



HISTOPATHOLOGICAL SPECTRUM OF GALLBLADDER DISEASES IN A TERTIARY CARE CENTER – A RETROSPECTIVE STUDY

Pathology

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ABSTRACT

BACKGROUND: Gallbladder disease is known to affect a substantial number of people throughout the world. In India, the disease prevalence is on the rise, largely attributable to dietary & lifestyle changes, thus causing a significant disease burden. The purpose of this study is to evaluate the varied histological manifestations of gallbladder pathology and their association with cholelithiasis. **MATERIALS & METHODS:** This retrospective study was conducted in the department of pathology, Kilpauk medical college from January 2018 to December 2018. The clinical data and the histopathological changes were evaluated. **RESULTS:** Of the 156 cases which were studied, 120 cases (77%) had gallstones. The mean age was 47 years. Females had a slight preponderance for gallbladder diseases with the Male: Female ratio being 1:2. 138 cases (89.8%) were diagnosed as chronic cholecystitis. 3 cases were diagnosed to have invasive malignancies. **CONCLUSION:** A diverse spectrum of diseases affect the gallbladder encompassing inflammatory conditions, parasitic infections, pseudoneoplastic lesions and neoplasms. Routine cholecystectomy specimens should be evaluated meticulously as incidental findings and diagnosis can be transformative.

KEYWORDS

Gallbladder, gallstones, cholelithiasis, carcinoma, histopathological spectrum

INTRODUCTION:

Disorders of gall bladder, the tiny hollow organ that stores bile and sits beneath the liver, affect a significant population of the world¹. Gallstones are the attributable cause for more than 95% of the various disorders, for which the known risk factors include alcohol intake, high calorie and high fat diet, obesity, female sex, older age group, diabetes mellitus, drugs and fluke infestations of the biliary tract^{1,2}. In India, the prevalence of gallstone induced disease is quite high, with various studies reporting prevalence rates ranging from 10% - 22%³.

Gall bladder cancer, one of the rare malignancies to occur in the gastrointestinal tract, has its highest incidence rate in India, with search of literature yielding an age standardized incidence rate of 21.5/100,000 women and 7.09/100,000 men in North India⁴. The strong correlation between gallstones and gall bladder cancer and its relatively poor prognosis warrant the need for preventive action like cholecystectomy to be done for gallstone diseases, even though the overall incidence of gall bladder cancer among such patients is 0.2%⁵. The composition of gallstones varies with etiology, with cholesterol stones being the majority followed by pigmented stones and mixed stones. The prevalence of gallstones varies with age, sex, and ethnicity⁶. The myriad of findings associated with cholelithiasis range from asymptomatic presentation to carcinoma. This study was undertaken to determine the histopathological spectrum of gall bladder diseases in cholecystectomy specimens and to evaluate their correlation with gallstones.

MATERIALS AND METHODS:

This retrospective study was conducted in the Department of Pathology, Kilpauk medical college over a period of one year from January 2018 to December 2018. A total of 156 cholecystectomy specimens were received, all of which were included in the study. The detailed clinical history which accompanied the specimens were noted. The specimens were fixed in 10% neutral buffered formalin. The nature of the gallstones when present, were noted. Sections were taken from fundus, body and neck for all specimens with additional sections taken when required. After processing, 4-micron thick sections were cut, which were stained with Hematoxylin & Eosin. Immunohistochemical analysis was performed when required. All the slides were reviewed and the histopathological changes were observed. The results were summarised and analysed in Microsoft Excel 2016.

RESULTS:

The age of the patients ranged from 16 years to 83 years with the mean age being 47 years. The age group commonly affected was between fourth and sixth decade of life, accounting for 57% of all cases. The overall male-female ratio was 1:2. However there was no gender predilection in the sixth and seventh decade, where the disease distribution was nearly equal. Overall, 77% cases were associated with gallstones. Table 1 depicts the age & gender distribution of gall bladder diseases in relation to gallstones.

Of the gallstones, mixed stones were the most common accounting for 55% of cases followed by pigment stones (28.3%). Cholesterol stones were more common among women (Figure 1). Table 2 depicts the type of gallstones and their distribution.



