



Histopathologic Spectrum of Gallbladder in Cholecystectomy Specimens

Shazia Aslam, Sadia Hameed, Arif Hussain, Muhammad Mudassar, Haseeb Ahmad Khan

ABSTRACT

Background: Cholecystitis is a common problem in adult population. Gross and microscopic examination of gall bladder has multiple findings. Presence of stones is one of the known etiologic factors to produce histopathological changes in gallbladder. It is also one of the predisposing factors for the development of gallbladder carcinoma. This study aims to find the histopathologic spectrum of gall bladder specimens received in pathology department after undergoing surgical intervention. **Objective:** To analyze the morphological spectrum of cholecystitis due to stones. To find out the possible risk factors for gall stone formation. To find out the frequency / prevalence of different types of gall stones. **Study Design:** Retrospective Study. **Settings:** Department of pathology, UMDC Faisalabad and at Meezan Lab Faisalabad-Pakistan. **Duration:** From January 15, 2015 to May 14, 2017. **Methodology:** This study was conducted on cholecystectomy specimens. All clinical data was taken from patient's histopathology request form and from patient's clinical record gross and microscopic features of gall bladder specimens were studied in correlation with presence or absence of gall stones. **Results:** The total number of cholecystectomy specimens studied were 664. There were 633 cases of chronic calculous cholecystitis, the highest incidence of these being in the age group of 31-40 years. In this, males were 132 and females were 532. All patients underwent ultrasonography to confirm the diagnosis. There were 31 cases of a calculus cholecystitis. On morphological analysis, the commonest gall stones were cholesterol stones and the commonest lesion was chronic cholecystitis by histopathology. **Conclusion:** This study concludes the predominance of chronic calculous cholecystitis in our study population. Among these cholesterol stones are more prevalent.

Keywords: Cholecystectomy, Calculous cholecystitis, Morphologic analysis.

Corresponding Author

Submitted for Publication: 20-01-2020

Accepted for Publication: 02-03-2020

DR. SHAZIA ASLAM, Associate Professor of Pathology, University Medical & Dental College, Faisalabad Pakistan

Contact / Email: +92 344-7903390, rayanjanba@gmail.com

Citation: Aslam S, Hameed S, Hussain A, Mudassar M, Khan HA. Histopathologic Spectrum of Gallbladder in Cholecystectomy Specimens. APMC 2020;14(1):92-6.

INTRODUCTION

The Gall Bladder is a small pear-shaped sac that stores and concentrates bile. It is connected to the liver (which produces the bile) by hepatic duct. When food containing fat reaches the small intestine, the hormone cholecystokinin is produced by discrete endocrine cells in intestinal wall and is carried to the gall bladder via the bloodstream. The hormone causes the gall bladder to contract, forcing bile into common bile duct. A valve, which opens only when food is present in the intestine, allows bile to flow from the common bile duct into the duodenum (upper intestine) where it functions in the process of fat digestion.¹

Sometimes the substances contained in bile crystallize in the gall bladder, forming gallstones. These small, hard concretions are more common in persons over 40, especially in women and obese individuals. They can cause irritation of the gall bladder mucosa that can lead to obstruction of biliary tree & inflammation of gall bladder mucosa. These events can result in severe episodes of pain.¹

Gall stone disease is a very common problem in the western world as well as in our country. 10% of the adult patients have asymptomatic gall stones. The prevalence varies with age, sex and ethnic group. Gall stones vary in their composition, majority being cholesterol and remaining being mixed and pigmented. Cholesterol stones are by far the most common type. Stones having rich component of bilirubin are termed as pigment stones. Gall stones also appear to be a common risk factor in development of carcinoma of gall bladder.²

