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Histopathological Study of Gall Bladder Lesions in Gurugram, Haryana

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Abstract
Background and objectives*: Gall bladder is one of the organs having a wide spectrum of disease ranging from congenital anomalies, calculi and its complications , non-inflammatory , inflammatory & neoplastic lesions Gall stones are one of the major cause of morbidity and mortality all over the world. Inflammatory processes in the gallbladder have been described as the causal factor for a metaplastic response from the gallbladder epithelium. The irritation factor caused by stones produces changes in cell differentiation, thereby resulting in an adaptive response to this aggression, i.e. the formation of gastric and intestinal metaplasia. Recent studies have suggested that these epithelial changes are distinct phases of the epithelial differentiation leading to dysplasia, the lesion that ultimately precedes adenocarcinoma of the gallbladder.*
Materials & Methods: *This is a one year prospective study of 129 cases which included all the cholecystectomy specimens received in department of Pathology, FMHS, SGT University from November 2015 to November 2016.*
Results: *In the present study total 129 patients were included where 108 were females and 21 were males. Histopathological findings depicted that chronic cholecystitis(34.11%) was the most prevalent. Besides these, hyperplasia, metaplasia, dysplasia and gall bladder carcinoma were observed in 10.07 %, 22.48 %, 5.42 % and 3.87 % of the patients respectively. Study also showed that female patients were more prone to premalignancy and malignancy.*
Conclusion: *The study revealed about histomorphological changes in epithelium of gall bladder after cholecystectomy where premalignant and malignant types were remarkable percentage though chronic cholecystitis was the commonest histopathological feature. Gradient ages may suggest that gall bladder carcinoma was developed from cholecystitis to carcinoma via hyperplasia, metaplasia and dysplasia.*
Keywords: *Cholecystitis, cholecystectomy, gallstones, gallbladder, carcinoma.*

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I. Introduction

The gall bladder is a hollow organ that sits beneath the right lobe of the liver. In adults the gall bladder measures approximately 8 cm in length and 4 cm in diameter whenfully distented.[1]Anatomically gall bladder is divided into three sections the fundus, body, neck.[2] Gallbladder is the organ which stores and concentrate bile and helps in digestion of fat.[3] The most common pathology found in gallbladder is cholelithiasis followed by cholecystitis. Gallstone afflict 10% -20% of adult population in developed countries.[4] The prevalence varies with age, sex and ethnic groups. Most patients were unaware of disease and remain asymptomatic for life. The current changes in lifestyles of individuals pertaining to indulgement in unhealthy fat rich food, lack of exercise, obesity and sedentary lifestyles have once again focused our attention to gallstones and diseases of gallbladder. Now a day a laparoscopic cholecystectomy is the treatment of choice and done routinely for gallstone diseases. It is difficult to diagnose distinctly benign and malignant lesions of gallbladder before surgery without histopathological examination.[5] Despite the concept by people that routine histopathology of cholecystectomy specimen plays a dismal role in themanagement of most patients[6], it plays an important role in clinicopathologic correlation of various lesions of gallbladder and helps in diagnosing premalignant conditions like carcinoma in situ and early carcinoma. This is the reason that each and every specimen of cholecystectomy should be evaluated in the histopathology laboratory.[7] On routine histopathologic examination of cholecystectomy specimens, the most commonly found pathology is cholelithiasis. Among other pathologies,

cholecystitis, both acute and chronic is common. Cholesterolosis, Hyperplasia, Metaplasia , Dysplasia and Malignant conditions are the less common pathological entities. Cholecystitis associated with cholelithiasis is common disease particularly found in fertile and fatty females in their 4th and 5th decades of age. It can also affect both male and children. This condition has increased in the past two decades due to increase intake of unhealthy fat rich food, lack of exercise, obesity and sedentary lifestyles. Common histopathological findings in chronic cholecystitis are thickening of wall, varying degrees of mononuclear and lymphocytic infiltration and fibrosis.[8] The aim of this study is to determine the frequency of various histopathological pattern in cholecystectomy specimens and to emphasize the importance of histopathologic examination of each and every specimen of gallbladder. The findings of the present study will hopefully help surgeons and histopathologists to get a coherent of the tissue changes in cholecystitis and remain vigilant for carcinomatous changes in the gall bladder associated with long standing cholecystitis associated with gall stones.