Figure 1: Cholesterol stones (above) and Pigmented Stones (below)

Table 1: Age & Gender Distribution

Age group	Calculus disease		Acalculous Disease	
	Male	Female	Male	Female
11-20	0	2	0	0
21-30	2	19	1	6
31-40	4	22	1	6
41-50	6	16	4	1
51-60	10	12	3	4
61-70	11	11	3	1
71-80	4	0	3	3
81-90	0	1	0	0
Total	37	83	15	21

Table 2: Distribution of Gallstones

Type of Stones	Gender		Total	Percentage
	Male	Female		
Mixed	24	42	66	55%
Pigment	11	23	34	28.3%
Cholesterol	2	18	20	16.7%
Total	37	83	120	100%

Table 3: Distribution of cases by histopathological diagnosis

Histopathological Diagnosis	Gallstones	
	Present	Absent
Acute Cholecystitis	3	3
Gangrenous Cholecystitis	3	0
Chronic Cholecystitis	107	32
Xanthogranulomatous Cholecystitis	2	1
Dysplasia	2	0
Carcinoma	3	0
Total	120	36

Table 4: Additional pathology in chronic cholecystitis

Additional Findings	Gallstones	
	Present	Absent
Papillary hyperplasia	3	0
Metaplasia	Antral	45
	Intestinal	5
Cholesterolosis	25	5
Adenomyomatous hyperplasia	7	0
Lymphoid follicles	3	0

Table 5: Premalignant & malignant lesions - Distribution

Lesion	Age	Sex	Stone
Low grade dysplasia	46	Male	Cholesterol
High grade dysplasia	67	Male	Mixed
Adenocarcinoma	61	Male	Mixed
Adenosquamous carcinoma	61	Female	Cholesterol
Adenosquamous carcinoma	68	Female	Cholesterol

The spectrum of histopathological diagnosis that were observed include acute cholecystitis (3.9%), gangrenous cholecystitis (1.9%), chronic cholecystitis (89.8%), xanthogranulomatous cholecystitis (1.9%), dysplasia (1.3%), and carcinoma (1.9%). Table 3 depicts the entire gamut of histopathological diagnosis of 156 specimens and their relationship to gallstones. The additional pathological findings that were observed in the cases of chronic cholecystitis include papillary hyperplasia, metaplasia, cholesterolosis, adenomyomatosis, and the presence of lymphoid follicles with overlapping morphology among these findings. Metaplasia was seen in 40% of cases of chronic cholecystitis. Cholesterolosis and antral metaplasia were observed in both calculous and acalculous chronic cholecystitis (Figures 2 & 3).

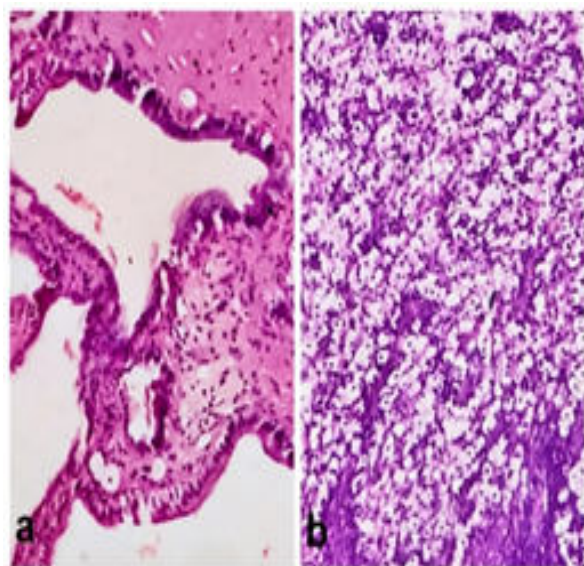


Figure 2: (a) Cholesterolosis - Accumulation of foamy macrophages in lamina propria; (b) Xanthogranulomatous cholecystitis - Transmural accumulation of foamy macrophages

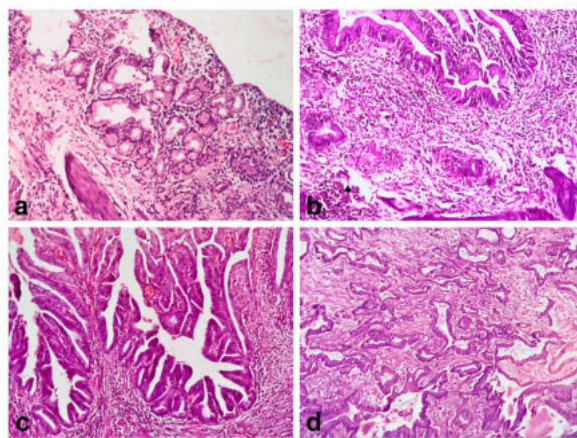


Figure 3: (a) Antral Metaplasia; (b) Low grade dysplasia; (c) High grade dysplasia; (d) Adenocarcinoma