Composition of bile has major role in formation of stones. The critical pathophysiological prerequisite for 'black' stone formation is biliary hypersecretion of bilirubin conjugates. It is due principally to hemolysis, ineffective erythropoiesis, or pathologic enterohepatic cycling of unconjugated bilirubin. The motility of gallbladder plays an important role in formation of gall stones. Second factor is the presence of proteins in the liver and bile that either promote or inhibit cholesterol crystallization into gallstones.³ Increased levels of the hormone estrogen as a result of pregnancy, hormone therapy, or the use of birth control pills, may increase cholesterol levels in bile and also decrease gallbladder movement, resulting in gallstone formation. Other factors are parity, smoking, alcohol, diabetes and obesity.⁴

Gall stone disease produces diverse histopathologic changes in gall bladder mucosa, namely acute inflammation, chronic inflammation, granulomatous inflammation, cholestolosis, dysplasia and carcinoma. The gall bladder mucus plays a regulatory role in cholelithiasis as it promotes the nucleation of stones. Mucus, calcium and lipids act in concert to form the gallstones.⁵

The aim of this study was to evaluate the morphologic features of gall bladder specimens of patients received in pathology department of UMDC, & Meezan lab Faisalabad after undergoing cholecystectomy.

Cholecystitis is one of the commonest problems that brings the patients to surgical outpatient department and in emergency. Inflammation of gall bladder can be acute, chronic or acute

event superimposed on chronic cholecystitis. The leading cause of cholecystitis in majority of cases is the presence of gall stones.⁶

Routine examination of gall bladder specimens on gross and microscopic examination reveals many interesting findings. Gall bladder containing stones must be surgically excised because they bear potential risk of development of malignant neoplasm. Pathological changes vary from inflammation to malignancy.

This study aims to quantify the various outcomes of routine gall bladder examination after undergoing cholecystectomy. Various patterns of histopathologic changes can be analyzed and possible risk factors can be focused to reduce the prevalence of disease.

METHODOLOGY

Study Design: Retrospective Study.

Settings: Department of pathology, University Medical & Dental College and at Meezan Lab. Faisalabad Pakistan.

Duration: From January 15, 2015 to May 14, 2017.

Sample Size: Total 664 cholecystectomies were studied.

Inclusion Criteria: Formalin fixed specimens of gall bladder with complete clinical data in attached histopathology request form.

Exclusion Criteria: Autolyzed specimen and cases with incomplete clinical information were excluded from the study.

Methods: Clinical and pathological data were reviewed. All cholecystectomy specimens received, were fixed in 10% formalin.

After overnight fixation in formalin the specimens were subjected to detailed gross examination. Sections were obtained from the fundus, body and neck of the gallbladder, and microscopic examination was done after routine tissue processing & hematoxylin and eosin staining.

RESULTS

A total of 664 cholecystectomy specimens were received during period of three years. The age range was from 8-90 years with mean age of 37. The gall bladder lesions were predominantly seen in females as compared to males. (Table 1)

Table 1: Sex distribution of patients

Females	532
Males	132
Total	664

In this study the number of cases was increasing with increase in patient's age so increasing age was found to be proportionately related to risk of development of cholecystitis. Majority of patients were of 4th and 5th decade of life. The age range was from 8-90 years. The age distribution of patients is given below in table 2.

Table 2: Age distribution of patients

Age group(years)	Number of patients
1-10	04
11-20	13
21-30	104
31-40	205
41-50	196
51-60	92
61-70	44
71-80	07
81-90	01

Majority of cases of cholecystectomy were found to be associated with gallstones. Only few cases were found to be without stones (Table 3).

Table 3: Various types of cholecystitis

Calculous cholecystitis	633
Acalculous cholecystitis	31

Among the calculous cholecystitis, stones present were cholesterol stones and pigment stones. Cholesterol stones were found in majority cases of cholecystitis (Table 4).