II. Materials And Method

The present study is done in the department of Pathology, S.G.T Medical college ,Gurugram, over a period of 1 year from November 2015 to November 2016. During the period, we received 129 cholecystectomy specimens from Department of Surgery, S.G.T Medical college, Gurugram and surrounding hospitals. Cholecystectomy specimens received in the department were fixed in 10% formalin and submitted to detailed gross examination. Three full thickness sections were obtained from fundus, body and neck of the gallbladder. Additional sections were taken from other grossly abnormal areas if present. Sections were processed and then stained with Haematoxylin and Eosin stain. The stained sections were examined microscopically for a variety of morphological changes in the diseased gallbladder.

III. Results

The total number of cholecystectomy specimens studied were 129. Among these 21(16.27%) were of males and 108(83.72%) were of females with M:F ratio 1:5.1. In this study, age ranges from 21-80 years. Maximum number of patients were between 31-40 years. Out of 129 cases, chronic cholecystitis with cholelithiasis were found in 44 cases(34.10%) , chronic cholecystitis in 22 cases(17.05%), acute on chronic cholecystits in 3(2.32%) cases, chronic cholecystitis with ulceration in 2(1.55%) cases, chronic cholecystitis with cholesterolosis in 6(4.65%) cases, followed by chronic cholecystitis with metaplasia which comprises 29(22.48%) cases. Out of 29 metaplasia cases , intestinal metaplasia found in 16 cases, pyloric metaplasia found in 13 cases. Remaining cases were different types of inflammation along with hyperplasia were found in 10 cases(7.75%), dysplasia in 3 cases(2.32%) and carcinoma of gall bladder were found in 5 cases(3.87%).

Table 1. Distribution of cases in correlation with age group and sex of the patient (n=129).

Age group	SEX		Total	P value
	FEMALE	MALE		
20-30	30 (90.91%)	3 (9.09%)	33 (100.00%)	0.417
30-40	35 (85.37%)	6 (14.63%)	41 (100.00%)	
40-50	16 (88.89%)	2 (11.11%)	18 (100.00%)	
50-60	15 (75.00%)	5 (25.00%)	20 (100.00%)	
60-70	10 (71.43%)	4 (28.57%)	14 (100.00%)	
70-80	2 (66.67%)	1 (33.33%)	3 (100.00%)	
Total	108 (83.72%)	21 (16.28%)	129 (100.00%)	

Table 2 .Histopathological Diagnosis Pattern Of Gallbladder

Histopathological Dignosis	AGE Group						Total	P value
	20-30	30-40	40-50	50-60	60-70	70-80		
Ac on CC	1 (3.03%)	1 (2.44%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (2.33%)	<.0001
Adenocarcinoma	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.00%)	0 (0.00%)	0 (0.00%)	1 (0.78%)	
CC	11 (33.33%)	4 (9.76%)	4 (22.22%)	2 (10.00%)	1 (7.14%)	0 (0.00%)	22 (17.05%)	
CC with atropic mucosa	0 (0.00%)	2 (4.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (1.55%)	
CC With CL with atropic mucosa	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (10.00%)	1 (7.14%)	0 (0.00%)	3 (2.33%)	
CC with Cholesterolosis	1 (3.03%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	1 (7.14%)	0 (0.00%)	3 (2.33%)	
CC with CL	11 (33.33%)	15 (36.59%)	3 (16.67%)	7 (35.00%)	8 (57.14%)	0 (0.00%)	44 (34.11%)	
CC with CL & ulceration	1 (3.03%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.78%)	
CC with CL and Cholesterolosis	1 (3.03%)	2 (4.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (2.33%)	
CC with CL Papillary	0 (0.00%)	1 (2.44%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.78%)	

Histopathological Dignosis	AGE Group						Total	P value
	20-30	30-40	40-50	50-60	60-70	70-80		
Hyperplasia								
CC with CL with epithelial hyperplasia	0 (0.00%)	2 (4.88%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (2.33%)	
CC with CL with focal pyloric metaplasia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.00%)	0 (0.00%)	0 (0.00%)	9 (6.97%)	
CC with CL with intestinal metaplasia	2 (6.06%)	2 (4.88%)	2 (11.11%)	1 (5.00%)	0 (0.00%)	0 (0.00%)	7 (5.43%)	
CC with Epithelial Hyperplasia	1 (3.03%)	2 (4.88%)	1 (5.56%)	1 (5.00%)	1 (7.14%)	0 (0.00%)	6 (4.65%)	<.0001
CC with focal pyloric metaplasia	0 (0.00%)	1 (2.44%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4(0.78%)	
CC with High Grade Dysplasia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.00%)	0 (0.00%)	0 (0.00%)	1 (0.78%)	
CC with intestinal metaplasia	2 (6.06%)	8 (19.51%)	4 (22.22%)	3 (15.00%)	0 (0.00%)	1 (33.33%)	9(6.97%)	
CC with Moderate dysplasia	2 (6.06%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (1.55%)	
CC with Ulceration of mucosa	0 (0.00%)	0 (0.00%)	1 (5.56%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.78%)	
Moderately differentiated Adenocarcinoma with infiltrating muscle	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (0.78%)	
Moderately differentiated Adenocarcinoma with intestinal differentiation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (0.78%)	
Signet Ring cell Carcinoma	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (14.29%)	0 (0.00%)	2 (1.55%)	
Total	33 (100.00%)	41 (100.00%)	18 (100.00%)	20 (100.00%)	14 (100.00%)	3 (100.00%)	129 (100.00%)	

