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A histopathological study of gall bladder in a tertiary care centre: An observational study

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Abstract
Introduction: Gallstone disease is a major health problem and a significant health issue worldwide. This research was carried out to study the varied histopathological changes, demographic correlation and association of gall bladder pathologies to cholelithiasis on 114 cholecystectomy specimens.
Materials and Methods: The present research was conducted at Department of Pathology, Prakash institute of medical sciences and research over a period of 3.5 years, July 2016 to December 2019. The gross examination was done after fixing the specimens in 10% formalin. Bits were given from fundus body and neck. Microscopic findings of the H&E-stained sections were noted.
Results: 46.5% of the samples were present in the age range of 50-70 years with high female preponderance. On Microscopic examination, chronic inflammation was found in 69.2% of the cases. Cholelithiasis was seen in 67.5% of the specimens. Acute, acute on chronic, eosinophilic, gangrenous, xanthogranulomatous cholecystitis and a single case of adenomyomatosis were also seen.
Conclusion: Gallstones produce a wide range of histopathological changes in mucosa which requires detailed histopathological analysis. The increasing rate of cholelithiasis calls for further research to signify its importance in diagnosis, demographic and future trends.

Keywords: Cholecystitis, histopathology, cholelithiasis

Introduction
Gallstone disease is a relatively common disease at global level and accounts for more than 90% of biliary tract disease [1]. Gallstones are known to cause high rates of morbidity in all parts of the world [2]. Due to changes in dietary pattern and westernization of diets with high fat, high calorie, low fiber meals, and increasing trends of alcohol consumption the incidence of cholecystitis and cholelithiasis has visibly displayed an upward shift in the last 30-40 years [3, 4]. Gallstones incidence is shown to vary with socio-demographic factors like age, sex, diet patterns, geographical location, drug history and comorbidities. A large number of the population remains unaware of their condition and lead an asymptomatic disease course [2]. Gallstones are solid deposits of the bile fluid, which can form within the gallbladder. They differ in size and shape and can be as minute as a grain of sand to as significant as a golf ball. Gallstones present when there is a chemical imbalance in the components of bile fluid that leads to precipitation of one or more of the constituents [5]. Gallstones can now commonly be seen on routine investigations. They are seen in all age groups, but the shows a rising trend with age [6]; and about one fourth of the female population above 60 years of age is bound to develop gallstone disease [7]. Cholelithiasis is associated with histopathological changes in gall bladder mucosa like acute and chronic inflammation, hyperplasia, metaplasia, dysplasia, cholesterolosis and carcinoma [8]. The objective of this study was to establish a histopathological correlation with demographic data and associate cholecystitis and cholelithiasis with their acuteness or chronicity of presentation.

Materials and Methods
This study was conducted in the department of pathology, Prakash institute of medical sciences and research center, over a period 3.5 years, July 2016 to December 2019. The study comprised of 114 gallbladder specimens received in the pathology department for histopathological evaluation. The specimens were fixed in 10% formalin. For each specimen, tissue sections were obtained to study the fundus, body and neck of gallbladder. Additional sections were taken from the specimen that appeared to have abnormal gross morphological changes. Routine tissue-processing was performed.

Routine Hematoxylin & Eosin staining and detailed microscopic evaluation of the sections were performed. The data was entered and analyzed in MS Excel and all results were shown in percentages. On microscopy, mucosa was examined for inflammation, cholesterolosis, dysplastic changes and carcinoma.

Results

A total of 114 cholecystectomy specimens were subjected for histopathological analysis. Sex ratio was 1.2:1 with female cases accounting for 55.2% and male cases accounting for 44.7%. Age range of cases studied was from 15 years to 79 years. Table 1 shows Age range of cases in study and sex distribution. Highest number of people were identified in Age range 50-60 years, closely followed by 60-70 years accounting for a net 46.5% together of all the samples.

Table 1: Age-group wise and gender-wise distribution of study cases (N=114)

Age Range	Number (N)	%
10-20 years	3	2.6
20-30 years	7	6.1
30-40 years	21	18.4
40-50 years	20	17.5
50-60 years	27	23.7
60-70 years	26	22.8
70-80 years	10	8.8
Gender	Number	%
Male	51	44.7
Female	63	55.2

