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## The spectrum of histopathological lesions in Gallbladder in cholecystectomy specimens

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### Abstract

**Background:** Gall bladder is very common organ to be affected by many pathological diseases which include wide spectrum of the lesions from congenital ones to inflammatory or premalignant and malignant lesions.

**Aim:** Study the spectrum of histopathological lesions in gallbladder in Cholecystectomy specimens.

**Material and Methods:** The study was conducted in the Department of Pathology, Muzaffarnagar Medical College, Muzaffarnagar. Total of 434 cholecystectomy specimen were studied.

**Result:** Maximum cases (231/434 cases) were of chronic cholecystitis followed by acute cholecystitis (28 cases), eosinophilic cholecystitis (3 cases), cholesterolosis (31 cases), follicular cholecystitis (11 cases), xanthogranulomatous cholecystitis (9 cases) and one case each of mucocele and porcelain gall bladder. Metaplasia was seen in 83 cases (19.12%), dysplasia in 16 cases (3.68%) and malignancy in 5 cases (1.15%).

**Conclusion:** Gall bladder with stones of prolonged duration associated with risk of premalignant and malignant conditions making histopathological examination necessary for timely recognition of lesion.

**Keywords:** Gall bladder, chronic cholecystitis, dysplasia, carcinoma

### Introduction

Gall bladder, a foregut organ is very common organ to be affected by many pathological diseases which include wide spectrum of the lesions from congenital ones to cholelithiasis, inflammatory or pre-malignant and malignant lesions [1]. It is one of the most common organ to be resected [2].

Gall bladder is a pear shaped structure lying on the visceral surface of right lobe of liver [3]. Histologically, it is lined by the tall columnar epithelium bathed with mucus which separates the mucosal cells from the bile [4]. It has three layers namely mucosa, muscularis and adventitia [5]. Cholelithiasis is the commonest etiology throughout the world. There is variation in the prevalence of cholelithiasis according to the age, sex and ethnicity [6]. In India, the prevalence of cholelithiasis is between 2- 29% while in Northern India, it is more prevalent that's why Northern India is known to be as stone belt. Cholelithiasis is a multifactorial disease [7], more prevalent in fatty fertile females of forty years until menopause but can occur in children and males also. Additional factors include age, genetic susceptibility, obesity, insulin resistance, alcohol consumption, increased triglyceride level, pregnancy and various drugs [7]. Ascorbic acid and Calcium [8], consumption of unsaturated fats [9] and dietary fibres [10] have the protective effect. Most of the patients are asymptomatic while some present with biliary colic or it's complications, commonest being the chronic cholecystitis, others are muscle hypertrophy, cholesterolosis, fibrosis and hyperplasia of mucus glands [6].

Gall bladder dyskinesia resulting in bile stasis is considered as the main pathology responsible for gall stone formation. Three factors namely mucus, calcium and lipid act together to promote the nucleation of the stones [11]. Stones are categorized as cholesterol stones, pigment stones and the mixed stones according to their composition [12]. These can be identified easily by their morphology e.g. cholesterol stones are single, oval and yellowish in color, pigmented stones are usually multiple and they are small in size and black colored. Mixed stones are multiple, multifaceted and can be of variable size [13].

Gall stones are responsible for the irritation of the columnar epithelium and is the main underlying cause for a number of histopathological changes like acute and chronic cholecystitis, cholesterolosis and pre-neoplastic conditions like metaplasia and dysplasia, ultimately culminating into the neoplasia [6, 11, 14]. That's why, patients with cholelithiasis need proper surveillance as most of the carcinoma of gall bladder are found in association of the stones [15, 16].

As the most of the patients are asymptomatic, gall bladder carcinoma is often diagnosed late incidentally on histopathological examination accounting for the grave prognosis.

Carcinoma gall bladder accounts for only 3% of all gastrointestinal malignancies. It is seen in patients of age more than 50 years and also more prevalent in females like other gall bladder pathologies. As it is diagnosed frequently in late stage, it has 5 year survival rate of only 1-5%. Most carcinomas are adenocarcinoma (approximately 84%), rest include adenosquamous, squamous and other rarer type of carcinoma [17].

Thus the present study was aimed to find out the histological changes in gall bladder and their association with various types of stones.

**Material and Method:** The present work was done in the Department of Pathology, Muzaffarnagar Medical College, Muzaffarnagar from June 2017 to May 2018. Total 434 cholecystectomy specimens were studied. Inadequate or autolysed specimens and specimens without complete medical records were excluded from the study.

