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Routine Histopathological Evaluation of All Cholecystectomy Specimens: Waste Of Resources Or A Justified Act? A Study From A Tertiary Care Centre In Greater Noida

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Abstract

Background: Gallstone disease is a major health problem and affect a substantial number of people throughout the world. Gall bladder is one of the important digestive organ which shows different histopathological changes. Different changes in dietary habit, obesity, oral contraceptive pills, alcohol etc., have shown increased pattern of cholecystitis and cholelithiasis and other pathological findings. This research was carried out to study the various histopathological pattern of gallbladder lesion and also help to differentiate non-neoplastic from neoplastic lesion thereby helping in further management

Materials & Methods: This retrospective study was conducted in Department of Pathology, Noida International Institute of Medical Sciences, Greater Noida for a period of 2-years, from January 2022 to December 2023. The data was retrieved from the medical records department after ethical approval from Institutional Ethics Committee. All histopathology reports and clinical data of 321 consecutive gall bladder specimen after elective and emergency cholecystectomy were retrospectively analyzed.

Results: A total of 321 cases of gall bladder specimen submitted for histopathological examination during the study period were included into the study. Of the 321 cases which were studied, chronic calculous cholecystitis was reported in 38% of cases. Females had a slight preponderance for gallbladder diseases with the Male: Female ratio being 1:6.2. 117 cases (36.45%) were diagnosed as chronic acalculous cholecystitis. 8 cases each of dysplasia and intestinal metaplasia were observed in this study.

On histopathologial evaluation, chronic calculous cholecystitis was most common findings followed by chronic acalculous cholecystitis. Cholesterolosis was associated with both chronic calculous as well as acalculous cholecystitis comprising all together 14% of this study. Other findings were acute on chronic cholecystitis, chronic follicular cholecystitis, xanthgranulomatous cholecystitis and eosinophilic cholecystitis. It was concluded that Chronic calculous cholecystitis was the most common histopathologcial findings and the common groups was 31-40 years.

Routine examination of cholecystectomy specimens grossly and microscopically is important for patient management In this present study case of gall bladder malignancy was not reported. However, intestinal metaplasia and dysplasia both were found in our study which were premalignant conditions that can eventually

lead to the development of carcinoma. It is very important to make sure that all cholecystectomy specimens undergone histopathological examination; with this, we can achieve timely diagnosis and early managements.
Conclusion: The incidence of chronic calculus cholecystitis are more common in female gender and mostly in third decade of life. Though malignancy of gall bladder is a rare condition but we strongly advocate routine histopathological examination of all the resected GB specimens in order to exclude pre-malignant or malignant condition as incidental findings and diagnosis can be transformative.

Keywords: Gall bladder, cholecystitis, dysplasia, hyalinizing stroma

Introduction

Gallbladder is the tiny hollow organ of digestive system which store bile and sits beneath the liver. Disordered gall bladder, which is mostly encountered with different histopathological changes including acute or chronic inflammation, mucosal changes, infection, benign polyps, pre-malignant and malignant conditions [1,2]. In the recent decades, there is increase in the incidence of cholecystitis and cholelithiasis because of changes in dietary pattern with high calorie and high fat diet, sedentary lifestyles, obesity, oral contraceptives, alcohol consumption [3,4]. In India, the prevalence of gallstone induced disease is quite high, with various studies reporting prevalence rates ranging from 10% - 22% [3]. Besides cholelithiasis and cholecystitis, the distribution of benign gallbladder diseases is quite diverse including acalculous conditions such as acalculous cholecystitis, cholesterolosis, polyposis of gallbladder and calculous cholecystitis which may or may not be associated with gallstones [5].

Cholecystectomy is the most commonly performed surgical procedure for gall bladder diseases. Majority of the cholecystectomy are done for cholelithiasis and its affects 10 to 20 % of adult population in developed countries [6]. Inflammation of gall bladder may be acute, chronic or acute superimposed on chronic. It almost always occurs in association with gallstones [7]. More than 95% of biliary tract disease is attributed to cholelithiasis and its prevalence increases with age from 21 to 80 years and higher in females than males [8,9]. All gall bladder containing stones should be removed surgically because of the risk of cancer, this being greater than the operative mortality risk[7].

