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Histopathological Profile of Cholecystectomy Biopsies in A Tertiary Care Teaching Hospital – A Retrospective Study

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ABSTRACT

Background: The gallbladder can present protean features on histopathological examination ranging from inflammation to premalignant changes and carcinoma and is a very common disorder in the population of northern belt of India.

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

Material and methods: A retrospective study of 800 cholecystectomy specimens from January 2013 to January 2016 was done in the Department of Pathology, F.A.A.M.C&H, Assam . Two cholecystectomy specimens were autolysed due to poor fixation and excluded from the study.

Results : Chronic cholecystitis (88.12%) was the most common finding in our study followed by cholesterolosis (4.75%) and various other mucosal pathologies of gallbladder. Female to male ratio was 4.6:1. Frequency of gallbladder cancer was 1.13%.

Conclusion : The study helped us to reveal the different patterns of gallbladder lesions on histopathological examination. Thorough sampling is very important for detection of incidental carcinoma.

KEYWORDS	Gallbladder cancer, Cholecystectomy, Cholesterolosis, Xanthogranulomatous cholecystitis, cholelithiasis

: Gallbladder is the most frequently encountered surgical specimen in a histopathology laboratory presenting with different histopathological changes ranging from inflammation comprising of acute , acute on chronic and chronic inflammation along with various mucosal changes of the gallbladder. Cholelithiasis is a common disorder affecting 10% to 20% of adult population in developed countries. More than 95% of biliary tract disease is attributed to cholelithiasis. Gallbladder cancer is the most common malignancy of the extra hepatic biliary tract. [1]

Incidental detection of gallbladder cancer in cholecystectomy specimen has been reported in 0.3 to 2% of all cholecystectomies performed for benign condition. [4,5] The need for histopathological examination of all cholecystectomy specimens is controversial but several studies showed that routine histopathological examination of all cholecystectomy specimen is favourable because of significant risk of incidental carcinoma. [6, 7] Women have a higher risk of developing gallbladder cancer than men. [8,9] The most important risk factor for gallbladder cancer (besides gender and ethnicity) is gallstones which are present in 95% of cases.

The estimated prevalence of gall stone disease in India is reported as between 2% and 29% with the disease being 7 times more common in North than in South India. [2 ,7] In early stage gallbladder cancer may be asymptomatic and most of them are well-known for their late presentation resulting in poor prognosis and high mortality. To improve the survival rate of gallbladder carcinoma patients, it is recommended to submit all cholecystectomy specimens for histopathological examination to rule out occult carcinoma. Porcelain gallbladder is a premalignant condition and prophylactic cholecystectomy is it's definitive management.[10]

This study was done to study the different pathological entities of the cholecystectomy biopsies on microscopic examination in our tertiary care teaching hospital and to find out how frequently we get gallbladder cancer in those specimens.

MATERIALS AND METHODS: Our study was a three years retrospective study of 800 cases of cholecystectomy biopsies from Jan' 2013 to Jan' 2016 in the Department of Pathology, Fakhruddin Ali Ahmed Medical College & Hospital, Barpeta, Assam. Two cholecystectomy specimens were autolysed due to poor fixation and so, excluded from our study. After gross morphological examination of the specimens of gallbladder obtained in 10% formalin fixative from either open surgery or laparoscopically, random sections of minimum three (3) numbers were taken and stained with H&E stain after processing. Additional sections were taken from any grossly abnormal area if present.We took 3 mm or more wall size as thickened gallbladder wall. Histopathological evaluation was done to detect the diverse changes in the gallbladder mucosa and wall. One case of porcelain gallbladder was also processed.

RESULTS AND OBSERVATION: Out of 2350 number of histopathological specimens received during the period of three years, 802cases (34.13%) belonged to cholecystectomy specimens, out of which two were found autolysed and excluded from the study thereby making the total number of cases 800(34.04%). On microscopic examination, we got predominantly chronic cholecystitis followed by cholesterolosis, empyema, xanthogranulomatous cholecystitis and various other pathological entities. Last but not the least; we got nine cases of gallbladder cancer. On gross examination, we got one case of porcelain gallbladder with extreme hardness which was microscopically confirmed to be mostly calcification and fibrosis.

Table-I : Spectrum of histopathological pattern in cholecystectomy specimens.

