

## Original Article

# Prevalence of Malignancy and Incidental Carcinoma in Routine Histopathology of Gall Bladder after Cholecystectomy for Gall Stones in the Age Group 30-60 Years

Mayurpankhi Saikia<sup>1</sup>, Junu Devi<sup>2</sup>

**Background :** Gall Bladder is the most commonly resected organ for various Pathological conditions and most common specimen received in the laboratory. Cholelithiasis is the most common cause of Cholecystectomy. Association of Cholelithiasis and Gall Bladder Carcinoma is strong. Gall Bladder Adenocarcinoma is a rare malignant tumor with insidious onset, rapid local invasion and progression. The frequency of incidental Carcinoma of Gall Bladder is also increasing and is estimated between 0.2% to 2.8%. Objectives of this study is to determine the various Gall Bladder lesion and detection of incidental Carcinoma in routine Histopathological study of Cholecystectomy specimens in 30-60 years age group.

**Materials and Methods :** Total 556 Cholecystectomy cases were enrolled in the study and it was done for a period of one year from August, 2015 to July, 2016. The specimens received were fixed in 10% formalin and were examine grossly and processed routinely. Sections were stain with Haematoxiline and Eosine stain and Microscopic findings were noted.

**Results :** out of 556 cases 124 were male 432 were female with M:F = 1:3.5. Most commonly affected age group is 30-40 years. Non-neoplastic (98.6%) cases are more than Neoplastic (1.4%) cases. Among Non-neoplastic cases most common Histopathological diagnosis was Chronic Cholecystitis (83.4%). All Neoplastic cases were malignant tumors involving the age group 40-60 years (P=0.04) and M:F=1:7. Histopathologically all were Adenocarcinoma. Prevalence of Gall Bladder Carcinoma was 1.4% and prevalence of incidental Carcinoma was 0.89%.

**Conclusion :** Routine Histopathological analysis of all Gall Bladder specimens after Cholecystectomy operation is mandatory for detection of various Pathological conditions and diagnosis of Gall Bladder Carcinoma specifically incidental Carcinoma which help in proper management the cases. However more studies with large numbers of cases are recommended for evaluation of incidence of incidental Carcinoma.

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**Key words :** Cancer, Gall bladder, Cholecystitis.

Gall bladder is among the most common surgically resected organs and the numbers of Cholecystectomies have increased more than 50% in the past decade<sup>1</sup>. It is affected by variety of non-neoplastic and Neoplastic lesions. More than 90% of Biliary diseases are attributed to Gall Stones. Moreover the most important risk factor for Gall Bladder cancer (besides gender and ethnicity) is Gallstones which are present in 95% of cases. Chronic trauma and inflammation can induce epithelial dysplasia, Carcinoma in situ and invasive cancer but a cause and effect relationship is not proven<sup>2</sup>. In India, carcinoma of Gall Bladder is much more common in women in North and Central part than in the West and the South<sup>3</sup>. The frequency of incidental Gall Bladder Carcinoma diagnosis in routine Cholecystectomy is estimated between 0.2 and 2.8%. Routine

Department of Pathology, Gauhati Medical College, Guwahati 781032

<sup>1</sup>MD, Assistant Professor

<sup>2</sup>MD, PhD, Associate Professor and Corresponding Author

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### Editor's Comment :

- Gall stone is the most important risk factor for Gall Bladder Carcinoma.
- After Cholecystectomy thorough sampling of Gall Bladder specimen is mandatory for diagnosis of incidental Carcinoma.

Histopathological examination of all cholecystectomy specimen is mandatory because of significant risk of incidental Carcinoma. Aim of this study is to determine the frequency of malignancy and incidental Carcinoma in routine cholecystectomy specimens.