This study aims to quantify the various outcomes of routine cholecystectomy specimens which is one of the frequently received specimens in the department of pathology. The different histopathological patterns which can be seen in gallbladder in chronic cholecystitis and their incidence can be known from this study. The socio-demographic characteristics of the patient can be analysed.

Materials & Methods:

This was a retrospective study conducted in the departments of Pathology ,Noida International Institute of Medical Science (NIIMS), Greater Noida over a period of two years from January 2022 to December 2023. Findings of a total 321 cholecystectomy specimens were included in this study. Information regarding age, gender and other relevant clinical data were collected from requisition form. All cholecystectomy specimens received in the Pathology Department were included in the study whereas persons with previous history of malignancy and chemotherapy were excluded from the study. Ethical approval from Institutional Review Committee, was taken.

Inclusion criteria

All patients who underwent cholecystectomy in the hospital during the study period were included in the study.

Exclusion criteria

1. Known case of Malignancy

2. Patient of chemotherapy.

All specimens were fixed in 10% formalin. Gross features of cholecystectomy specimens were recorded. Three sections each from neck, body and fundus were taken. In cases with any growth, irregularity in the wall, calcification, necrosis etc more sections were taken. Standard grossing techniques were followed. Appropriate areas were selected, grossed, processed,

Volume 7, Issue 3; May-June 2024; Page No 379-387

sectioned, and stained with haematoxyline and eosin dye. Microscpoic examination of histopathological examination was done on formalin fixed and paraffin processed tissues. Different histological findings were noted in various layers of cholelithiasis and cholecystitis gallbladder which are compared with each other. The observations were noted in pre-designed proforma and analyzed. Statistical analysis of the data was done using SPSS software.

Results:

A total of 321 patients who had undergone cholecystectomy were studied for a period of two years. Among these patients, 277 cases were of female (86.3%) and 44 cases were of male (13.7%).The age of the patients ranged from 15 years to 83 years with maximum number of patients being 31 to 40 years. In this study maximum number of females patients were found in the Age group between 31-40years followed by 21-30. 35 cases each of 41-40 and 51-60 year age group were recorded. Males patients were mainly found in the age group between 31-40 years followed by 41-50years of age. 2 males and 9 female were between age group 11-20 whereas, 2 males and 3 females patients were above 70 year age as shown in (Table 1)

Table 1: Age and gender wise distribution of gall bladder specimens

Age group(years)	**Male (n)**	**Female(n)**	**No. of cases**	**Total (n%)**
11-20	**2**	**9**	11	**3.43**
21-30	9	88	97	30.22
31-40	12	92	104	32.4
41-50	10	35	45	14.01
51-60	3	35	38	11.9
61-70	6	15	21	6.54
>70	2	3	5	1.5
TOTAL	44	277	321	100

Majority of patients (89.7%) presented with upper abdominal pain of varying duration. Other symptoms were depicted in [Table 2]

Table 2: Presenting symptoms in patients

Presenting Symptoms	No. of Patients (%)
Pain in Upper abdomen	288 (89.7%)
Hyperacidity after fatty meal/intolerance to fatty food	21 (6.5%)
Nausea or vomiting	8 (3.5%)
Heaviness in right hypochondrium	4 (1.2%)

All 321 cases underwent microscopic evaluation and were categorized histologically. In specimens with more than one findings, the predominant pattern was used for categorization (one condition per case) [Table 3]. The majority of cases had chronic inflammation, of which chronic calculous cholecystitis was predominant comprising 38% %, followed by chronic acalculous cholecystitis in 36.45% cases. Chronic acalculous

Volume 7, Issue 3; May-June 2024; Page No 379-387

cholecystitis with cholesterolosis was seen in 8.45 cases whereas 5.61 % of such cases also showed stones. The other spectrum of histopathological diagnosis that were observed include acute on chronic cholecystitis (6.9%), follicular cholecystitis (2.5%), xanthogranulomatous cholecystitis (1.24%), and Eosinophilic cholecystitis (0.9) [Table 3]. Histopathological findings are depicted in Figure 1-2.