Histopathological diagnosis		Number (Total = 800)	Percentage
Benign (98.87%)	Chronic cholecystitis	705	88.12%
	Chronic cholecystitis with cholesterolosis	38	4.75%
	Empyema	13	1.62%
	Acute on chronic cholecystitis	9	1.12%
	Eosinophilic cholecystitis	4	0.50%
	Chronic granulomatous cholecystitis	1	0.13%
	Xanthogranulomatous cholecystitis	6	0.75%
	Mucocele	4	0.50%
	Chronic cholecystitis with epithelial dysplasia	6	0.75%
	Chronic cholecystitis with intestinal metaplasia	2	0.25%
	Chronic cholecystitis with squamous metaplasia	2	0.25%
	Porcelain gallbladder	1	0.13%
Malignant (1.13%)	Adenocarcinoma	9	1.13%

Out of nine (1.13%) cases of gallbladder cancer, only two cases were preoperatively diagnosed and rest (0.87%) was all incidental gallbladder cancers.

Serial No	Age (years)	Sex	Histopathological differentiation
1	35	M	Moderately differentiated
2	30	F	Well differentiated
3.	38	F	Well differentiated
4	45	F	Well differentiated
5	50	F	Well differentiated
6	50	F	Well differentiated
7	60	F	Well differentiated
8	60	F	Moderately differentiated
9	60	F	Moderately differentiated

Table-II: Adenocarcinoma of gallbladder based on histopathological differentiation

Age Group	Male	Female	Total
11-20 years	4 (0.5%)	20 (2.5%)	24 (3.0%)
21-30 years	24 (3.0%)	203 (25.37%)	227 (28.37%)
31-40 years	37 (4.63%)	207 (25.87%)	244 (30.5%)
41-50 years	41 (5.13%)	125 (15.63%)	166 (20.75%)
51-60 years	19 (2.37%)	69 (8.63%)	88 (11.0%)
61-70 years	16 (2.0%)	28 (3.5%)	44 (5.5%)
71-80 years	0 (0%)	6 (0.75%)	6 (0.75%)
81-90	0 (0%)	0 (0%)	0 (0%)
91-100	1 (0.13%)	0 (0%)	1 (0.13%)
Total	142 (17.75%)	658 (82.25%)	800(100.0%)

Table- III: Showing the age and sex distribution of patients with gallbladder diseases

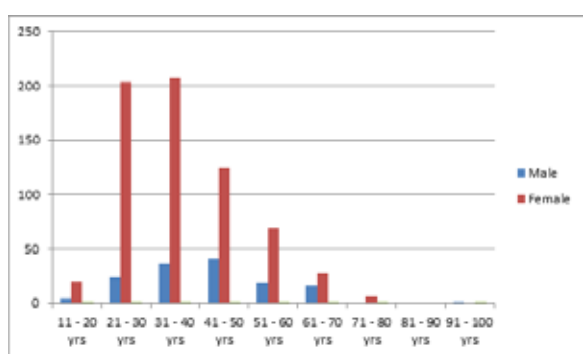

Chart I: Showing the age and sex distribution of gallbladder diseases

DISCUSSION: Gallstone disease is supposed to be one of the most common disorders of the biliary tract. In Northern India, the prevalence of gallbladder disease is 6.2%, 4.4% in males and 7.3% in females together with prevalence of gall stones being 4.1%, 1.9% in males and 5.5% in females.[11]

Gallbladder disease poses to be a common surgical health issue requiring cholecystectomy and one of the major causes of morbidity and mortality in the world. 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.[12]

Gallstones bear a potential increase risk of developing carcinoma gallbladder. Carcinoma gallbladder though rare is the most common malignancy of the biliary tract.[13]

In the present study, out of 800 cholecystectomy specimens, 705 specimens belonged to chronic cholecystitis(88.12%) thus making it the most common histopathological finding.