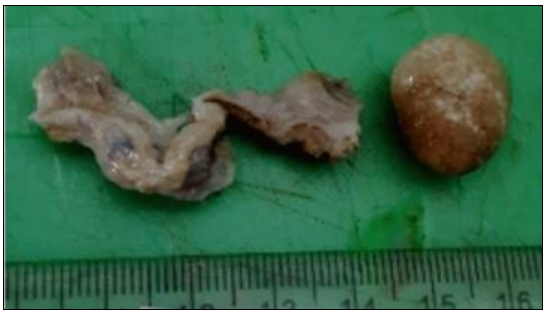

Fig 1: Cut open cholecystectomy specimen with single gallstone

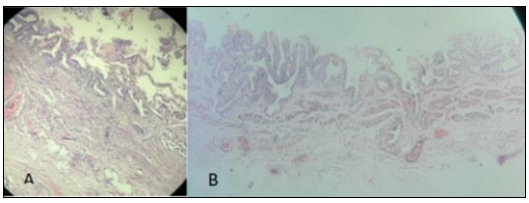

Fig 2: (A&B) Chronic Cholecystitis

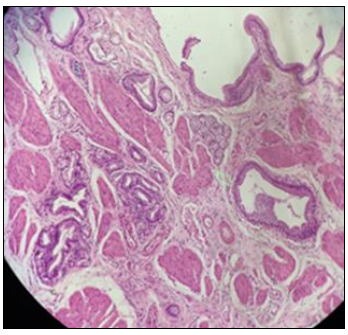

Fig 3: Adenomyomatosis

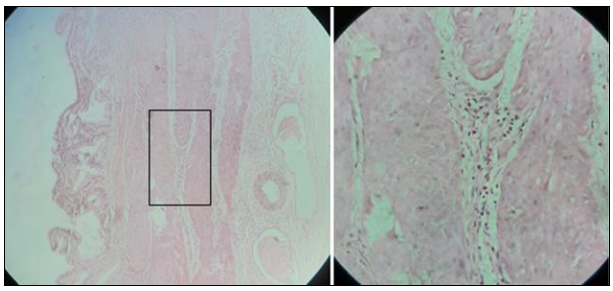

Fig 4: Eosinophilic cholecystitis

Specimens were analyzed on histopathological features and the type of inflammatory cells, out of which Chronic inflammation accounted for majority of the cases accounting for 69%. Acute inflammation was found in 6.1% and acute on chronic inflammation was seen in 16.6% of the specimens. Cholelithiasis was found in 77 specimens (67.5% of the specimens) out of which 57 specimens were of Chronic Cholecystitis. Table 2 shows the data of Cholecystitis based on histopathology findings and their association with Cholelithiasis.

Table 2: Distribution of lesions and association with Cholelithiasis (N=114)

Impression	N	%	Number of specimens with Cholelithiasis
Acute Cholecystitis	7	6.1	2
Chronic Cholecystitis	79	69.2	57
Acute on Chronic Cholecystitis	19	16.6	13
Adenomyomatosis	1	0.8	1
Eosinophilic Cholecystitis	5	4.3	2
Gangrenous Cholecystitis	2	1.7	1
Xanthomatous Cholecystitis	1	0.8	1

One case (0.8% of sample) of adenomyomatosis with chronic cholecystitis was seen in a 65-year-old female associated with Cholelithiasis. It was characterized by hyperplastic changes involving the gallbladder wall. Mucosa showed hyperplastic epithelium, mucosal glands forming clusters were seen invaginating into the hyperplastic muscularis layer (Fig: 3). Five cases of Eosinophilic Cholecystitis, two cases of Gangrenous Cholecystitis and one case of Xanthogranulomatous Cholecystitis were also seen.

Discussion

Gallstones are largely considered a serious health problem in developed countries, affecting about 10% to 15% of the worldwide adult population [9]. Cholelithiasis is one of the leading causes of tertiary care interventions related to gastrointestinal diseases. Most of the patients will be asymptomatic while some may experience biliary colic, nausea, vomiting, fatigue and rarely pruritis [10]. Therefore, most gallstones are not found on clinical examination and referred as clinically "silent," and might be diagnosed on incidental ultrasonographies for other investigative indications [11]. On the basis of multiple studies, it has been proven that Gallstone formation is multifactorial. Non-Modifiable factors include Advancing age, Female gender, Familial history, and ethnicity. Whereas Modifiable factors comprise of Diet with high calorie and carbohydrate content, low fiber, pregnancy, decreased physical activity, obesity and metabolic diseases [12]. Modifiable factors may also include rapid weight loss and intake of certain drugs

(estrogen, octreotide, diuretics) [13]. Female preponderance for cholecystitis has been noted in our study, which is similar to the findings in several other studies. Few studies have also reported the sex ratio to be as high as four times to six times while the present study showed a sex ratio of 1.2:1 [14]. The present study also showed trends of age distribution with high rate of incidences in advanced age groups of fifth to seventh decades of life, similar to other studies [14]. Geographical distribution of Cholecystitis has been notably high along the Karachi to Kolkata belt in the south east Asia region which may be associated to diet patterns and behavioral lifestyles of the populations residing in the area [15]. In the present study 69.2% of the specimens showed Chronic cholecystitis on histopathological analysis which is similar to recent studies in Baltimore showing 65% Chronic inflammation in Cholecystitis [16].

Adenomyomatosis was originally characterized as a precancerous lesion but is currently recognized as a benign modification of the normal gallbladder histology [17]. The exact altering pathogenesis of adenomyomatosis in gallbladder is still unclear which hinders with its histopathological diagnosis and further treatment [17]. Gallbladder adenomyomatosis is a condition identified by proliferation of epithelium and muscle hypertrophy of the gallbladder wall with dilatation of the mucosa through the thickened muscle layer known as the Rokitansky-Aschoff sinuses [17]. Whilst adenomyomatosis is a benign condition, histopathological analysis is of vital importance since gallbladder carcinoma is one of the most fatal conditions with challenging treatments [18].

Conclusions

Chronic cholecystitis is the most common histopathological finding in gall bladder disease. Gallstones produce a wide range of histopathological changes in mucosa which requires detailed histopathological analysis. The increasing rate of cholelithiasis calls for further research to signify its importance in diagnosis, demographic and future trends. A detailed evaluation of all cholecystectomy specimens should be performed for suitable interventions.

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