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Histopathological spectrum of gall bladder lesions and association with cholelithiasis

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Abstract

Introduction: Cholelithiasis is one of the major cause of mortality and morbidity especially in females. Mucosal alterations in gall bladder are associated with stones.

Aims and objectives: Present study was planned to evaluate histopathological changes in cholecystectomy specimens and their correlation with presence and type of stones.

Material and methods: A total of 432 cholecystectomy specimens sent for histopathological examination were included in the study. Association with age, sex, mucosal changes, presence or absence of stones, type and number of stones were seen.

Results: Male to female ratio was 1:6 with major age group was between 31 -40 years. Premalignant and malignant lesions were associated with females and increased age. Mixed type of stones were most commonly found and also were associated with premalignant and malignant lesions.

Conclusion: All cholecystectomy specimens should be thoroughly examined for various mucosal alterations and also if stones found should be properly evaluated for number and type.

Keywords: cholelithiasis, cholecystectomy, stones

Introduction

Cholelithiasis is one of the major gastrointestinal disorders, which is formed due to metabolic problems of hepatobiliary system [1]. It is a major cause of morbidity and mortality throughout the world [2]. The estimated prevalence of gall stone disease in India is 2-29% with 7 times more common in North India than in South India [3, 4].

Gallbladder stones are of various types, cholesterol, mixed and pigmented. Morphologically, cholesterol stones are single, large, oval and yellowish while pigmented stones are multiple, small, black. Mixed stones are multiple, multifaceted and of variable size [5].

Cholelithiasis cause various changes is gallbladder mucosa ranging from acute cholecystitis, chronic cholecystitis, polyp, empyema, eosinophilic cholecystitis, metaplasia, hyperplasia, dysplasia to carcinoma [6].

The study was conducted to determine the histological spectrum of gall bladder lesions and its association with cholelithiasis in patients undergoing cholecystectomy.

Material and method

This prospective study was conducted in the Department of Pathology, LLRM Medical College, Meerut between 1/7/17 to 31/12/17. All the cholecystectomy specimens whether open or laparoscopic sent to the Department of Pathology were included in the study.

Gall bladder specimens were subjected to gross and microscopic examination. Stones if present were assessed by the morphological type. The various histological changes observed in the gall bladder were analyzed in correlation with the type of gall stone.

Results

Out of total 432 cholecystectomy specimens 398 (92.12%) had calculi and 34 (7.87%) were without calculus. Of the 398 cases of calculus cholecystitis, 56 (14.6%) were males and 342 (86%) females. Majority 130 (32.6%) were in 31-40 age group. (Table 1).

Table 1: Age and sex wise distribution of calculus and acalculous disease.

	Calculus	disease		Acalculous	disease		
Age group	**Male**	**Female**	**Total**	**Male**	**Female**	**Total**	**Grand total**
11-20	00	12	12	00	02	02	14
21-30	11	103	114	02	05	07	121
31-40	12	118	130	01	10	11	141
41-50	07	65	72	01	11	12	84
51-60	15	33	48	00	01	01	49
61-70	11	07	18	00	00	00	18
71-80	00	04	04	00	01	01	05

Total	56	342	398	04	30	34	432
%	14.6	85.4	100	11.8	88.2	100	

Chronic cholecystitis was the most common histopathological alteration associated with 354/398 (88.9%) calculus and 32/34 (94.1%) calculus disease. Acute cholecystitis was the second most common histopathological change seen in 36/398 (9%) calculus and 02/34 (5.8%) acalculous cases.

Adenoma, dysplasia and carcinoma represented 02/398 (0.5%) 04/398 (1%) and 02/398 (0.5%) of cases of calculus disease while no case of adenoma dysplasia and carcinoma was seen to be associated with acalculous disease. (Table 2)

Table 2: Frequency of histopathological alternation is calculus and acalculous disease.

