A Histopathological Study of Cholecystectomy Specimens
(Research Paper)

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Abstract
Background - Cholecystectomy specimen (gallbladder) is the most frequently encountered surgical specimen in a histopathology laboratory. It shows different histopathological changes ranging from inflammation to premalignant changes and carcinoma. Incidental detection of gallbladder cancer in cholecystectomy specimen has been reported in 0.3 to 2% of all cholecystectomies performed for benign condition.

Aims and objectives: To study the different histopathological entities of the cholecystectomy specimens and to find out the frequency of gallbladder cancer in these specimens.

Material and methods: The present study is based on histopathological analysis of 400 cholecystectomy specimens from June 1, 2014 to May 31, 2016 in the Department of Pathology, Tezpur Medical College and Hospital, Tezpur, Assam.

Results: Chronic cholecystitis (86.25%) was the most common finding in our study followed by cholesterolosis (7.50%) and various other mucosal pathologies of gallbladder. Female to male ratio was 4.71:1. Frequency of gallbladder cancer was 1.25%. The frequency of incidental carcinoma in the study was 0.75%.

Conclusion: The study gives the different histopathological patterns of cholecystectomy specimens that attended our institute. to reveal the different patterns of gallbladder lesions on histopathological examination. Thorough histopathological analysis of cholecystectomy specimens is important to detect incidental carcinoma.

Keywords: Gallbladder cancer, Cholecystectomy, Cholesterolosis, Xanthogranulomatous cholecystitis, Granulomatous cholecystitis, Adenocarcinoma.

Introduction
Cholecystectomy specimen (gallbladder) is the most frequently encountered surgical specimen in a histopathology laboratory (1). It shows different histopathological changes ranging from inflammation to premalignant changes and carcinoma.
Gallbladder disease poses to be a common health issue worldwide, which require cholecystectomy (2). Earlier, western countries were more prone to the gallbladder pathologies, but nowadays it is on a rise in Asia probably because of increase in calorie and fat intake, decrease in fiber in their diet together with sedentary lifestyle (2). The prevalence of gallbladder disease in Northern India is 6.20% comprising 4.40% in males and 7.30% in females.

Cholelithiasis is a common disorder affecting 10% to 20% of adult population. It is common among female. More than 95% of biliary tract disease is attributed to cholelithiasis. The prevalence of gall stones in Northern India is 4.1% comprising 1.9% in males and 5.5% in females.

Carcinoma gallbladder though rare is the most common malignancy of the biliary tract (2). Women have a higher risk of developing gallbladder cancer than men (3, 4). The most important risk factor for gallbladder cancer (besides gender and ethnicity) is gallstone. Gall bladder cancer is a late presentation disease; hence the prognosis is poor and associated with high mortality rate. Several studies showed that routine histopathological examination of all cholecystectomy specimens is needed because of significant risk of incidental carcinoma. Incidental detection of gallbladder cancer in cholecystectomy specimen has been reported in 0.3 to 2% of all cholecystectomies performed for benign condition (5, 6).

Aims and objectives
The present study is carried out to study the different histopathological entities of the cholecystectomy specimens in our institute and to find out the frequency of gallbladder cancer in these specimens.

Materials and Methods
The study was carried out on 400 cholecystectomy specimens received in the Department of Pathology, Tezpur Medical College and Hospital, Tezpur, Assam for histopathological examination in the period of two years from June 1, 2014 to May 31, 2016. Data regarding their clinical profile was collected from the Surgery department of the institute.

A total of 400 cholecystectomy specimens underwent biopsy interpretation. The specimens collected for the study was sent by the Surgery department of the institute fixed in 10% formalin. The specimens were observed grossly in the Pathology department as per guideline described by standard text book of surgical pathology (1) and findings were noted in the note sheet. The biopsy tissues were then sectioned (minimum three) and processed in the conventional manner as described by J D Bancroft and Marilyn Gamble (7). Additional sections were taken from abnormal gross area of the specimens. After completion of processing, they were made in paraffin blocks and cut in rotatory microtome of about 3-5μ thickness. The sections were stained by conventional Haematoxylin and Eosin, mounted in DPX and examined under microscope. The microscopic slides were viewed under low power field and high power field. The findings were noted and a histopathological diagnosis was done.