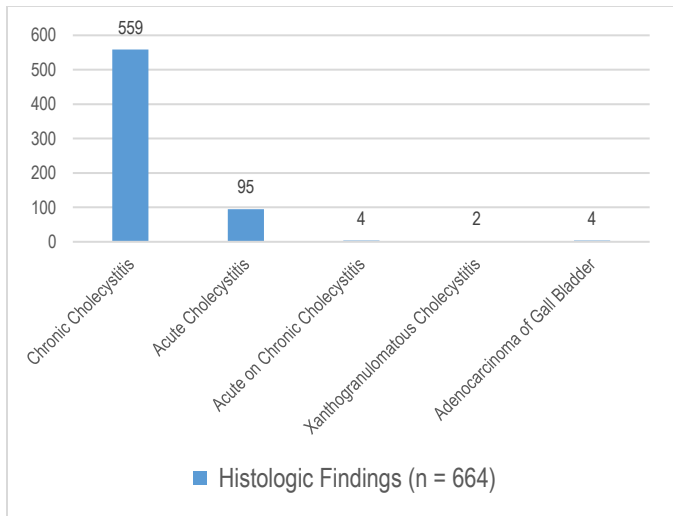
Table 4: Classification of gall stones on the basis of their morphology

Number of stones	Morphology	Number of cases as per gross morphology
Cholesterol	Solitary, oval, large & yellow	584
Pigment	Brownish, black stones	49
Total		633

Histologic features of various types of cholecystitis are given in (Table no 5).

Table 5: Distribution of cases according to histologic examination

Histologic findings	Number of cases
Chronic cholecystitis	559
Acute cholecystitis	95
Acute on chronic cholecystitis	04
Xanthogranulomatous cholecystitis	02
Adenocarcinoma of gall bladder	04
Total number	664



The serosal surface of the gall bladder was found normal in majority of surgical specimens on gross examination. Presence of congested blood vessels in serosa was a significant finding that was present in almost 90% cases. Gall bladder wall thickness was found normal in majority cases of chronic cholecystitis while it was markedly thickened in surgical specimens of patients who had experienced acute episode. Majority of surgical specimens had multiple stones. The gall stone size varied from 0.3 cm to 5 cm in diameter.



Figure 1: photograph of gall bladder



Figure 2: photograph of gall bladder shows a mass in wall of gall bladder

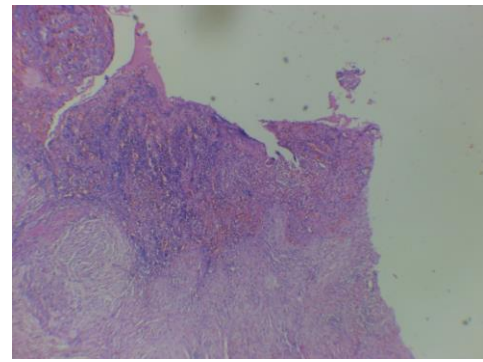


Figure 3: Photograph of gall bladder showing ulceration of surface and mixed acute and chronic inflammation