### MATERIALS AND METHODS

The present study is a cross sectional study carried out in the Department of Pathology, Gauhati Medical College and Hospital, Guwahati done for a period of one year from August, 2015 to July, 2016. The study was approved by Institutional Ethical Committee of Gauhati Medical College and Hospital, Guwahati vide letter number NO.MC/02/2015/218. All total 556 cases (sample size) of Cholecystectomy Specimens (30-60

years) received in the Department of Pathology, GMCH were included and analysed. Specimens received in a poorly preserved or autolysed State were excluded. Detail gross examination of formalin fixed specimens were done and subjected to histopathological processing and paraffin blocks preparation.

Sections were cut at 3-5 micron thickness and stained by Hematoxylin and Eosin and mounted in Dibutylphthalate Polystyrene Xylene (DPX) and examined under the microscope. Pathological diagnosis was made and classified.

**OBSERVATIONS AND RESULTS**

Out of 556 cases majority of cases (293, 52.7%) were in the age group of 30-40 years followed by 26.4% in 41-50 years age group and 20.9% in 51-60 years age group respectively. In gender distribution out of 556 cases 124 were male and remaining 432 were females with a M:F =1:3.4. Females are more commonly affected by Gall Bladder disease than males (Table 1, Fig 1).

Clinically patients had varied symptoms that included pain in right hypochondrium (91.9%), nausea or vomiting (5.9%), fever (0.9%), weight loss (0.7%), right hypochondriac mass (0.5%). In the present study maximum numbers of cases 548(98.56%) were non neoplastic in nature and 08 (1.4%) cases were neoplastic lesions. Among the non-neoplastic lesions 529(96.5%) cases were inflammatory lesions and rest 19 (3.4%) were pre-malignant lesions (Fig 2).

Among the inflammatory lesions we got maximum cases of Chronic cholecystitis, followed by other benign

Histopathological Diagnosis	No of cases	Percentage (%)
Chronic cholecystitis	464	83.45 %
Acute on chronic cholecystitis	14	2.52 %
Xanthogranulomatous cholecystitis	15	2.70 %
Chronic cholecystitis with cholesterolosis	16	2.88 %
Follicular cholecytitis	5	0.90 %
Eosinophilic cholecystitis	5	0.90 %
Empyema GB	1	0.18 %
Mucocele GB	3	0.54 %
Chronic cholecystitis with Intestinal metaplasia	8	1.44 %
Chronic cholecystitis with Antral metaplasia	6	1.08 %
Chronic cholecystitis with Epithelial Dysplasia	5	0.90 %
Chronic cholecystitis with Adenomyomatosis	5	0.90 %
Cholesterol Polyp	1	0.18 %
Neoplastic	8	1.44 %
Total	556	100 %

lesions. All 8 neoplastic lesions were malignant tumours and all of them were adenocarcinoma.

A total of 8 cases were diagnosed to have Gall Bladder carcinoma by histopathological examination. The male to female ratio was 1:7.

They were between the ages 40-60 years old. Only 3 out of 8 cases were clinically suspected to have Gall Bladder Carcinoma. Others were diagnosed as Chronic Calculus Cholecystitis clinically. Incidence of incidental Gall Bladder Carcinoma in our study was 0.89%. The patients had varied symptoms that included pain in right hypochondrium, vomiting and weight loss.

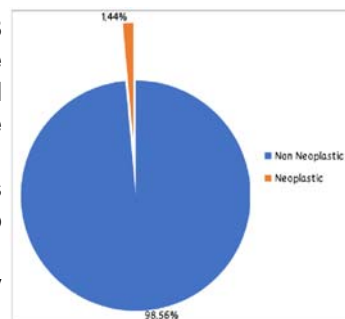


Fig 2 — Pie Diagram Showing Distribution of Gall Bladder Les

Sex	Age Group (in years)			Total
	30-40	41-50	51-60	
Male	61	34	29	124(22.3%)
Female	232	113	87	432(77.7%)
Total	293(52.7%)	147(26.4%)	116(20.9%)	556(100%)