Lesion	Calculus	%	Acalculous	%	Total	%
Acute cholecystitis	36	9.0	02	5.8	38	8.7
Chronic cholecystitis	354	88.9	32	94.2	386	89.3
Adenoma	02	0.5	00	0	02	0.4
Dysplasia	04	1.0	00	0	04	0.8
Carcinoma	02	0.5	00	0	02	0.4
Total	398	99.12	34	7.88	432	100

Table 3 represents changes associated with chronic cholecystitis. There were 386 cases of chronic cholecystitis of which chronic nonspecific cholecystitis was commonest 312 /386 (80.8%). These cases were further subcategorized in relation to presence or absence of gallstones.

Table 3: Epithelial and stromal alternations associated with chronic cholecystitis

Sr. No.	Lesion	Calculus disease	Acalculous Disease	Total
1	Chronic nonspecific cholecystitis	284(80.2)	28(87.5)	312(80.8)
2	Chronic cholecystitis with cholesterosis	18(5)	00(0)	18(4.6)
3	CC with metaplasia	30(84)	00(0)	30(7.7)
a	Pyloric /Antral	24(6.7)	00(0)	24(6.2)
b	Intestinal	06(1.60	00(0)	06(1.5)
4	CC with cholesterosis and metaplasia	03(0.8)	00(0)	03(0.8)
5	CC with hyperplasia	06(1.6)	00(0)	06(1.5)
6	CC with cholesterosis and hyperplasia	03(0.8)	01(3.1)	04(1.0)
7	Xanthogranulomatous cholecystitis	02(0.5)	02(6.2)	04(1.0)
8	Eosinophilic cholecystitis	02(0.5)	00(0)	02(0.5)
	Total	354(100)	32(100)	386(100)

On evaluating the type of stones, three types of stones were found. Mixed stone was the most common type found in 44/56 (78.5%) and 84 /342 (83%) of males and females respectively, followed by cholesterol stones comprising of 06/56 (10.7%) and38/342 (11.1%) respectively. Pigmented stones were least commonly found 6/56 (10.7%) and 20/342 (5.8%). (Table4)

Table 4: Gender wise distribution of types of stone (n=398)

Type of stone	Male	%	Female	%	Total	%
Mixed	44	78.6	284	83	328	82.5
Cholesterol	06	10.7	38	11.2	44	11.0
Pigmented	06	10.7	20	5.8	26	6.5
Total	56	100	342	100	398	100

Table -5 showed histopathological changes charges is relation to types of stones. From the results, it was found that most common histopathological change associated with all the three types of stones was chronic cholecystitis (354/398) followed by acute cholecystitis (36/398)

Table 5: Histopathological charges in relations to types of stones

Lesion	Mixed	Cholesterol	Pigmented
Acute cholecystitis	25	06	05
Chronic cholecystitis	295	38	21
Adenoma	02	00	00
Dysplasia	04	00	00
Carcinoma	02	00	00
Total (398)	328	44	26

Table-6 demonstrated the epithelial and stromal alternation is chronic cholecystitis and their correlation with the types of stones chronic nonspecific cholecystitis was most commonly observed finding associated with mixed stones 252/295.

Table 6: Epithelial and stromal alterations in chronic cholecystitis and their correlation with the types of stones

Lesion	Mixed stone (295)	Cholesterol (38)	Pigmented stone (21)
Chronic nonspecific CC (284)	252	23	09
Cholesterosis (06)	04	02	00
CC with Cholesterosis (18)	12	06	00
CC with metaplasia (30)	18	02	10
a. Pyloric	12	02	07
b. Intestinal	06	00	03
CC with Cholesterosis with metaplasia (03)	02	01	00
CC with hyperplasia (06)	03	01	02
CC with Cholesterosis and hyperplasia (03)	02	01	00
Xanthogranulomatous (02)	01	01	00
Eosinophilic CC (02)	01	01	00

While evaluating the number of stones, single stones were found in 90/398= (22.6%) and multiple stones in 308/398= (77.3%) cases.

