

ORIGINAL RESEARCH

A RETROSPECTIVE HISTOLOGICAL STUDY OF GALLBLADDER DISEASE

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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 a tertiary medical centre in Patna from January 2020 to December 2020. 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 (88.5%) were diagnosed as chronic cholecystitis. 1.92% 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 sits¹ beneath the liver, affect a significant population of the world. 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. In India, the prevalence of gallstone induced disease is quite high, with various^{2,3} studies reporting prevalence rates ranging from 10% - 22%.

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 of⁴ 21.5/100,000 women and 7.09/100,000 men in North India. 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 the⁵ overall incidence of gall bladder cancer among such patients is 0.2%. 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, and⁶ ethnicity. 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.

METHODS

This retrospective study was conducted in a tertiary medical centre in Patna over a period of one year from January 2020 to December 2020. 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 for 24 hours 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 53% of all cases. The overall male-female ratio was 1:2. However there was no gender predilection in the sixth 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.

Age group	Calculous 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

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. Table 2 depicts the type of gallstones and their distribution.

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%

The spectrum of histopathological diagnosis that were observed include acute cholecystitis (3.9%), gangrenous cholecystitis (1.9%), chronic cholecystitis (89.1%), 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.

Histopathological Diagnosis	Gallstones	
	Present	Absent
AcuteCholecystitis	3	3
GangrenousCholecystitis	3	0
ChronicCholecystitis	107	32
XanthogranulomatousCholecystitis	2	1
Dysplasia	2	0
Carcinoma	3	0
Total	120	36

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.

Additional Findings	Gallstones		
	Present	Absent	
Papillaryhyperplasia	3	0	
Metaplasia	Antral	45	6
	Intestinal	5	0
Cholesterolosis	25	5	
Adenomyomatoushyperplasia	7	0	
Lymphoidfollicles	3	0	

All the premalignant and malignant lesions of the gallbladder were associated with gallstones, with cholesterol and mixed stones being present. 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.

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

DISCUSSION

Gallbladder disorders encompass a spectrum of etiologies. However, inflammatory diseases of gallbladder are the predominant group⁷ throughout the world. 97% of cases in our study were of inflammatory pathology. The prevalence of gallbladder disorders in India varies

with⁸ ethnicity with studies reporting rates up to 29%. Gender and age are strongly associated with incidence of gallbladder disease, with female sex & older age being important risk factors, as⁹ evidenced by this study and several other studies. 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 (53%) 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^{10,11} study of 78 patients (66%). 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^{11,12} Thamilselvi et al (Mixed – 54%). 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^{10,11,12} (Pigmented – 10%), thus highlighting the North-South difference^{10,11,12}. Chronic cholecystitis constituted the majority of the cases (89.1%) 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 for¹³ invasive adenocarcinoma. Xanthogranulomatous cholecystitis, the clinical and radiological mimicker of malignancy, is characterized by the diffuse thickening of gallbladder, which on histology shows diffuse inflammation with¹⁴ foamy macrophages and other inflammatory cells. 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^{15,16} squamous cell carcinomas and adenosquamous carcinomas.

CONCLUSION

Diseases of gallbladder are common and on the rise. The histopathological spectrum of gallbladder 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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