Table 3. Distribution of cases showing metaplasia according to age group (n=29).

AGE Group	**No. of cases**	**%**
20-30	4	13.79
30-40	12	41.38
40-50	6	20.69
50-60	6	20.69
60-70	0	0.00
70-80	1	3.45
Total cases	29	100

Table 4. Distribution of cases showing hyperplasia according to sex of the patient

Sex	**No. Of Cases**	**%**
Female	7	70.00
Male	3	30.00
Total Cases	10	100

Table 5. Distribution of total cases of malignancy according to age group (n=5).

Age Group	Neoplasm		Total	P value
	Present	Absent		
20-30	0 (0.00%)	33 (100.00%)	33 (100.00%)	<.0001
30-40	0 (0.00%)	41 (100.00%)	41 (100.00%)	
40-50	0 (0.00%)	18 (100.00%)	18 (100.00%)	
50-60	1 (5.00%)	19 (95.00%)	20 (100.00%)	
60-70	2 (14.29%)	12 (85.71%)	14 (100.00%)	
70-80	2 (66.67%)	1 (33.33%)	3 (100.00%)	
Total	5 (3.88%)	124 (96.12%)	129 (100.00%)	

Table 6. Sex-wise distribution of malignant cases of gall bladder

Sex	Neoplasm		
	Present	Absent	Total
FEMALE	5 (4.71%)	101 (95.28%)	106 (100.00%)
MALE	0 (0.00%)	23 (100.00%)	23 (100.00%)
Total	5 (3.87%)	124 (96.12%)	129 (100.00%)

IV. Discussion

Gall stone disease (cholelithiasis) is one of the most prevalent gastrointestinal diseases. Cholelithiasis is common with incidence ranging from 10% to 20% of world population. The estimated prevalence of gall stone disease in India has been reported as 2% to 9%. Acute calculous cholecystitis is precipitated in 90 % of cases by obstruction of neck or cystic duct by a stone. It is the primary complication of gall stones and the most common reason for emergency cholecystectomy.The present study was carried out on 129 cholecystectomy specimens to determine the histopthological spectrum and frequency of gallbladder disease. Histopathology not only establishes a tissue diagnosis in gallstone disease but also contributes towards understanding its etiopathogenesis. It can also help in planning future treatment modality.Chronic cholecystitis is associated with premalignant lesions such as hyperplasia, metaplasia, dysplasia and neoplasia. The clinical presentation of gall bladder malignancy is non specific and symptoms are similar to those of acute or chronic cholecystitis.

Hyperplasia is a common preneoplastic respose to stimulus. Microscopically cells resemble normal cells but are increased in numbers.In hyperplasia pseudostratification of epithelium occurs , nuclear crowding occurs, presence of tall columnar cells is there.The gallbladder epithelium is prone to various metaplastic changes, including pyloric gland metaplasia, intestinal metaplasia which lead to dysplasia sometimes.Metaplasia is the reversible replacement of one differentiated cell type with another mature differentiated cell type.