Fig 1: Pigmented stones

Fig 2: Cholesterol stones

Fig 3: Mixed stones

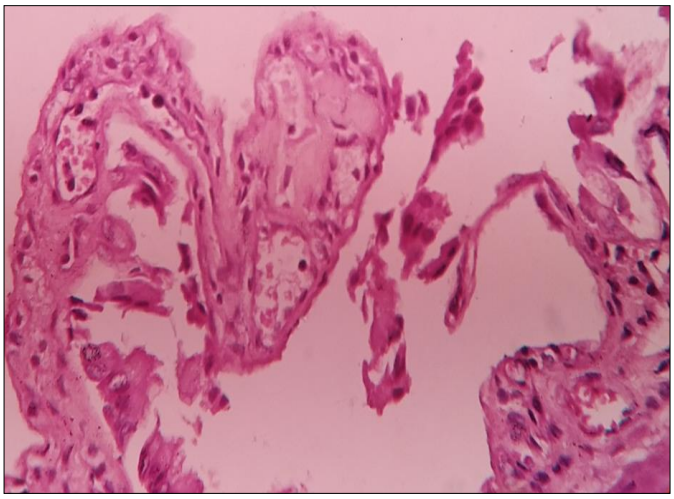

Fig 4: Cholesterosis Gall Bladder; denuded mucosa with foamy macrophages in lamina propria (10x), H&E

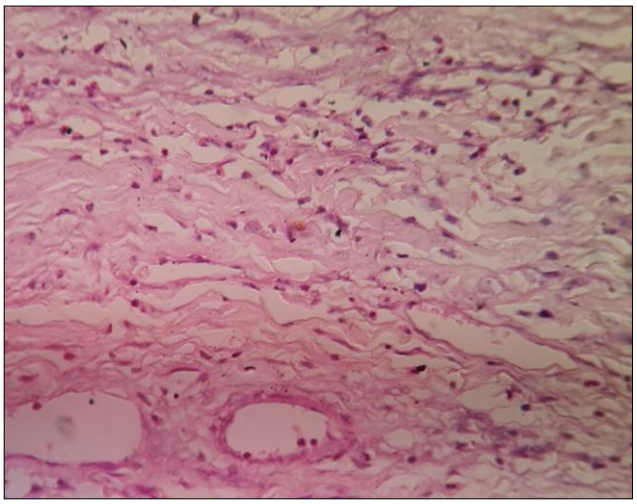

Fig 5: Chronic cholecystitis; mixed inflammatory infiltrate up to serosa (40x), H&E

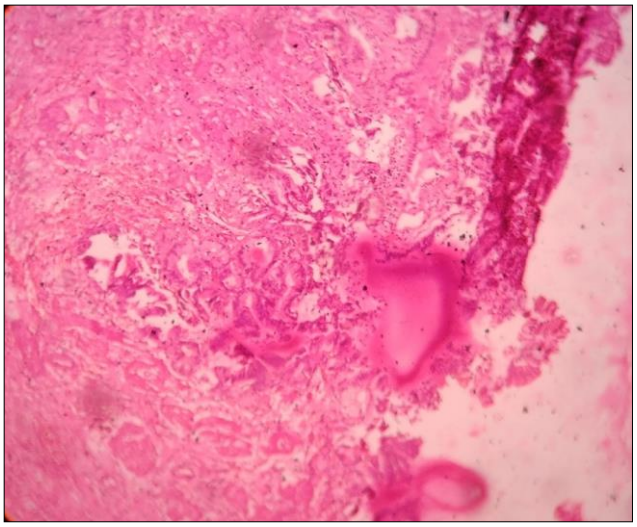

Fig 6: Adenocarcinoma gall bladder; Glandular epithelium wth dysplastic features infiltrating deep in muscle layer (10x), H&E