The specimens were collected in 10% formalin and fixed for 24 hours. Then sections were taken from fundus, body and neck of gall bladder after observing the gross morphological details of all specimens and stones, if present. Additional sections were taken from abnormal appearing mucosa. Sections were stained with Hematoxylin and Eosin stain after the processing. The stained slides were then studied thoroughly under microscope to observe the changes in mucosa.

**Results:** In the periods of 12 month, 434 cholecystectomy specimens were analysed. Age of the patients ranged from 11-80 years and the commonest age group with gall bladder disease was the 4<sup>th</sup> decade, seen in 115 cases (26.5%) (Figure 1). The mean age of presentation was being 41.69 years. Females were more commonly affected (345 cases, 79.49%) while only 89 cases (20.5%) were seen in males, so the female to male ratio was 3.9:1 (Figure 2).

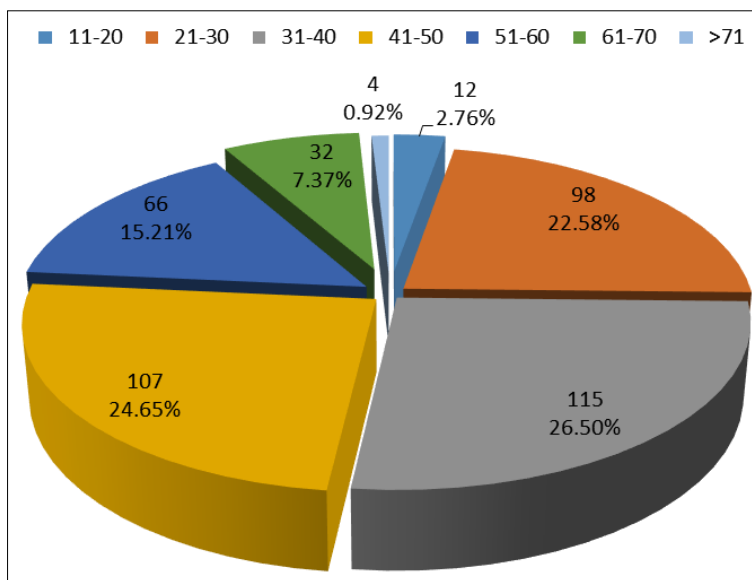


Fig 1: Age wise distribution

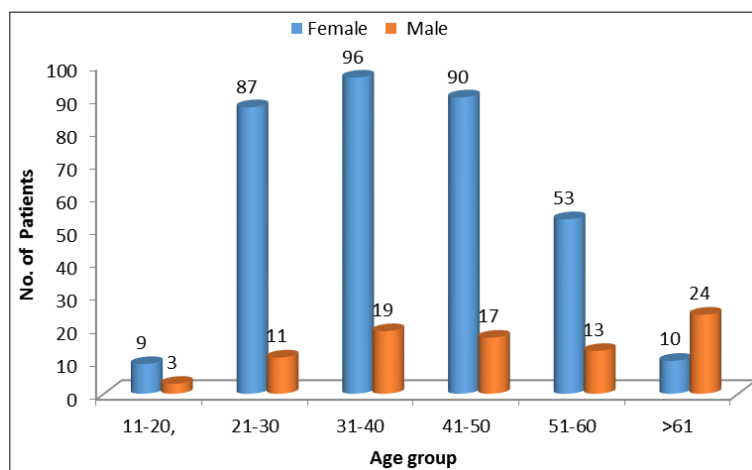


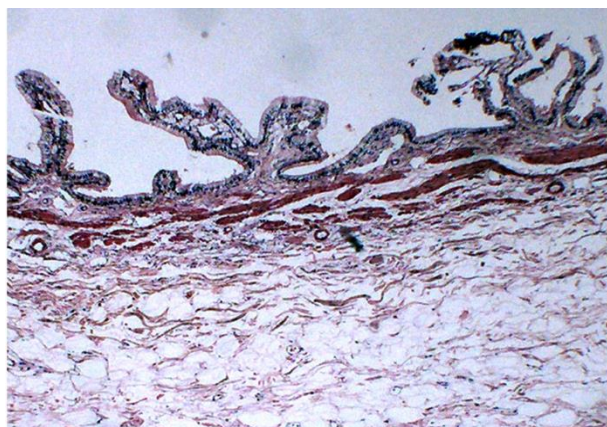
Fig 2: Sex-wise distribution

On gross examination, 192 (44.2%) gall bladder were of normal size, 208 were contracted and 34 gall bladder were edematous and distended. Out of total 434 cases, gall stones were present in 382 cases (88.02%) out of which multiple stones were seen in 263 cases and the rest 52 (11.98%) were acalculus gall bladder. Mixed stones were most common, seen in 210/382 cases (54.97%) followed by cholesterol and pigment stones in 93/382 cases (24.34%) and 79/382 cases (20.68%) respectively. On histopathological examination, non-neoplastic lesions were seen in 429/434 cases and were