Table 3: Distribution of cases by histopathological diagnosis

Histopathological Diagnosis	**No. of cases**	**Percentage(%)**
Chronic acalculous cholecystitis	117	36.45
Chronic calculous cholecystitis	122	38
Chronic calculous cholecystitis with cholesterolosis	18	5.61
Chronic acalculous cholecystis with cholesterolosis	27	8.4
Follicular cholecystitis	8	2.5
Acute on chronic cholecystitis	22	6.9
Xanthogranulomatous cholecystitis	4	1.24
Eosinophilic cholecystitis	3	0.9
Total	**321**	**100**

The additional pathological findings that were observed in both chronic calculous cholecystitis and chronic acalculous cholecystitis include papillary hyperplasia, intestinal and pyoric metaplasia, and hyalinization. 8 out of 321 cholecystectomy specimens showed mild to severe dysplasia (2.4%).[Table 4, 5] **.** Out of 27 cases of chronic cholecystitis with cholesterolosis, 2 cases were associated with papillary hyperplasia and 1 case with pyloric metaplasia. One case of chronic cholecystitis with cholelithiasis and cholesterolosis also show pyloric metaplasia as additional findings.

Table 4: Additional pathology in chronic cholecystitis

Additional Findings	**No. of cases**
Dysplasia	7
Hyalinisation	1
Papillary Hyperplasia	6
Pyloric Metaplastic	4
Intestinal Metaplasia	5
Both papillary hyperplasia & pyloric metaplasia	1

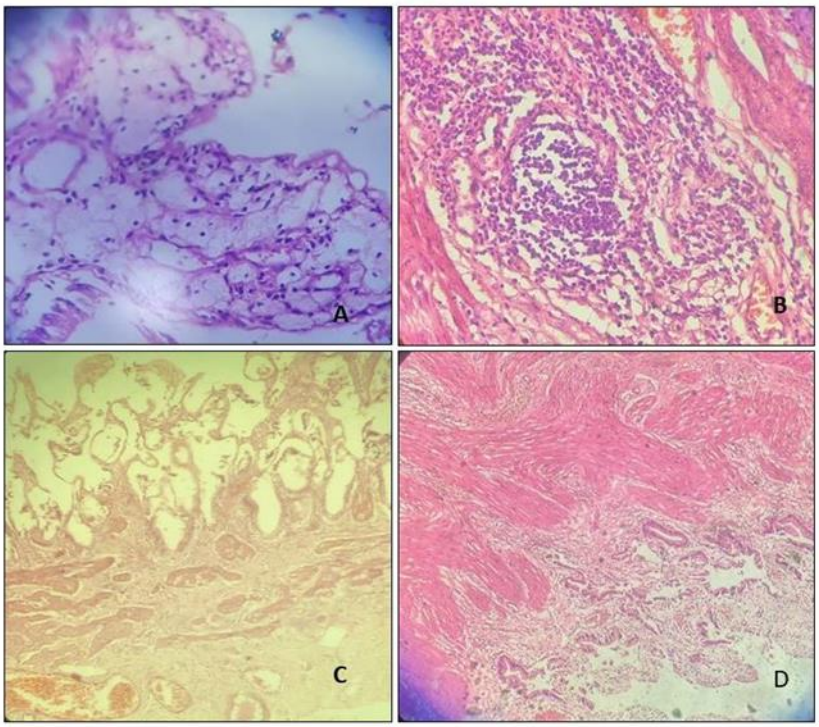
Volume 7, Issue 3; May-June 2024; Page No 379-387