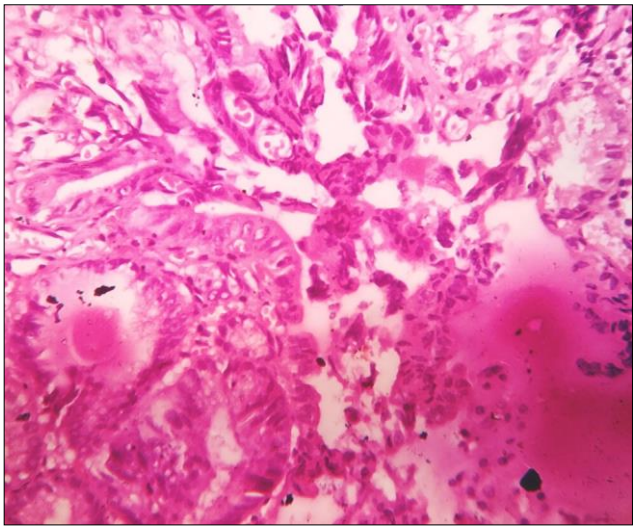

Fig 7: Adenocarcinoma gall bladder; Glandular epithelium with dysplastic features in form of loss of polarity, nuclear pleomorphism and atypical mitosis (40x), H&E

Discussion

Disease of gall bladder is one of the major cause of morbidity and mortality in our country. It changes with the geographical area, age, sex and dietary habits [3].

In our study age group involved was 11 to 80 years with maximum cases were of 31-40 years for both male and female. Minimum age of the patient was 12 years while maximum age was of 80 years, both were females. Male to female ratio was 1:6. All these are comparable to other studies [3, 7, 8]. Female sex hormones and their metabolites are responsible for high incidence of gallstones in females. When divided age according to presence or absence of gallstones, similar age group (31-40 yrs) was involved maximally.

In our study gallstones cause various types of cholecystitis and associated lesion. (398/432) (92.12%). However about 8% of cases were not associated with presence of stones. These results are very much similar to other studies [3, 9].

The various lesions noted with gallstones include acute and chronic cholecystitis and associated epithelial and stromal alternation, dysplasia and carcinoma.

Chronic cholecystitis was observed in 354/398 cases of gallstones (88.9%) which is similar to study done by Stanchu *et al*. [10].

Metaplasia was observed in 30/354 cases of which pyloric metaplasia comprised 80% (24/30) of cases similar to study by Stanchu *et al*. [10]. Metaplastic changes are most commonly associated with mixed stones (18/30) (60%) very close to that of Mathur *et al*. (66%) [11].

Elfing *et al*. [12] purposed the hypothesis that primary cholelithiasis causes secondary hyperplasia because of mechanical irritation caused by the calculi. In our study hyperplasia was seen in 9/354 (2.5%). Of the 398 cases associated with calculi. Adenoma, dysplasia and carcinoma were found in02/398 (0.5%) 04 /398 (1%) and 02/398(0.5%) of cases associated with calculi. This is similar to study done by Dattal *et al*. [13] all affected patients were females and were of advanced age group [14, 15, 16, 17]. mixed stones were most commonly associated with carcinoma [18, 19]. The increased risk of gall bladder carcinoma is related to higher incidence of cholelithiasis in women. Female sex hormones are main etiological factors in pathogenesis. So early menarche, early first pregnancy, multiple pregnancies, and delayed menopause may increase the risk [20].

In our study mixed stones are most common variety of gallstones (328/398 =82.4%) while cholesterol and pigmented 26/398 11% and 26/398 =6.5% of cases respectively [3, 17].

Single stones were found is 90/398= (22.6%) and multiple stones in 308/398= (77.3%) cases [8].

Conclusion

Gallstone disease cause various histological changes in gallbladder which varies from simple inflammation cholecystitis to various mucosal alterations such as cholesterosis, hyperplasia, metaplasia, dysplasia to carcinoma. Mixed types of stones are most common type and are associated with premalignant and malignant lesions.

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