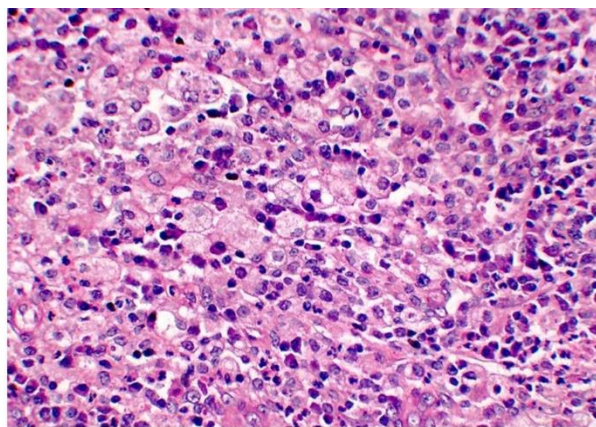
common in 4<sup>th</sup>-5<sup>th</sup> decade. Maximum cases (231/434 cases) were of chronic cholecystitis (Fig 3) followed by acute cholecystitis (28 cases), eosinophilic cholecystitis (3 cases), cholesterosis (31 cases), follicular cholecystitis (11 cases), xanthogranulomatous cholecystitis (9 cases) (Fig 4) and one case each of mucocele and porcelain gall bladder (Table 1). Metaplasia was seen in 83 cases (19.12%). Dysplasia was reported in 16 cases (3.68%) (Fig 5). Stones were present in 15 / 16 cases (Table 1).

**Table 1:** Association of histomorphological lesions with gall stones

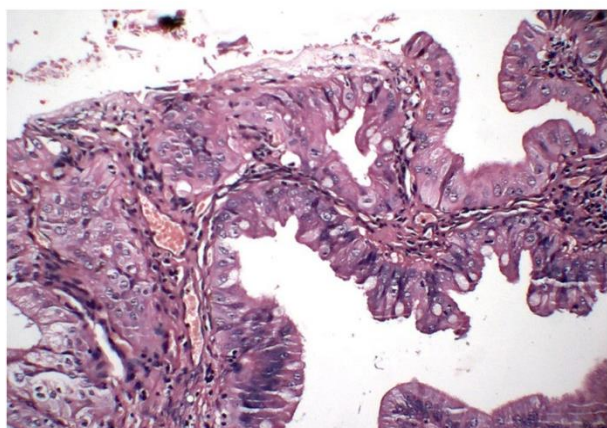
Histopathological finding	Total no. of cases	GB with stones	Percentage	GB without stone	Percentage
Acute cholecystitis	28	23	82.14%	05	17.85%
Eosinophilic cholecystitis	03	01	33.33%	02	66.66%
Chronic cholecystitis	231	206	89.17%	25	10.82%
Follicular cholecystitis	11	07	63.63%	04	36.36%
Cholesterosis	31	28	90.32%	03	9.36%
Xanthogranulomatous cholecystitis	09	06	66.66%	03	33.33%
cholegranulomatous cholecystitis	02	02	100%	00	00
Mucocele	01	01	100%	00	00
Adenomyomatosis	13	10	76.92	03	23.07%
Porcelain gallbladder	01	00	00	01	100%
Metaplasia	83	81	97.59%	02	2.40%
Dysplasia	16	15	93.75%	01	6.25%
Carcinoma	05	03	60%	02	40%
Total	434	382	88.02%	52	11.98%



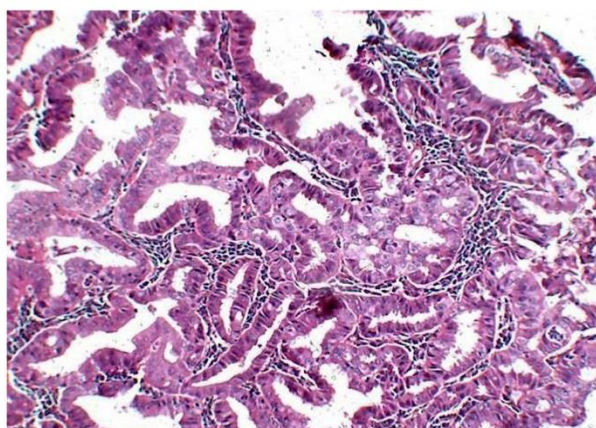
**Fig. 3 -** Gall bladder showing chronic cholecystitis 200x H&E



