International Journal of Clinical and Diagnostic Pathology

ISSN (P): 2617-7226
ISSN (E): 2617-7234
www.patholjournal.com
2021; 4(4): 70-74
Received: 01-08-2021
Accepted: 03-09-2021

Dr. Menka Shah
Professor in Pathology, Pramukh swami Medical College, Bhai Kaka University, Karamsad, Gujarat, India

Dr. Krishna Panchal
Resident in Pathology, Pramukh swami Medical College, Bhai Kaka University, Karamsad, Gujarat, India

Corresponding Author:
Dr. Menka Shah
Professor in Pathology, Pramukh swami Medical College, Bhai Kaka University, Karamsad, Gujarat, India

Histopathological spectrum of diseases in gall bladder

Dr. Menka Shah, Dr. Krishna Panchal

DOI: https://doi.org/10.33545/pathol.2021.v4.i4b.423

Abstract
Context: The histopathological spectrum of diseases in gall bladder ranges from inflammation to benign to malignant lesions. The present study was undertaken to emphasize on the need of histomorphological analysis of all gall bladder specimens, for the diverse findings that may be identified.
Methods: A cross-sectional observational study was undertaken at a tertiary care teaching hospital in Central Gujarat, India where clinical, radiological and pathological findings of 360 cholecystectomies specimen were studied between April 2016 to May 2021 (5 years).
Results: A female preponderance (M:F ratio =2:3) with a predilection for the fifth and sixth decade of life was noted in the total 360 specimens studied. Histomorphological spectrum included cholelithiasis [222 cases (61.1%)] followed by cholecystitis [107 cases (29.7%)] and neoplasms [24 cases (6.6%)].
Conclusion: The present study supports the dictum that histopathological analysis of all cholecystectomy specimens should be done, as it may reveal a wide spectrum of abnormalities, undiagnosed by clinical and imaging studies.

Keywords: gall bladder pathology, cholecystitis, cholesterosis, adenomyoma, cholangiocarcinoma

1. Introduction
The gallbladder, a foregut derivative organ, is a pear-shaped sac that lies in a shallow fossa on the visceral surface of the right hepatic lobe, which functions as a reservoir of the bile [1]. Diseases of gall bladder is one of the common gastrointestinal manifestations encountered worldwide [2]. Gallbladder pathology is a frequent source of patient's complaints, presenting as pain in epigastrium and right upper quadrant of abdomen radiating to interscapular area, right scapula and shoulder which is usually associated with nausea, vomiting, jaundice, anorexia, fever and chills. Sometimes gall bladder diseases produce symptoms and signs to such an extent that removal of gall bladder remains the only treatment [3].
Gallbladder is involved in wide spectrum of diseases ranging from non-neoplastic diseases like congenital anomalies, calculi and its complications, non-inflammatory, inflammatory to the neoplastic lesions [4]. Cholecystitis and cholelithiasis appear to be increasing in incidence over past couple of decades in India and in western world due to increased intake of high fatty and high calorie diet and due to alcohol intake [5]. Benign tumours and tumour like conditions affecting the gall bladder include cholesterol polyps, adenomatous hyperplasia, adenomyomatous hyperplasia, papillomas, adenomas, paraganglioma etc. Malignancies of gall bladder include most commonly adenocarcinoma and rarely adenosquamous carcinomas, squamous cell carcinoma, small cell carcinoma, lymphomas, and sarcomas [6].
Best Practise Recommendations (BPRs), published by The Royal College of Pathologists in October 2019, titled "Histopathology and cytopathology of limited or no clinical value" emphasizes that all gallbladder specimens should be examined, as significant pathology may be present with normal gross morphology [7]. The present study was undertaken to emphasize the same by quantifying the histomorphological outcomes of the routine gall bladder examination following cholecystectomy procedure.

2. Materials and Methods
2.1 Study Design: The present study is a cross-sectional observational study undertaken at a tertiary care teaching hospital in Central Gujarat, India where clinical and laboratory data of all cholecystectomies done between April 2016 to May 2021 (5 years) were analysed. Clinical details and histopathological data were retrieved from the integrated Hospital Management Information System and Laboratory Information System of the institute.

2.2 Inclusion Criteria: All cases that had removal of gall bladder by cholecystectomy for a suspected primary pathology of the gall bladder.

2.3 Exclusion Criteria: All the cases where the gall bladder was removed as part of other surgeries were not included in the study.

2.4 Methodology: Samples received in the Surgical Pathology section of the Central Diagnostic Laboratory of the institute were fixed in 10% formalin. Gross examination findings to include presence of stones, growths, polyps, wall of gall bladder with mucosal changes and other gross abnormalities were noted. A minimum of three sections were given (neck, body and fundus). Additional sections were given whenever indicated. Tissue sections were processed in automated tissue processor and paraffin blocks were prepared. The sections were cut into 3–5-micron thickness and stained in Haematoxylin and Eosin stain and studied them under light microscopy.

2.5 Data Analysis: The relevant clinical data, imaging and ancillary tests findings, relevant gross examination findings and the detailed histopathology reports were noted in pre-designated proforma. The data were then analysed for descriptive analysis and frequency distribution in Microsoft Excel 2016.

3. Results

The present study consists of analysis of lesions of gall bladder received in histopathology section of department of pathology from May 2016 to May 2021 i.e., of 5 years. The total number of surgical pathology specimens received during this period were 22,266 out of which, there were 360 gall bladder excision specimens. Of the 360 specimens, majority [297 cases (82.50%)] were removed laparoscopically, while 63 specimens (17.50%) were excised by an open cholecystectomy. The age of the patients ranged from 4-89 years (Figure 1). The mean age of presentation was 45.6 years. There was female predilection with 216 females (60%) and 144 males (40%); the male: female ratio being 2:3.