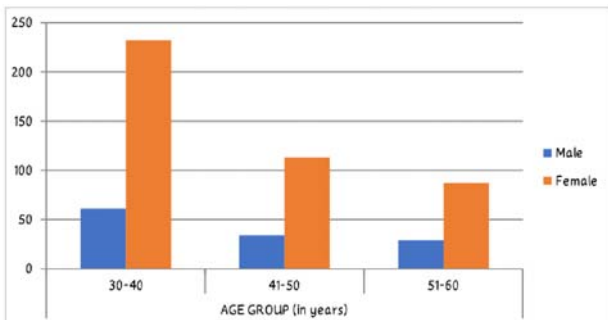


Fig 1 — Bar Diagram Showing Age and Sex Distribution of Gall Bladder Lesions

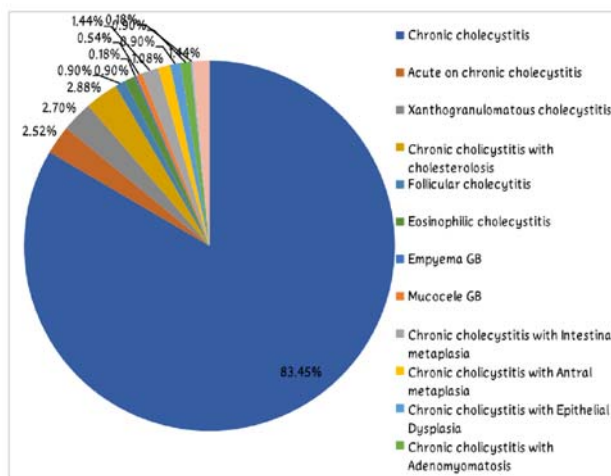


Fig 3 — Pie Diagram Showing Total Distribution of Gall Bladder Lesions

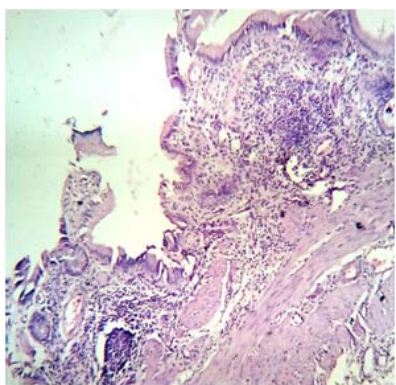


Fig 4 — Microscopic Image of Chronic Cholecystitis (10x40), H&E Stain



Fig 5 — Gross Picture of Strawberry Gall Bladder

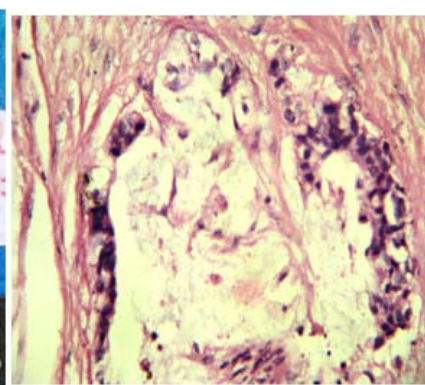


Fig 6 — Microscopic Image of Mucinous Adenocarcinoma Gall Bladder (10x40, H&E)

Macroscopically 2 of the 8 cases showed polypoidal growth, 1 case showed nodular mucosa and others showed thickened and normal Gall Bladder Wall. All of them were Adenocarcinoma histopathologically of which 3 cases were of well differentiated Adenocarcinoma, 2 cases each of moderately differentiated Adenocarcinoma and Papillary Adenocarcinoma and 1 case of mucinous adenocarcinoma.