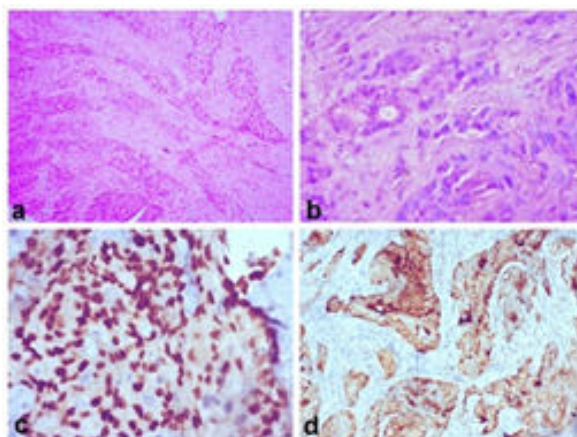


Figure 4: (a), (b) Adenosquamous carcinoma - Sheets, nests and glands of tumour cells; (c) p63 - Positive in malignant squamous cells; (d) CK7 - Positive in malignant glandular cells

Adenomyomatous hyperplasia was seen in 5% of chronic cholecystitis. Table 4 depicts the distribution of cases of chronic cholecystitis with additional findings and their relationship to gallstones.

All the premalignant and malignant lesions of the gallbladder were associated with gallstones, with cholesterol and mixed stones being present (Figures 2, 3, & 4). All three invasive malignancies occurred in the seventh decade. Two cases of dysplasia were observed in male patients. Table 5 summarizes the premalignant and malignant lesions and their relationship with gallstones.

DISCUSSION:

Gallbladder disorders encompass a spectrum of etiologies. However, inflammatory diseases of gallbladder are the predominant group throughout the world⁷. 97% of cases in our study were of inflammatory pathology. The prevalence of gallbladder disorders in India varies with ethnicity with studies reporting rates up to 29%⁸. Gender and age are strongly associated with incidence of gallbladder disease, with female sex & older age being important risk factors, as evidenced by this study and several other studies⁹. In our study gallbladder disorders were twice more prevalent in women than men, with the disease occurring in girls even in the second decade. Majority of the patients (57%) were in the fourth to sixth decade of life, which was similar to the findings observed by Dattal DS et al in a study of 1371 patients (69%) and that which was noted by Thamilselvi et al in a study of 78 patients (66%)^{10,11}.

The incidence of pigment gallstones is higher in south India, but the most common type of stones tends to be that of mixed type, as was the case in our study. The incidence of mixed stones (55%) was in concordance with the study done by Patil et al (Mixed - 57%) and Thamilselvi et al (Mixed - 54%)^{11,12}. The incidence of pigmented stones (28.3%) was in concordance with the study done by Thamilselvi et al (Pigmented - 38%) as opposed to that which was observed in the studies done by Patil et al (Pigmented- 6%) and Dattal DS et al (Pigmented - 10%), thus highlighting the North-South difference^{10,11,12}.

Chronic cholecystitis constituted the majority of the cases (89.8%) in this study. Some of the associated findings seen in our study are histological mimickers of malignancy like papillary hyperplasia which can mimic intraepithelial neoplasia. Extensive antral metaplasia or intestinal metaplasia can occur with chronic cholecystitis irrespective of the presence of gallstones. The presence of metaplasia indicates chronic inflammation which should ring an alarm bell to look for evidence of dysplasia or invasive malignancies. Adenomyomatous hyperplasia characterized by cystically dilated glands within the wall of the gallbladder can sometimes be present which can be mistaken for invasive adenocarcinoma¹³.

Xanthogranulomatous cholecystitis, the clinical and radiological mimicker of malignancy, is characterized by the diffuse thickening of gallbladder, which on histology shows diffuse inflammation with foamy macrophages and other inflammatory cells¹⁴. Three cases were reported during the study period, two of which were associated with gallstones.

Carcinoma of gallbladder, though rare is associated with poor prognosis. The two cases of adenosquamous carcinoma were associated with cholesterol stones, emphasizing the fact that large cholesterol rich stones are more frequently found in association with squamous cell carcinomas and adenosquamous carcinomas^{15,16}.

CONCLUSION:

Diseases of gallbladder are common and on the rise. The histopathological spectrum the disorder includes congenital anomalies, inflammatory disorders, infections, pseudoneoplastic lesions, benign neoplasms and malignant neoplasms. Gallstones, the most frequent offender can present with a finding as innocuous as an asymptomatic imaging feature or be associated with lethal malignancies. Nonetheless, routine cholecystectomy specimens should be evaluated meticulously as incidental findings and diagnosis can be transformative.

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