Total	**24**

Table 5: Additional pathology in chronic cholecystitis with cholelithiasis

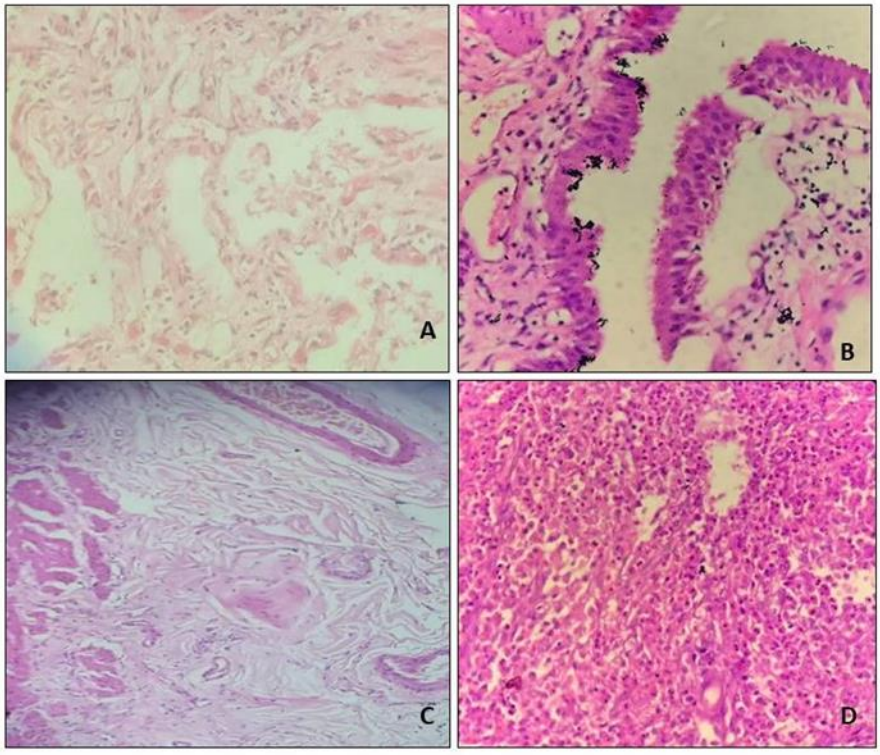
Additional Findings	**No. of cases**
Dysplasia	1
Hyalinisation	2
Papillary hyperplasia	5
Pyloric Metaplasia	4
Intestinal Metaplasia	3
Total	**15**

Figure 1A-D: A- Cholesterolosis [H&E, 40X], B- Follicular Cholecystitis [H&E, 40X], C- Papillary Hyperplasia [H&E, 20X], D- Muscle Hyperplasia [H&E, 20X]



Volume 7, Issue 3; May-June 2024; Page No 379-387

Figure 2 A-D: A- Eosinophilc Cholecystitis [H&E, 40X], B- Dysplastic epithelium [H&E, 40X], C- Hyalinising stroma [H&E, 20X], D- Xanthogranulomatous cholecystitis [H&E, 40X]



Discussion:

Gall bladder disorders encompass a spectrum of etiologies. However, inflammatory diseases of gall bladder are the most common findings throughout the worlds. Gall bladder diseases require surgical removal procedure, cholecystectomy. The excised gall bladder is evaluated routinely by histopathological examination and pathological features are identified. In this study we determined the histopathological spectrum of cholecystectomy specimen and demographic characteristics of the patients.

In the present study females were more affected with male to female ratio of 1:6.2 which is in concordance with study done by Tyagi et al (1:6.5) & Siddiqui et al. (1:7)[10,11]. The majority of the patients in this study were between the age group of 31- 40 years which is consistent with the study conducted by Narendra et al.[12].

Out of 321 cases, 288 cases (89.7%) were complaining of pain in upper abdomen followed by intolerance to fatty food(6.5%) and nausea or vomiting(3.5%). In the study of S Siddiqui et al. 91.4% cases presented with pain in upper abdomen.

Histopathologically, the most common diagnosis was Chronic calculus cholecystitis (38%) followed by chronic acalculus cholecystitis (36.45%) . Similar study was also done by Kulkarni AM et al in which cases of Chronic calculus cholecystitis was 57.76% and chronic acalculus cholecystitis cases was 22.35%.[13] Cholesterolosis is associated with both calculous cholecystitis (5.61%) as well as acalculous cholecystitis (8.4%) . Histopathological examination of cholesterolosis showed the thickened wall, aggregated cholesterol with yellowish streaks and foamy macrophages in lamina propria of gall bladder. Similar to our study pathak et al and Bhatt et al also observed cholesterolosis as findings of cholecystectomy specimens comprising 7.87% % and 9.75% of total cases respectively [14,15].