**Fig. 4 -** Xanthogranulomatous cholecystitis 400x,H&E



**Fig. 5 -** Dysplasia with intestinal metaplasia 200x H&E



**Fig. 6 -** Well differentiated adenocarcinoma.200x, H&E

**Fig 3, 4, 5, 6:** Photographs showing different histopathological lesions.

Dysplasia was more common with cholesterol stones, seen in 10/15 cases (66.66%) followed by pigment stones in 3/15

cases (20%) and mixed stones in 2/15 cases (13.34%). Only 5 cases of malignancy was seen (1.15%) and all were

common in 5<sup>th</sup>- 6<sup>th</sup> decade. Adenocarcinoma was reported in 4 cases (80%) and papillary carcinoma in one case (20%) (Fig 6). Out of 5 cases of malignancy, 3 cases (60%) were seen in gall bladder harbouring stones while rest 2 cases (40%) were seen in acalculus gall bladder (p value 0.049 i.e.

statistically significant) (Table 2). Cholesterol stones were seen in 2/3 cases while only one case was seen in association of mixed stone. Thus, most of the histomorphological lesions were associated with gall stones (p value 0.0001 which is highly significant).

**Table 2:** Distribution of cases of dysplasia and carcinoma with stones

Histopathology	No. of cases	GB with stone	GB without stone
Dysplasia	16	15 (93.75%)	01 (6.25%)
Carcinoma	05	03 (60%)	02 (40%)

## Discussion

Cholelithiasis is a very common world wide illness among the various gastro-intestinal disorders, needing cholecystectomy. There is a long list of the lesions that are associated with the stones which can be either inflammatory namely cholecystitis, cholesterolosis, adenomyomatosis, polyps or can be premalignant like metaplasia, hyperplasia, dysplasia or even the frank malignancy. They may present initially as gall bladder thickening or small mass, picked up by an expert radiologist but all cases are not diagnosed ultrasonographically. Hence, it has been a traditional practice to send all cholecystectomy specimens for histopathological examination<sup>[6]</sup>.

In the present study, all patients ranged between the age group of 11 to 80 years. Most of them were in 4<sup>th</sup> decade (26.49%). Majority were females (79.49%) males being only 20.51%. Thus, female to male ratio was 3.9: 1. Similar findings were observed by Sumit *et al.*<sup>[18]</sup> who studied 184 cholecystectomy cases. Age of the patients varied from 11 to 80 years, with majority of the patients in 4<sup>th</sup> decade. Female preponderance was seen (F: M ratio is 1.5:1). Khan MR *et al.*<sup>[19]</sup> studied 360 gall bladder specimens, females being 79% and males 21% thus female to male ratio was 3.86:1 and the maximum patients (30.2%) were between 31-40 years. The findings were also consistent with the work done by Banerjee *et al.*<sup>[20]</sup>.

Gall bladder was contracted in 47.9% cases, normal size in 44.2% cases and enlarged in 7.8% cases in the present work. In a study by Banerjee *et al.*<sup>[20]</sup> 66.7% gall bladder were shrunken, 20% were of normal size and in 13.3% cases, gall bladder were distended.

In our study, 382/434 cases (88.02%) were associated with stones while 52 cases (11.98%) were without stones. This is in concordance with the study by Dattal DS *et al.*<sup>[21]</sup> who found stones in 91.8% cases while only 8.2% gall bladders were without stones. Multiple stones were found in 263/382 gall bladder (68.84%) while 119 (31.15%) cases had single stone. Similar findings were observed by Goyal S *et al.*<sup>[22]</sup> They found multiple stones in 69.64% and single stone in 30.35% patients. Similarly, Khanna R *et al.*<sup>[23]</sup> also observed that the multiple stones (85%) were more common finding than the solitary ones (15%). Thus, all these studies indicate that the cases with multiple stones are more commonly symptomatic. In this study, mixed stones were seen in 54.97% cases, cholesterol stones in 24.32% cases and in 20.68% cases, black pigment stones were found. These findings were consistent with the study of Mathur SK *et al.*<sup>[6]</sup> Goyal S *et al.*<sup>[22]</sup> and Baig SJ *et al.*<sup>[24]</sup> who observed that mixed stones are more prevalent than the cholesterol and pigment stones.