Dysplasia is indicative of an early neoplastic process. In dysplasia cell maturation and differentiation are delayed. Epithelial dysplasia consist of an expansion of immature cells, with a corresponding decrease in the number and location of mature cells. In dysplasia there is pseudostratification of epithelium , nuclear crowding and disorganization of epithelium.Carcinoma of gall bladder is the most common malignancy of extrahepatic biliary tract. Gall bladder cancer is at least twice as common in women than in men. Carcinoma of gall bladder shows two patterns of growth : infiltrating and exophytic. Most carcinomas of gall bladder are adenocarcinomas. Some of the carcinomas are papillary in architecture and are well to moderately differentiated: others are infiltrative and poorly differentiated to undifferentiated.In present study all the cases of cholelithiasis ranged between 20 to 80 years . Cholelithiasis cases were seen upto 80 years of age while cases of carcinoma gall bladder were seen in higher age group. The youngest patient was 20 year old and eldest was 80 year old. The majority patients were in 3rd decade. A similar study was carried out by Sumit et al, over a period of 1 year. The study included 184 cases of cholecystectomy specimens.The age of the patients varied from 20 to 80 years. The maximum patients were in 4th decade of life.[9]

In the study of 129 cases, 44 cases of chronic cholecystitis with cholelithiasis were detected , 33 cases were females and 11 cases were males.In a similar study by Mondal et al, 786 cholecystectomy specimen were studied, maximum number of cases of chronic cholecystitis with cholelithiasis were 627;524 were females and 103 were males.[10]In the present study of 129 cases, Hyperplasia of the gall bladder epithelium was present in 10(7.75%) cases.Maximum cases seen in age group of 30-40 years which comprised of 4 cases. It was followed by the age group 40-50 years which comprised of 3 cases. The age group 20-30 years shows only 2 cases of hyperplasia. 1 case each were seen in age group of 50-60 year and 60-70 year.Out of 10 hyperplasia cases, 7 cases were found in females and 3 cases were found in males . In a similar study by Khanna R et al on 140 cholecystectomy cases. Epithelial hyperplasia was observed in 26 cases(18.57%).Out of 26 hyperplasia cases, 20 cases were found in females and 6 cases were found in males.[11]

In the present study of 129 cases, 29 gall bladder epithelium showed metaplasia i.e.(22.48%) . Out of these 12 were seen in age group of 30-40 years. 6 cases each were seen in the age groups 40-50 and 50-60 years. 4 cases were seen in younger age group of 20-30 years. 1 case was found in the age group of 70-80 years. Out of 29 cases of metaplasia , 24 cases were found in females and 5 cases were found in males. A similar study was carried out by Khanna R et al to on 140 cholecystectomy specimens. At microscopy, metaplasia as seen in 45 cases. Maximum number of cases of metaplasia were seen in age group of 30-40 years.In the study of 129 cases, total number of cases of gall bladder epithelium showing dysplasia is 3 (2.32%) . 1 case each were seen in the age group of 30 – 40 , 40 – 50 and 50-60 years. Out of 3 cases of dysplasia 2 cases were found in females and 1 case was found in male.In a similar study by Sanjay et al, on 400 cholecystectomy specimens, dysplasia was found in 20 cases(5.0%).[12]

In the study of 129 cases total no of cases of malignancy is 5(3.87%). Malignancy was detected in patients above 50 years of age constituting maximum cases of 2 i.e.(40%)(one patient each seen in age group of 60-70 years and 70-80 years.) Only 1 case was seen in age group of 50-60 years. All 5 cases of malignancy were found in females.Our study findings are consistent with the study of Tereda T et al. It was conducted on 540

cholecystectomies and gall bladder carcinoma was detected in 12 cases(2.22%). Out of 12 cases of malignancy 9 cases were found in females and 3 cases were found in males. Despite advance in diagnostic and surgical modalities , gallbladder carcinoma is still characterized by late diagnosis and poor prognosis except when incidentally diagnosed at an early stage after cholecystectomy for cholelithiasis

V. Summary And Conclusion

The present study revealed that the most common age group for the gallbladder disease is found to be 31-40 years. The females being more affected than males.In this study the maximum number of patients were seen in the group of chronic cholecystitis with cholelithiasis which comprises of 44 cases followed by 29 cases of metaplasia , chronic cholecystitis in 22 cases, 10 cases of epithelial hyperplasia , 3 cases of dysplasia , 3 cases of cholesterolosis and 5 cases of carcinoma of gall bladder. Carcinoma of gall bladder was observed after 50 years of age with maximum cases were seen in age group 60-70 years. No case of carcinoma was seen before the age of 50. Carcinoma of gall bladder was observed in 5 cases and all 5 cases were females. 2 cases each were seen in two different age group 60-70 years and 70-80 years. Only 1 case was in age group of 50-60 years.Above all, all these observations may suggest an association between gallstones, cholecystitis and development of Gall bladder carcinoma. The factors in the gallstones, which mainly play for transformations of gallbladder into pre-malignancy or malignancy, are to be investigated thoroughly.

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