HISTOPATHOLOGICAL EXAMINATION OF CHOLECYSTECTOMY SPECIMENS- ROUTINE OR SELECTIVE?
Kalisetty Suresh Babu¹, Kondapaturu Lakshmi Chandrasekhar², Dogga Hemanth Saikumar³, Yendeti Hemraj⁴, Kandan Nivetha⁵

¹Assistant Professor, Department of General Surgery, King George Hospital, Andhra Medical College, Maharanipeta, Visakhapatnam, Andhra Pradesh.
²Postgraduate, Department of General Surgery, King George Hospital, Andhra Medical College, Maharanipeta, Visakhapatnam, Andhra Pradesh.
³Postgraduate, Department of General Surgery, King George Hospital, Andhra Medical College, Maharanipeta, Visakhapatnam, Andhra Pradesh.
⁴Postgraduate, Department of General Surgery, King George Hospital, Andhra Medical College, Maharanipeta, Visakhapatnam, Andhra Pradesh.
⁵Postgraduate, Department of General Surgery, King George Hospital, Andhra Medical College, Maharanipeta, Visakhapatnam, Andhra Pradesh.

ABSTRACT

BACKGROUND
The objective of routine histopathological examination of all cholecystectomy specimens is to confirm the clinico-radiological diagnosis, identification of unsuspected findings including incidental gallbladder malignancy. This study is to assess the need for routine or selective histopathological evaluation of gallbladder specimens following cholecystectomy. We wanted to determine as to whether routine histological examination of every cholecystectomy specimen is justified.

MATERIALS AND METHODS
Patients undergoing cholecystectomy either by open or laparoscopic technique were included. The American Joint Committee on Cancer (AJCC) Tumour Nodal Metastasis (TNM) system was the reference for staging carcinoma gallbladder. Cholecystectomy done as a part of other surgical procedures like liver resection, Whipple procedure & prophylactic cholecystectomies done for sickle cell anaemia were excluded.

RESULTS
Adenocarcinoma of gallbladder was detected in 1.14%, out of 176 cases on histopathological examination. Frequency was more in females and the mean age of occurrence was 31 years. Both patients underwent open cholecystectomy and had well and moderately differentiated adenocarcinoma on histopathology respectively.

CONCLUSION
All cases of invasive carcinoma of the gall bladder showed macroscopic abnormal appearance either pre- or intra-operatively. A more selective policy for histological examination of the gall bladder specimens would not miss any invasive malignancy. It would significantly reduce the workload for a pathologist, be more cost-effective and still remain safe for the patients.

KEYWORDS
Gall Bladder Carcinoma, Cholelithiasis, Cholecystitis, Cholecystectomy.
Though signs and symptoms are often nonspecific, the symptoms to be considered as prime importance are right hypochondriac pain, anorexia, loss of weight without intention, obstructive jaundice features (late sign), ascites, especially in elder individuals. Palpable mass per abdomen is a late sign.

Most of the gall bladder carcinomas are adenocarcinomas, which includes various subtypes like papillary, nodular and tubular. Squamous, adenosquamous and anaplastic types are rare entities. Papillary type has an overall better outcome due to its localization to the gall bladder. The spread of disease is mainly by lymphatics, venous drainage and direct spread to liver parenchyma. Histologically, gall bladder differs from intestines histology in lacking muscular is mucosa and submucosa, thus lymphatics are present in sub serosal layer.

Therefore, cancers not invading the muscular layer have minimal risk of nodal involvement. Thus, intraoperatively about 25% tumours are localized disease, 35% have regional lymph nodal involvement or extension into liver parenchymal tissue and approximately 40% have distant metastasis.

The frequency of incidental gallbladder carcinoma diagnosis in routine cholecystectomy is estimated between 0.2 and 2.8%.

Despite all the advancements in the imaging techniques the suspicion is usually intra-operative, where localized malignancies are found to be difficult to differentiate from chronic cholecystitis, cancer, the tumour is most commonly found to be nodular and infiltrative, with thickening of gall bladder wall, often extending into the entire gall bladder. And the confirmation of malignancy can only be done by histological assessment.

Selective approach for sending cholecystectomy specimens for histopathology is not favoured as yet, as it can result in missing discrete pathologies and premalignant benign lesions such as porcelain gallbladder, carcinoma-in-situ, and early carcinomas.3

MATERIALS AND METHODS

This descriptive study was carried out at the Department of General Surgery Andhra medical college, Visakhapatnam, from September 2016 to October 2018. Patients undergoing cholecystectomy either by Open or Laparoscopic technique were included. Cholecystectomy done as a part of other surgical procedures like liver resection, Whipple procedure & prophylactic cholecystectomies done for sickle cell anaemia were excluded & autolysed specimens were excluded from the study.

Detailed histopathology reports and detailed records of the patients found to have malignancy were obtained from notes and electronic database to evaluate preoperative laboratory, ultrasound and intra-operative findings. The American Joint Committee on Cancer (AJCC) Tumor Nodal Metastasis (TNM) system was the reference for staging carcinoma gallbladder.

RESULTS

Patients (n=176), undergoing routine cholecystectomy specimens were included. Majority (63%) were female, with a male to female ratio of 1:1.7. Mean age was 42.25 years. Gallstones were found in 93.75% patients. Chronic cholecystitis was the commonest (80.68%) pathology followed by acute cholecystitis in 18.17%. There were no cases of carcinoma in situ.

None of the macroscopically normal specimens have malignancy. There were no incidental carcinomas in this study.