Results and Observation
The study included 400 cholecystectomy specimens for histopathological evaluation. The age of the patient ranged from 12 years to 87 years. Majority of patients were in the age group of 31-40 years (Cite Table-1). Out of 400 cases, 330 (82.50%) were female and 70 (17.50%) were male with a male female ratio 4.71:1 (Cite Figure-1).

![Fig. 1- Sex distribution of study the cases.](image-url)
Table 1- Age and sex distribution of the study cases.

| Age Gr. | Male       | Female     | Total     |
|---------|------------|------------|-----------|
| 11-20 yrs | 1(0.25%)   | 9(2.25%)   | 10(2.50%) |
| 21-30 yrs | 10(2.50%)  | 89(22.25%) | 99(24.75%)|
| 31-40 yrs | 18(4.50%)  | 119(29.75%)| 137(34.25%)|
| 41-50 yrs | 22(5.50%)  | 68(17.00%) | 90(22.50%)|
| 51-60 yrs | 10(2.50%)  | 30(7.50%)  | 40(10.00%)|
| 61-70 yrs | 8(2.00%)   | 12(3.00%)  | 20(5.00%) |
| 71-80 yrs | 0(0.00%)   | 3(0.75%)   | 3(0.75%)  |
| 81-90 yrs | 1(0.25%)   | 0(0.00%)   | 1(0.25%)  |
| Total    | 70(17.50%) | 330(82.50%)| 400(100%) |

Out of 400 numbers of cholecystectomy specimens, on histopathological interpretation, 395 (98.75%) specimens showed non-neoplastic pathology and 5 (1.25%) specimens showed neoplastic pathology (Cite Figure 2).

Figure 2- Neoplastic and non-neoplastic distribution of study cases.

Amongst non-neoplastic we got predominantly inflammatory lesions mostly chronic cholecystitis followed by cholesterolosis, empyema, xanthogranulomatous cholecystitis, eosinophilic cholecystitis and various other pathological entities as shown in Table 2. We got one case of chronic cholecystitis with intestinal metaplasia, one case chronic cholecystitis squamous metaplasia and one case of chronic cholecystitis with epithelial dysplasia among the non-neoplastic specimens, which can be considered as pre-malignant lesions but not true neoplastic lesions. So these three cases were included in the non-neoplastic category instead of neoplastic category in the study. Out of 5 neoplastic lesions, we found benign tumour as nil. All 5 neoplastic lesions were malignant tumours and all of them were adenocarcinoma. One was moderately differentiated adenocarcinoma, which was a male patient of 40 years age. Remaining 4 were well differentiated adenocarcinoma, which were female of age group 30-60 years age. Out of 5 cases of gall bladder cancer, only two cases were pre-operatively diagnosed and rests were all incidental gallbladder cancer. The frequency of incidental carcinoma in the study was 0.75%.

Table2- Histopathological spectrum of cholecystectomy specimens.

| Histopathological Diagnosis                        | Number & % |
|---------------------------------------------------|------------|
| Chronic cholecystitis                             | 345(86.25%)|
| Chronic cholecystitis with cholesterolosis        | 30 (7.50%) |
| Empyema                                           | 5 (1.25%)  |
| Acute on chronic cholecystitis                    | 5 (1.25%)  |
| Eosinophilic cholecystitis                        | 2 (0.50%)  |
| Granulomatous cholecystitis                       | 1(0.25%)   |
| Xanthogranulomatous cholecystitis                 | 2 (0.50%)  |
| Mucocele                                          | 2 (0.50%)  |
| Chronic cholecystitis with epithelial dysplasia    | 1 (0.25%)  |
| Chronic cholecystitis with intestinal metaplasia   | 1 (0.25%)  |
| Chronic cholecystitis squamous metaplasia          | 1 (0.25%)  |
| Benign                                            | 0 (0.00%)  |
| Malignant (i) Adenocarcinoma                      | 5 (1.25%)  |

Discussion

Gallbladder disease poses to be a common health issue worldwide, which require cholecystectomy. We did histopathological study of 400 cholecystectomy specimens during the study period.