Fig 7 — Gross Picture of Gall Bladder Carcinoma

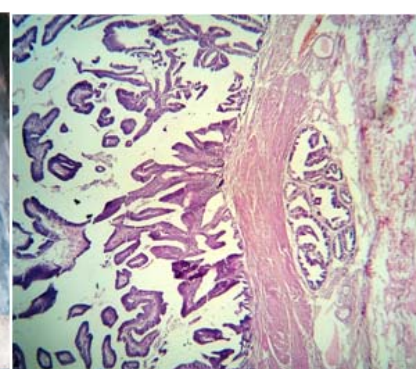


Fig 8 — Microscopic Image of Papillary Adenocarcinoma Gall Bladder (10x10, H&E)

In our study the p- value for the age of Neoplastic lesions is 0.04 which is <0.05 and it is statistically significant. Male to female ratio in Gall Bladder Carcinoma was found to be 1:7. Increased frequency of Gall Bladder Carcinoma in females suggested a possible role of hormonal factors.

**DISCUSSION**

Frequency of Gallstones increases with age, more after 40 years of age and becomes 4 to 10 times more likely in older individuals. The risk factors predisposing to Gallstones formation include Obesity, Diabetes mellitus, Estrogen and Pregnancy.

In our present study, the peak age group among both male and female affected by Gallbladder diseases in general was 30-40 years group which is consistent with studies by Mohan H, *et al* (2005)<sup>4</sup>, Nailesh Shah, *et al* (2010)<sup>5</sup>, Sabina, *et al* (2013)<sup>6</sup>. But there are some studies like, Arati NA, *et al* (2013)<sup>7</sup> & Gajendra Singh, *et al* (2016)<sup>8</sup> who had maximum numbers of patients in the 41 to 50 years age group. In our study we found female pre-ponderance. The male to female ratio was found to be 1 : 3.5. which is consistent with the studies by Nailesh Shah, *et al* (2010)<sup>5</sup>, Mustafa Mazlum, *et al* (2011)<sup>9</sup>, Arati NA, *et al* (2013)<sup>7</sup>.

In the present study out of 556 Cholecystectomy

specimen, 464 specimen belong to Chronic Cholecystitis (83.45%) thus making it the most common histopathological findings and this value is similar with the other studies like Sabina, *et al* (2013)<sup>6</sup>, Sunil Kumar KB, *et al* (2015)<sup>10</sup>. We got 15 cases of Xanthogranulomatous Cholecystitis (2.75%) which is consistent with the studies by Tadasi Terada, *et al* (2013)<sup>11</sup>, Gudeli Vahini, *et al* (2015)<sup>12</sup> & Nidhi Awasthi, *et al* (2015)<sup>13</sup>. Xanthogranulomatous Cholecystitis is diffusely infiltrated by macrophages and other inflammatory cells. On macroscopic examination, showed marked wall thickening and mimic with Carcinoma grossly. So its microscopic diagnosis is important.

In our study the incidence of Follicular Cholecystitis was 0.90% which is consistent with studies by Mohan, *et al* (2005)<sup>4</sup> & Gudeli Vahini, *et al* (2015)<sup>12</sup>. The incidence of Cholesterol Polyp was 0.18% which is consistent with the study reported by Faisal G Siddiqui, *et al* (2013)<sup>14</sup>. There were 16 cases (2.87%) of Cholesterolosis

Table 3 — Age Distribution of Gall Bladder Carcinoma	
Age in years	No of cases (%)
30-40	1 (12.5%)
41-50	6 (75.0%)
51-60	1 (12.5%)

Table 4 — Characteristics of Patients With Gall Bladder Carcinoma

Pre-operative diagnosis of GBC	Clinical diagnosis	Macroscopic appearance	Type
Yes	Suspected GBC	Polypoidal growth	Papillary Adenocarcinoma extending up to serosa
No	Chronic calculus cholecystitis	Thickened GB	Well differentiated Adenocarcinoma extending up to muscle layer
No	Chronic calculus cholecystitis	Normal GB Wall	Well differentiated Adenocarcinoma infiltrating up to serosa
Yes	Suspected GBC	Nodular mucosa	Moderately Differentiated Adenocarcinoma
Yes	Suspected GBC	Polypoidal growth	Papillary Adenocarcinoma extending up to serosa
No	Chronic calculus cholecystitis	Thickened GB	Moderately Differentiated Adenocarcinoma
No	Chronic calculus cholecystitis	Normal GB Wall	Well Differentiated Adenocarcinoma
No	Chronic calculus cholecystitis	Thickened GB	Mucinous Adenocarcinoma

