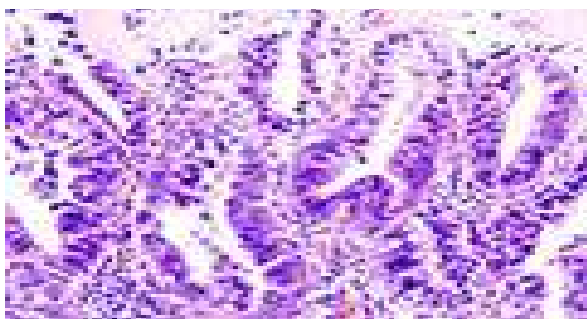
There were 35 incidental carcinomas with 4 gross abnormalities in this series. Subsequent staging revealed 25 adenocarcinomas in stage T1b, 9 in stages T2 and 1 in T3 stage.



Gallbladder adenocarcinoma lymphatic invasion histopathology.



Incidentally discovered gallbladder cancer (adenocarcinoma) following a cholecystectomy.



## Gallbladder adenocarcinoma histopathology

### Discussion

Gallbladder cancer is the most common malignancy of the extrahepatic biliary tree.<sup>1</sup> It is usually detected at an advanced stage and is associated with a dismal prognosis.<sup>3</sup> Although early-stage tumours are associated with good prognosis, the preoperative detection of tumours that are more likely to benefit from surgical resection is difficult.<sup>7</sup> The clinical presentation of early GBC is non-specific and symptoms are similar to those of acute or chronic cholecystitis. Although an expert radiologist can detect the presence of early lesions in the form of focal gallbladder wall thickening or lesions of small mass, not all cases of early GBC present with an obvious lesion on abdomen ultrasonography.<sup>7</sup> Some of the small lesions missed on preoperative ultrasound can be picked up on gross examination of the cholecystectomy specimen. Histopathological examination of the cholecystectomy specimen facilitates the detection of tumours that are not apparent even on gross examination of the specimen.<sup>8</sup> Hence, it has been traditional practice to send all cholecystectomy specimens for HPE.

In this study, females outnumbered males with male to female ratio of 1:4. Female predominance is also reported in many studies. The mean age  $32.25 \pm 5.3$  years ranging from 19 to 80 years, slightly higher than that reported in other studies (12). Over ninety one per cent patients presented with pain upper abdomen and dyspeptic symptoms. A where all patients had upper abdominal pain. None of the patients in our study had any evidence of malignancy either clinically or on ultrasound examination.

The most common histopathological finding in our study was chronic cholecystitis; (92.3%) specimens were reported as chronic inflammation with mucosal ulceration, denudation, metaplasia to dysplasia and wall infiltration by chronic inflammatory cells like neutrophils, macrophages, plasma cells and varying degrees of fibrosis. A similar study by Memon [13] also reports chronic cholecystitis as major histopathological finding, identified in 64.8% cases.

Empyema of the gallbladder is often difficult to distinguish from uncomplicated acute cholecystitis [12]. In this study, 3 (1.3%) cases were reported as acute cholecystitis with empyema of gallbladder. This is in stark contrast to 31.5% cases of empyema associated with cholecystitis as reported by Memon [13]. Mucocele of the gallbladder has an incidence of 3 percent. In this study, 31 cases presented as cholecystitis with mucocele; reported incidence of mucocele is, however, several times higher (14/15). Gallbladder polyps have an incidence ranging from 4.6 to 6.9 per cent [15]. In our study, 50 cases of gallbladder polyp was identified. In our series, incidental carcinoma of gallbladder was found in 35 cases (5.7%). These gallbladders showed no gross abnormality per-operatively. The incidence of gallbladder malignancy in this series was considerably low compared to other studies, which show an incidence varying from 6.9 to 12 per cent [14, 15]. All patients in our series presented with longstanding history of chronic cholecystitis. There were no symptoms or signs suggestive of underlying malignancy in any patient; gallbladder malignancy usually does not have any characteristic clinical features with over 90 per cent of patients presenting with symptoms of acute or chronic cholecystitis. Although ultrasound has a high diagnostic accuracy for both advanced and early gallbladder cancer [20], none of the 35 cases carcinomas in this series were picked on preoperative ultrasound. In addition, all six gallbladder specimens showed no macroscopic evidence of malignancy when they were opened during surgery. Similar

observations and recommendations are made by other studies [16,17]. The issue of routine histopathology of all gallbladder specimen therefore remains unresolved; the need to send every specimen for histopathology or otherwise therefore depends on the expertise of the ultrasonologist as it depends on the skill of the operating surgeon. We, however, advocate routine histopathology of all gallbladders removed at surgery since the subsequent report would provide evidence of malignancy on solid grounds.

Although there are myriad of premalignant conditions, carcinoma gallbladder has a strong association with gallstones [17]. The strong association between the two warrants attention paid to histopathology of specimen in all cases undergoing cholecystectomy for cholelithiasis, irrespective of presence or otherwise of any gross abnormalities. It is widely reported that long standing mucosal irritation by the stones cause atypical cellular changes and increased cellular proliferation. It has been hypothesized that in long standing cases, these areas of hyperplasia progress to metaplasia and carcinoma-in-situ [18]. Studies confirm presence of such changes in the vicinity of gallbladder carcinoma [18].

### Conclusion

The histopathological spectrum of gallbladder after cholecystectomy is extremely variable. Incidental diagnosis of carcinoma gallbladder is not rare; we discovered evidence of malignancy in 35 (.5.7%) cases on subsequent histopathological examination of gallbladder specimen, which showed no gross features of cancer. These cases had no symptoms suggestive of underlying malignancy nor was cancer reported on any of cases would have been failed to identify with disastrous results; We therefore, strongly advocate routine histopathology of all cholecystectomy specimens. Old patients and patients having long duration symptoms are

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