Regarding the age of the patients in the study, it ranged from 12 years to 87 years and maximum numbers of patients were in the 31 to 40 years group. Similar results were observed by other authors like Mohan et al 2005, Khan et al 2014, Unisa et al 2011 (8,9,10). But there are some studies like Mittal et al 2010, Bawasaheb et al 2013, Arathi NA et al 2013 and Awasthi N 2016 (11,12,13) who had maximum number of patients in the 41 to 50 years age group. Deranged cholesterol mechanism which increases with age probably leads to increase in prevalence of gallstone formation and bile saturation.
Out of 400 cases 330 (82.50%) were female and 70 (17.50%) were male with a male female ratio 4.71:1, which was consistent with other studies. Females were more affected than males in gallstone diseases probably due to sedentary habits and sex hormones’ role.

In our study, 86.25% cholecystectomy specimens belonged to chronic cholecystitis. This value is similar with other study like Khan S, Jetley S, Hussain M 2013 (77.70%), Awasthi N 2014 (79.80%), Samroo AG., Jarwar M, Ali SA, Nzamani NB, Memon AS 2013 (66.41%) and Khan F, Manzoor A, UI Haq MB 2014 (89.15%) (9,14,15,16).

In our study, 30 cases of cholesterolosis (7.50%) which was similar to Mohan et al, Sabina et al and Faran et al. The age of patients with cholesterolosis ranged from 24 -70 years with mean of 39.2 years out of which 25 (83.33%) were females and 5 (16.67%) were males which was almost similar to a study by Khairy et al (17).

We found two cases (0.50%) of Xanthogranulomatous cholecystitis in our study, which shows marked wall thickening and mimic with carcinoma grossly. Its microscopic diagnosis is therefore important. We found one case of granulomatous cholecystitis and 2 cases of eosinohic cholecystitis in our study. We also found 1 case of chronic cholecystitis with epithelial dysplasia, 1 case of chronic cholecystitis with squamous metaplasia and 1 case of chronic cholecystitis with intestinal metaplasia in our study among the non-neoplastic specimens, which can be considered as pre-malignant lesions but not true neoplastic lesions. So these three cases were included in the non-neoplastic category instead of neoplastic category in our study. This gives a variety of inflammatory and pre-malignant histopatholical pattern of the study cases.

In our study we found 1.25 % cases on neoplastic lesions. We did not found any benign tumour but all 5 cases (1.25%) as malignant tumours. All malignant cases were adenocarcinoma, which is similar with other studies like Khan F et al 2014 (0.21%), Mohan et al 2005 (1.09%), Shrestha R et al 2007 (1.40%), Ghirima et al 2011 (1.28%), Kaur et al 2012 (0.78%), Khoo JJ et al 2005 (0.62%) and Mittal R et al 2010 (1.00%) (4, 8, 18, 19, 20, 21, 22). Out of 5 cancer cases two were pre-operative diagnosed and three were incidental carcinoma. The frequency of incidental carcinoma in the study was 0.75%. Other studies shows that the frequency of incidental gallbladder cancer is between 0.2% to 2.8% either intra operatively or post operatively diagnosed.

Conclusion

Gallbladder disease poses to be a common surgical health issue requiring cholecystectomy world wide. Thorough sampling of the cholecystectomy specimens and routine histopathological examination is of utmost importance to detect non neoplastic complications and incidental gallbladder cancer. The main strength of this study is that it gives the most comprehensive picture of different histopathological pattern and frequency of incidental diagnosis of gall bladder cancer of cholecystectomy specimens done in the institute. The major limitations of this study include the small sample size and short study period.

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