associated with Chronic Cholecystitis and was characterized by infiltration of foamy macrophages in the mucosa, which is consistent with studies by Nailesh Shah, *et al* (2010)<sup>15</sup>, Mohammed Tayeb, *et al* (2015)<sup>16</sup>. Incidence of Eosinophilic Cholecystitis was 0.89% which is consistent with studies by Tariq Sarfaraz, *et al* (2015)<sup>17</sup>, Gudeli Vahini, *et al* (2015)<sup>12</sup>. However, histopathological diagnosis of these Gall Bladder lesions has no prognostic value.

In the present study, it was observed that prevalence of non-neoplastic lesions were more. Among the non-neoplastic lesions maximum number of cases were inflammatory lesions (96.5%) rest were pre-malignant lesions. The occurrence of non-neoplastic lesion in Gall Bladder in present study is 98.55% which is consistent with studies by NT Damora, *et al* (2013)<sup>18</sup> & Gajendra Singh, *et al* (2016)<sup>8</sup>.

Cholelithiasis produces mucosal epithelial changes that represent the precursors lesions of carcinoma. A Gallstone mainly injure the Mucosal Epithelium and thus causes changes like Metaplasia, Dysplasia and Neoplasia. There is presence of inter-relationship between Antral Metaplasia, Intestinal Metaplasia, Dysplasia and Carcinoma. Hence Histopathological examination is important in every case of Cholecystectomy specimens.

Incidence of Gall Bladder Carcinoma (GBC) in our study was 1.43% which is consistent with the studies by Nailesh Shah, *et al* (2010)<sup>5</sup>, Ghimire P, *et al* (2011)<sup>19</sup>, Chin KF, *et al* (2012)<sup>20</sup> Mohammed A Bawaheb (2013)<sup>21</sup>, Gulwani HV, *et al* (2015)<sup>22</sup>, Taha MM, *et al* (2015)<sup>23</sup>. All the 8 cases of Gall Bladder Carcinoma were in the age range of 41 to 50 years and is found among females which is quite similar to other studies. Increased frequency in females suggested a possible role of Hormonal Factors.

Incidence of incidental Gall Bladder Carcinoma in our study was 0.89% which is consistent with studies by Dipti Kalita, *et al* (2013)<sup>24</sup>, Hamdani, *et al* (2012)<sup>25</sup>, Ghimire, *et al* (2011)<sup>19</sup>, R Shreshtha, *et al* (2010)<sup>26</sup> & Medhi KB, *et al* (2016)<sup>3</sup>.

Adenocarcinoma showing varying degrees of differentiation was the most common type of malignancy in our study which is consistent with findings of studies by Nailesh Shah, *et al* (2010)<sup>15</sup>, Mustafa Mazlum, *et al* (2011)<sup>9</sup>, Nissar Hussain Hamdani, *et al* (2012)<sup>25</sup>, Mohammed A Bawaheb, (2013)<sup>21</sup>, Faisal G Siddiqui, *et al* (2013)<sup>14</sup>, Ramesh S Waghmare, *et al* (2014)<sup>27</sup>, Gudeli Vahini, *et al* (2015)<sup>17</sup> & Taha MM, *et al* (2015)<sup>10</sup>.

#### CONCLUSION

This study has highlighted the importance of proper histological examination for diagnosis of various lesions of Gall Bladder especially Carcinoma which was not suspected upon clinical nor macroscopic examination. GBC was not always associated with gallstones but may clinically mimic Gallstone disease. Adenocarcinoma was the predominant histological type of GBC. Increased rate of incidentally diagnosed Gall Bladder cancer was found in our study which reinforces the importance of thorough sampling and routine histopathological examination of all cholecystectomy specimens. Further studies with large sample size is recommended for determination of actual value of incidental Carcinoma.

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