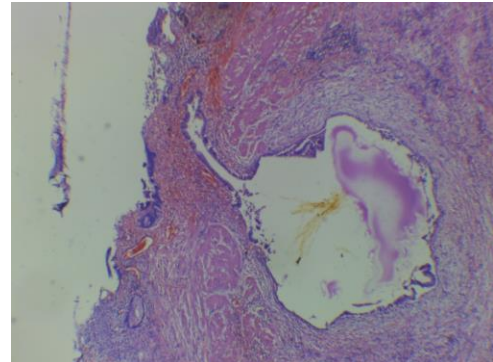


Figure 4: formation of Rokitansky Ashoff sinuses in a case of cholecystitis

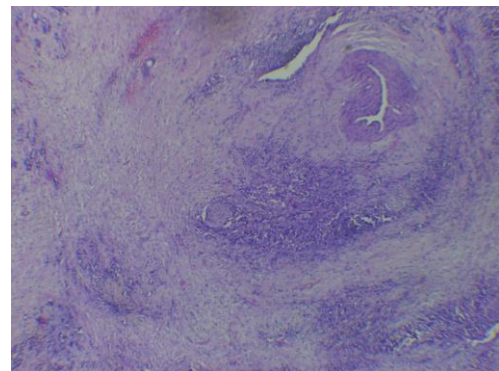


Figure 5: presence of perineural invasion in gall bladder carcinoma

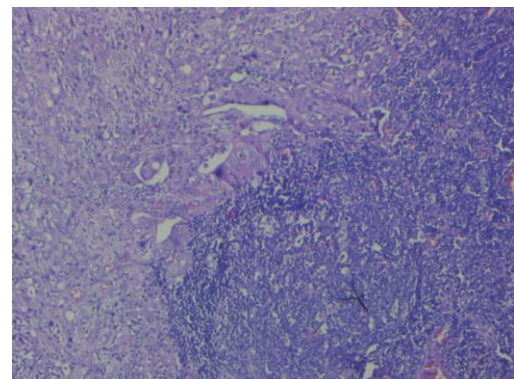


Figure 6: Presence of metastatic carcinoma in lymph node isolated from neck of gall bladder

DISCUSSION

An important finding in all collaborative population studies was a strong relationship between history suggestive of previous gallstones or gall bladder diseases and subsequent risk for cholecystitis & gall bladder cancer.⁷ Pure stones of cholesterol or calcium bilirubinate may be present without evidence of any significant inflammation. Thickening of gall bladder wall is striking feature in cholecystitis.⁸

In our study, Gall stone disease was predominantly seen in females (80.12%) as compared to males (19.87%). Female sex hormones appear to play a role, especially between the ages of 30 and 50 years. Zafar SN *et al.* studied the morphologic features of gall bladder in 415 cholecystectomy specimens. Females were more affected with male to female ratio of 1:6.5. Most of the cases were seen in 4th & 5th decade. Associated cholelithiasis were seen in 85.3% of cases.⁹ These results coincide with results of our study.

Two cases of xanthogranulomatous cholecystitis included in our study were of age 35 and 40 years respectively. These results were different from a study done by Singh N *et al* in which he reported the cases of xanthogranulomatous cholecystitis in 6th and 7th decade of life.¹⁰ Di Ciaula *et al* found that the commonest age group for cholelithiasis was below 30 years.¹¹

Certain risk factors for development of gall stones are well established. Female gender and increasing age are important risk factor. Modifiable risk factors are obesity, sedentary life style contributing to hypomotility of gall bladder. Obese patients have increased incidence of cholecystitis.

The reproductive age group (21-30, 31-40 & 41-50) is the most commonly affected age group in this study. This finding supports that reproductive hormones play important role in cholecystitis. Women with more pregnancies and longer lengths of fertility periods appear to have a higher likelihood of developing gallstones than those who remain nulliparous.^{12,13} Another study that correlates the estrogen receptors and cholesterol biosynthesis found that estrogen in particular stimulates the HMG-Co-A reductase enzyme causing increased synthesis of cholesterol and thus putting women at an increased risk of supersaturation. Further supporting the link between estrogen and gallstones, it was determined that postmenopausal women on estrogen replacement therapy were found to have an increased incidence of gallstones. Progesterone may also contribute to gall stone disease by inhibiting gallbladder contraction and promoting hypomotility and bile stasis.¹⁴

CONCLUSION

The most commonly involved age group for cholelithiasis is found to be 30-50 years. Female are more commonly affected than males. Cholelithiasis was found the most common inciting factor for cholecystitis. Chronic cholecystitis was the common histopathologic diagnosis. Cholesterol stone was the most common type of stone comprising 87.95 %, followed by pigment stones. Early cholecystectomy is treatment of choice in symptomatic patients as cholelithiasis is important inciting factor in pathogenesis of carcinoma of gall bladder. Histopathology of gall bladder specimen is very significant as this provides a lot of

information regarding spectrum of many diseases. It also provides many important incidental findings. If risk factors are analyzed prevention can be done for malignant cases.

LIMITATIONS

Biochemical analysis of gallstones could not be done for logistics reason in the current study.

SUGGESTIONS / RECOMMENDATIONS

Cholecystectomy must be done on earlier basis in cases of cholecystitis incited by cholelithiasis due to risk of development of adenocarcinoma of gall bladder.