On histopathological examination, present study revealed

maximum cases of chronic cholecystitis in 231/434 cases (53.22%). Similar findings were observed by Baig SJ *et al.*<sup>[24]</sup> and Tyagi SP *et al.*<sup>[25]</sup> they found chronic cholecystitis in 60% and 50.8% cases respectively.

Acute cholecystitis accounted for 6.45% cases while Kaur *et al.*<sup>[26]</sup> Khan S *et al.*<sup>[27]</sup> and Sharma I *et al.*<sup>[28]</sup> showed 2.60%, 2.70% and 2.60% cases of acute cholecystitis respectively.

Cholesterolosis was seen in only 31 cases (7.14%) which was similar to the work done by Giri S *et al.*<sup>[18]</sup> who reported cholesterolosis in 7.61% cases.

Only the 3% cases of adenomyomatosis was reported which was in concordance with the study of Terada<sup>29</sup> who showed 3.68% of it.

Follicular cholecystitis was found in 2.53% cases. Kaur A *et al.*<sup>26</sup> and Mohan *et al.*<sup>30</sup> showed similar findings, follicular cholecystitis being 2.08% and 2.30% respectively.

Only 3 cases (0.69%) were of eosinophilic cholecystitis which was in concordance with the study of Kaur *et al.*<sup>[26]</sup> (0.78% cases).

Xanthogranulomatous cholecystitis was diagnosed in 9 cases (2.07%). Shah H *et al.*<sup>[31]</sup> and Vahini G *et al.*<sup>[32]</sup> showed xanthogranulomatous cholecystitis in 2.0% and 1.81% cases respectively.

Metaplasia refers to the adaptive replacement of one type of epithelium with other that can sustain the adverse effects. Metaplasia was found in 83 cases (19.12%) which was in concordance with the study of Dattal DS *et al.*<sup>[21]</sup> who observed 15.56% cases of metaplasia, but Seretis C *et al.*<sup>[33]</sup> observed metaplasia in 25.6% cases.

Dysplasia is indicative of an early neoplastic process. Present work showed dysplasia in 16/434 cases (3.68%) which was consistent with the study of Kaur *et al.*<sup>[26]</sup> who found 3.64% cases of dysplasia. Similarly, Jain BB *et al.*<sup>[34]</sup> observed 4% cases of dysplasia. But this was in discordance with the studies done by Khanna R *et al.*<sup>[23]</sup> and Duarte *et al.*<sup>[35]</sup> (8.5% and 16% cases of dysplasia respectively). Similarly, Mukhopdhyay S *et al.*<sup>[36]</sup> found dysplasia in 5% cases.

Gall bladder carcinoma was diagnosed in only 5 cases (1.15%). This observation was similar to the studies done by Selvi *et al.*<sup>[13]</sup> Mohan *et al.*<sup>[30]</sup> and Pradhan *et al.*<sup>[37]</sup> showing malignancy in 1.20%, 1.09% and 1.05% cases respectively. Kaur A *et al.*<sup>[26]</sup> found carcinoma in 0.78% cases. Vahini G *et al.*<sup>[32]</sup> in their study found carcinoma in 4.5% cases. This was in discordance to the present study. Shah H *et al.*<sup>[31]</sup> showed 2% cases of carcinoma which is in close proximity to the results of our study.

Present study showed 15 cases (out of 16 cases) associated with stones (93.75%) while out of 5 cases of gall bladder carcinoma, 3 cases were seen in calculus gall bladder (p

value 0.0001, indicate statistical significant association of dysplasia and carcinoma with stones). Dattal DS *et al.* [21] observed that 90.48% cases of dysplasia were seen in association with stone while all malignancy were seen in calculus gall bladder. Similar findings were also observed by Jain *et al.* [34] who had seen dysplasia in 88.8% cases associated with stones and only 11.1% cases were without stones. They found 78.5% cases of carcinoma in calculus gall bladder and only 21.4% cases in gall bladder having no stones. Thus, all these studies indicate that the dysplasia and carcinoma are highly associated with stones.

### Conclusion

Wide variety of gall bladder lesions are associated with stones including the neoplasia. Risk of premalignant and malignant conditions are more with stones of prolonged duration, indicating the urgent need for routine histopathological examination to ensure the early recognition of malignancy for better prognosis.

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