STUDY	CHRONIC CHOLECYSTITIS
Awasthi N (2014) [14]	584 out of 732 cases diagnosed (79.8%)
Khan S, Jetley S, Hussain M (2013) [7]	280 out of 360 cases diagnosed (77.7%)
Somroo A.B , Jarwar M, Ali SA, Nizamani NB, Memon A S (2008) [15]	346 out of 521 cases diagnosed (66.41%)
Khan F, Manzoor A, Ul Haq M B (2014) [9]	838 out of 940 cases diagnosed {89.15%)
Present study (2016)	705 out of 800 cases diagnosed (88.1%)

Table IV: Comparing different studies in the diagnosis of chronic cholecystitis

The studies were found similar to our study. Regarding the age of patients in the study, it ranged from 13 years to 94 years and maximum number of patients was in the 31 to 40 years group i.e. the third decade. Similar results were observed by other authors like Mohan et al,[2] Khan et al,[7] Unisa et al[11]. But there are some studies like Mittal et al[21], Bawasaheb et al[23], Arathi NA et al[22] and Awasthi N[14] who had maximum number of patients in the fourth decade.

Out of 800 patients, 658 (82.25%) were female patients and 142(17.25%) were males. The female to male ratio was 4.6:1 which was consistent with other studies.[6,7] Females were more affected than males in gallstone diseases probably due to sedentary habits and sex hormones' role in most women population in India promoting the gallstone formation. Deranged cholesterol mechanism which increases with age probably leads to increase in prevalence of gallstone formation and bile saturation.[18,19, 20]

Xanthogranulomatous cholecystitis usually presents with marked wall thickness and mimics carcinoma grossly. It can extend to the surrounding adjacent tissues,[7, 16] so it's diagnosis on microscopy is very important.

STUDY	XANTHOGRANULOMATOUS CHOLECYSTITIS
Khan et al (2014)[9]	0.1%
Khan et al (2013)[7]	3.6%
Mohan et al (2005)[2]	2.3%
Awasthi N(2012)[14]	1.8%
Present study (2016)	0.75%

Table-V: Comparing the incidence of Xanthogranulomatous cholecystitis in different studies.

Out of the 9 (1.13%) cases of adenocarcinoma of gall bladder diagnosed on microscopy, there were 8 females(88.9%) & 1 male(11.1%) and two cases were pre clinically diagnosed.

STUDY	GALL BLADDER CANCER
Mohan et al (2005)[2]	1.09%
Shrestha R et al (2007)[3]	1.4%
Khan et al (2013)[7]	2.22%
Ghimire et al (2011)[6]	1.28%
Kaur et al (2012)[24]	0.78%
Khoo J J et al (2005)[17]	0.62%
Mittal R et al (2010)[21]	1.0%
Khan et al {2014}[9]	0.21%
Present study (2016)	0.87%)

Table- VI: Comparing the incidence of gall bladder cancer in cholecystectomy specimens in different studies.

The frequency of incidental gallbladder cancer is said to be between 0.2% to 2.8% either intra operatively or post operatively diagnosed.[25, 26] In India, prevalence in gallbladder cancer, which ranks among first 10 cancers in ICMR registries on national level is seen in northern and north eastern states of Uttar Pradesh, Assam, Bihar, West Bengal and Orissa.[29,30]

In our study, we had a single male patient, 35 years of age diagnosed with gallbladder cancer. The female population is mostly affected by gallbladder cancer. It increases after 45 years of age and at 65 years, it is maximum.[28] But in our study, a varied age group ranging from 30 - 60 years with mean age being 47.6 years was seen along with a peak in the sixth decade (33.3%), all females. Other studies have shown the mean age of occurrence to be 53.56 years, 56.2 years, 56.7years etc [3,17 , 21]. Awareness towards health and medical accessibility nowadays may be the reason of lowering of the age of diagnosis as gallbladder cancer is usually, a silent disease.

Our study had 38 cases of cholesterolosis (4.75%) which was similar to Mohan et al, Sabina et al and Faran et al. [2 ,7, 9] The age of patients with cholesterolosis ranged from 24 -70 years with mean of 39.2 years out of which 30(78.9%) were females and 8(21.1%) were males which was almost similar to a study by Khairy et al .[27]

CONCLUSION: The study revealed a diverse histopathological pattern of gallbladder lesions in cholecystectomy specimens. Chronic cholecystitis was the most common histopathological diagnosis followed by acute on chronic cholecystitis, cholesterolosis, empyema, mucocele, xanthogranulomatous cholecystitis, eosinophillic cholecystitis, metaplasia, epithelial dysplasia and last but not the least adenocarcinoma of the gallbladder. Increased rate of incidentally diagnosed gallbladder cancer was found in our study which reinforces the importance of thorough sampling and routine histopathological examination of all cholecystectomy specimens

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