CONFLICT OF INTEREST / DISCLOSURE

Authors declare that they have no competing interests.

ACKNOWLEDGEMENTS

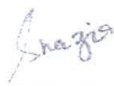



Authors would like to acknowledge Laboratory staff of Meezan Lab & UMDC Pathology department for their support.

REFERENCES

1. Srinivasan G, Inba S. Study of histopathologic spectrum of gall bladder in cholecystectomy specimens. *Int J Res Med Sciences*. 2019;7(2):593-9.
2. Jessari M, Rashid B. Dietary patterns and risk of gall bladder diseases: A hospital-based case control study in adult women. *J Health Popul Nutr*. 2015;33(1):39-49.
3. Kumar H, Kini H, Tiwari A. Histologic evaluation of 400 cholecystectomy specimens. *J Pathol Nepal*. 2015; 5(10):834-40.
4. Huang J, Chang C, Wang J, Lin J, Shau W, Lee Ph. Nationwide epidemiologic study of severe gallstone disease in Taiwan. *BMC Gastroenterol*. 2009;9:63.
5. Portincasa P, Molina M, Garruti G, Wang D. Critical care aspects of gallstone disease. *J Crit Care Med*. 2019;5(1):6-18.
6. Ahmed W, Iqbal M, Ahmed I. Is there any Change in Demographic Pattern of Patients with Cholelithiasis? *IMJ*. 2017;9(2):75-9.
7. Dinsel O, Goksu M, Hamit Sinan H. Importance of routine histopathological examination of a gallbladder surgical specimen: Unexpected gallbladder cancer. *JLMC*. 2018;14(6):1325-9.
8. Singh A, Singh G, Kaur K, Goyal G, Siani G and Sharma D. Histopathologic changes in gall bladder mucosa associated with cholelithiasis: A prospective study. *Niger J Surg*. 2019;25(1):21-5.
9. Zafar SN, Obirizee A, Adesibaakan B, Cornwell EE, Fullul TM, Tran DD. Optimal time for early laparoscopic cholecystectomy for acute cholecystitis. *JAMA Surg*. 2015;150(2):129-36.
10. Singh N, Arora R. Incidence of various types of gallstones in patients of cholelithiasis in patients of cholelithiasis in North India. *Jemds*, 2015;4(97):213-4.
11. Di Ciaula, Wang DQ, Molina M. Bile acids and cancers: direct and environmental dependent effect. *Ann Hepatol*. 2017;16(3):87-105.
12. Park Y, Kim D, Lee JS, Kim YN, Choi D et al. Association between diet and gallstones of cholesterol and pigment among patients with cholecystectomy: a case-control study in Korea. *JHPN*. 2017;36:39.

13. Baidya R, Sigdel B, Baidya NL. Histopathologic changes in gall bladder mucosa associated with cholelithiasis. J Pathol Nepal. 2012;2:224-5.
14. Mittal R, Jesudason R, Nayak S. Selective histopathology in cholecystectomy for gallstone disease. Indian J Gastroenterol. 2010;29(1):26-30.

AUTHORSHIP AND CONTRIBUTION DECLARATION

AUTHORS	Contribution to The Paper	Signatures
Dr. Shazia Aslam Associate Professor, Pathology University Medical & Dental College, Faisalabad Pakistan	Manuscript Writing, Data Analysis, Results Completion, Discussion, References, Writing	
Prof. Dr. Sadia Hameed Professor & Head of Pathology Department University Medical & Dental College, Faisalabad Pakistan	Data Collection, Technical Review, Histopathological Review	
Prof. Dr. Arif Hussain Professor of Pathology University Medical & Dental College, Faisalabad Pakistan	Literature Review	
Dr. Muhammad Mudassar Associate Professor & Head of Pathology Department Batterjee Medical & Dental College, Jeddah Saudi Arabia	Proof Reading	
Dr. Haseeb Ahmad Khan Assistant Professor, Pathology FMH College of Medicine & Dentistry, Lahore Pakistan	Histopathological Slides Review, Proof Reading	