The remaining spectrum of histopathological diagnosis that were observed include acute on chronic cholecystitis(6.9%), Follicular cholecystitis(2.5%), xanthogranulomatous cholecystits(1.24%) and eosinophilic cholecystitis(0.9%) . Benkhadoura et al and Bhatta S et al also reported similar percentages of cases of acute on chronic cholecystitis(96.9%) and follicular cholecystitis(2.78%) respectively.[16,17].

Volume 7, Issue 3; May-June 2024; Page No 379-387

Follicular cholecystitis (FC) is a rare entity found characterized by prominent lymphoid follicles in the lamina propria distributed throughout the gallbladder wall.It is found in 0.1–1 % of patients with chronic cholecystitis.[18,19]

Xanthogranulomatous cholecystitis (XGC) is a rare condition, initially identified by Christensen and Ishak in 1970 and later referred to as XGC by McCoy *et al*. in 1976. It is characterized by a destructive inflammatory reaction that can be focal or diffuse [20]. The chronic inflammation caused by XGC is marked by the production of xanthogranulomas, extensive proliferative fibrosis, and the infiltration of macrophages and foam cells into the gallbladder wall [21]. In present study xanthogranulomatous cholecystitis was observed in 1.24% cases which were similar to study of Bhatta et al. and sharma I et al.[22]

Eosinophilic cholecystitis (EC) is a rare form of cholecystitis that was first described in 1949[23]. The prevalence of EC ranges from 0.25% to 6.4% as reported in various studies across the world[23,24,25]. EC is characterized by a dense transmural infiltration of eosinophils making up 90% or more of the leukocytic infiltration[26].In our study 3 cases of eosinphilic cholecystitis (0.9%) were reported which is in concordance with the study of Memis B et al (1.1%).[27]

The additional pathological findings that were observed in the both calculous and acalculous chronic cholecystitis include papillary hyperplasia(3.42%), pyloric (2.49%)and intestinal (2.49%)metaplasia, hyalinization (0.93%)and dysplasia(2.49%) which is in concordance with study done by Kanimozhi.S et al.[28] . 8 out of 321 cases were showing dysplasia from which 7 cases were observed in chronic acalculous cholecystitis and 1 case was assoiated with chronic calculous cholecystitis. Dysplasia was also observed in the study of kanimozhi et al and sharma I et al.

In this present study cases of gall bladder malignancy was not reported . However, out of 321 cases 8 cases were showing mild to severe dysplasia (2.49%) and intestinal metaplasia was observed in 8 cases. Intestinal metaplasia and dysplasia both are premalignant conditions that can eventually lead to the development of carcinoma. Imperatively, most of the patients who presented with these premalignant conditions belonged to the older age groups. This indicates that an increased age at presentation increases the risk of a malignant transformation [29,30]. If not detected early, these lesions can orchestrate the pathogenesis that underlies the development of GBC. It is therefore necessary to evaluate the histopathology of each GB specimen, irrespective of its macroscopic appearance intraoperatively. Doing so can aid the early detection of carcinoma in high-risk patients, thus preventing the risk of progression to advanced disease.

Conclusion:

GB disease remains a major indication for cholecystectomy. The risk factors for developing chronic cholecystitis was seen in female gender of age group 31-40 years. Our study strongly recommends routine histopathological examination of all cholecystectomy specimens for the detection of various variants of chronic cholecystitis . Of these, chronic calculous cholecystitis, chronic acalculous cholecystitis and cholesterolosis, remain the most prevalent. Furthermore, a macroscopic absence of remarkable features does not preclude the presence of an underlying premalignant or malignant lesions. Thus,we strongly advocate routine histopathological examination of all the resected GB specimens in order to exclude premalignant ailments such as intestinal metaplasia and dysplasia. Left undetected, these lesions can progress to GB adenocarcinoma , which is noted to have a particularly undesirable prognosis Hence, we recommend comprehensive histopathological examination of all gall bladder samples for timely diagnosis and quick intervention.

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Volume 7, Issue 3; May-June 2024; Page No 379-387

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Volume 7, Issue 3; May-June 2024; Page No 379-387

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Volume 7, Issue 3; May-June 2024; Page No 379-387