![Figure 1](image)

**Figure 1**

![Figure 2](image)

**Figure 2**

<table>
<thead>
<tr>
<th>Histopathology</th>
<th>Male</th>
<th>Female</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Cholecystitis</td>
<td>54</td>
<td>80</td>
<td>134 (76.15)</td>
</tr>
<tr>
<td>Acute on Chronic Cholecystitis</td>
<td>10</td>
<td>16</td>
<td>26 (14.77)</td>
</tr>
<tr>
<td>Acute Cholecystitis</td>
<td>3</td>
<td>5</td>
<td>8 (4.54)</td>
</tr>
<tr>
<td>Gangrenous Gall Bladder</td>
<td>2</td>
<td>4</td>
<td>6 (3.40)</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>0</td>
<td>2</td>
<td>2 (1.14)</td>
</tr>
</tbody>
</table>

*Table 1. Histopathological Report (n=176)*

Incidence of adenocarcinoma of gallbladder was 1.14% (n=2). Frequency was more in females and the mean age of occurrence was 31 years. Both patients underwent open cholecystectomy and had well and moderately differentiated adenocarcinoma on histopathology. Both patients underwent open cholecystectomy.
DISCUSSION
In our study we have included 176 cases presenting to the OPD of department of surgery, King George Hospital, Andhra medical college Visakhapatnam with symptomatic gall stones, confirmed by imaging studies and admitted for further management. Duration of study was from September 2016 to October 2018.

Frequency of gallbladder carcinoma exhibits a marked variability throughout the world. Asia is a high risk continent. The frequency of intra or post-operative incidental gallbladder carcinoma diagnosis is estimated between 0.2 to 2.8%. Gallbladder carcinoma is asymptomatic in 15-30% of cases or presents with atypical symptoms. Diagnosis is often made at an advanced stage with a poor prognosis. The stage of disease at the time of presentation determines the microscopic tumour clearance (R0) and thus outcome of the surgery. Good prognosis is anticipated in patients with gallbladder carcinoma discovered as an incidental finding mostly because early stage of diagnosis require only cholecystectomy.

At present, the only hope of a cure in the case of gall bladder adenocarcinoma is offered by surgery. The extent of curative R0 resection depends on the stage of the disease at the time of diagnosis. It ranges from simple cholecystectomy for Tis to pT2a and radical cholecystectomy including segment 4a and 5 of the liver and regional lymphadenectomies for pT2b. In T3 and T4 tumours with no lymph nodal involvement or no peritoneal metastasis, complete excision of the tumour with an extended hepatectomy (Couinad’s segments (IV, V, VI, VII, and VIII) should be done for adequate clearance of the tumour. This aggressive approach has resulted in increasing the survival rate of T3 and T4 tumours.

The accurate pre-operative diagnosis of gall bladder carcinoma is very difficult, and it is during the operation that suspicion or clinical diagnosis of malignancy is made. However, in each case, a gross macroscopic abnormality of the gall bladder was easily identifiable and prompted the surgeon to send the specimen for histological examination. These series confirm that there was not a single case of invasive adenocarcinoma of the gall bladder that would have been missed if only macroscopically abnormal specimens were examined. Chronic cholecystitis was the commonest (80.68%) pathology followed by acute cholecystitis in 18.17%. There were no cases of carcinoma in situ. None of the macroscopically normal specimens have malignancy. There were no incidental carcinomas in this study.

Present study confirms that combined with pre-operative suspicion, and the intra-operative findings can help to diagnose gallbladder carcinoma. The gross abnormalities can guide to send the specimen for histopathology and make definite histological diagnosis. Literature is filled with evidence to support a more selective policy towards histopathological examination. Multiple series have confirmed the safety, efficacy and rationality of sending macroscopically normal specimens for histopathology while not missing a single case of invasive adenocarcinoma of gallbladder. Darmas et al reported incidental gallbladder carcinoma in 0.3% i.e. in only four of 1452 patients for whom cholecystectomy specimens were examined over a period of 5 years, all four of whom demonstrated mass on gross examination of the cholecystectomy specimen and two of those showed pre-operative suspicions of malignancy. In a prospective comparative study by Romero-González et al it was concluded that it was safe not to send almost half (46%) of cases for histopathology by considering pre-operative, intra-operative and post-operative evidence pointing towards malignancy.

CONCLUSION
All cases of invasive carcinoma of the gall bladder showed gross macroscopic abnormal appearance either pre- or intra-operatively. A more selective policy for histological examination of the gall bladder specimens would not miss any invasive malignancy. It would significantly reduce the workload for a consultant pathologist, be more cost-effective and still remain safe for the patients.

REFERENCES
[1]

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>USG Findings</th>
<th>Gross Examination</th>
<th>Type of Tumour</th>
<th>Site of Tumour</th>
<th>Grade</th>
<th>Stage</th>
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</thead>
<tbody>
<tr>
<td>27</td>
<td>F</td>
<td>Mass Replacing the Gall Bladder</td>
<td>Irregular, Cauliflower Like Exophytic Mass From Fundus Invading the Underlying Wall</td>
<td>Papillary Adenocarcinoma</td>
<td>Fundus</td>
<td>High Grade</td>
<td>T3N0M0</td>
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<tr>
<td>70</td>
<td>F</td>
<td>Polyp in The Gall Bladder &gt;1 cm</td>
<td>Irregular Growth Projecting into The Lumen from Fundus</td>
<td>Papillary Adenocarcinoma</td>
<td>Fundus</td>
<td>High Grade</td>
<td>T2N0M0</td>
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</tbody>
</table>

Table 2. Patients with Gall Bladder Adenocarcinoma