Clinical Presentation: All the patients presented with pain in right hypochondriac region (100%), accompanied by vomiting in 159 cases (44.1%), by fever in 76 cases (21.1%), by nausea 174 cases (48.3%), by fullness in 32 cases (8.89%), by diarrhoea in 16 cases (4.4%) and abdominal lump in 24 cases (6.6%). 3 patients presented with pain and lump in abdomen (1.47%). Per abdominal examination showed that 49 cases (3.6%) had presented with abdominal rigidity, while 24 cases (6.6%) had a lump in the right hypochondriac region; the rest of the patients had no significant findings.

Gross Examination: The wall of the gall bladder was thinned out in majority of specimens i.e., there were 276 specimens (76%) in which the wall thickness ranged from 4-6 mm. The wall showed thickening in 86 specimens (24%). Of the various gross examination findings noted, mucosal aberrations included in various combinations, congestion [341 (94%)], loss of mucosal folds [328 (91%)], occasional polyps [13(3.61%)], perforations [21(5.83%)] and growths [14(3.88%)], detailed in table 1.

Table 1: Gross examination findings in cholecystectomy specimens. (n = 360)

Gross findings	No. of cases (%)
Congested	341 (94%)
Loss of mucosal folds	328 (91%)
Velvety	265 (73%)
Perforation	21 (5.83%)
Polyp	13 (3.61%)
Growth	14 (3.88%)
Haemorrhage	1 (0.2%)

Microscopic Examination: Epithelial aberrations were noted in 340 cases, with only 20 specimens (5.5%) showing normal mucosa. Of the various alterations noted, focal ulceration [239 (66.3%)], atrophic changes [69 (19.1%)], complete sloughing [16(4.4%)], hyperplastic changes [07(1.9%)] and antral metaplasia [03(0.8%)]; as detailed in table 2.

Table 2: Microscopic mucosal alterations in the gall bladder specimens (n = 360)

Mucosal alterations	No. of cases (%)
Ulcerated	239 (66.30%)
Atrophic	69 (19.10%)
Sloughed	16 (4.40%)
Hyperplastic	7 (1.90%)
Necrosis	5(1.30%)
Antral metaplasia	3 (0.80%)
Erosion	1 (0.20%)
Normal	20 (5.50%)

Final Histopathological Diagnosis: In the present study, a wide spectrum of lesions of gall bladder was observed on histopathology, which is shown in Figure 2.

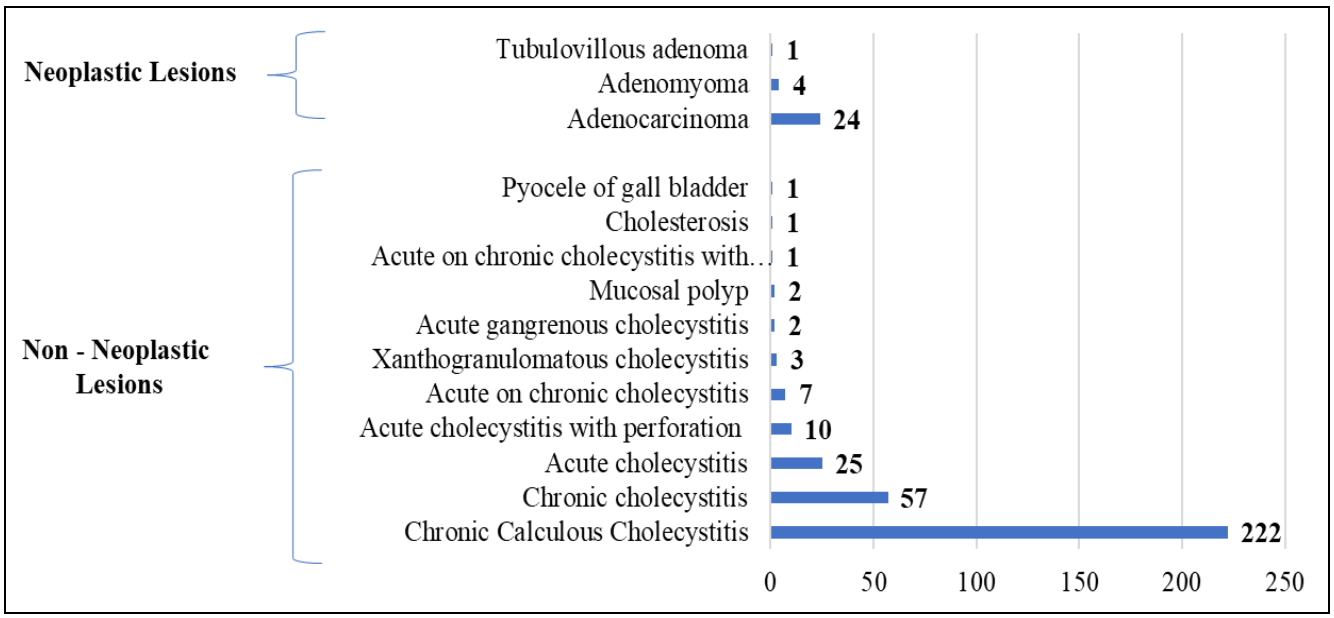

Fig 2: Histopathological Diagnoses (n=360)

24 cases (6.6%) of malignancies were diagnosed on histopathological diagnosis; all of them being adenocarcinoma of gall bladder.

6. Discussion

Gall bladder diseases affect a significant portion of population and present with a diverse clinical and histopathological spectrum.[8] The number of cholecystectomies has increased more than 50% in the last decade [9].

The frequency of gall bladder specimens among total surgical pathology specimens have shown considerable variation in the literature. In the study done by Rashmi H K *et al*[10], the gall bladder specimens constituted 0.89% of total surgical pathology specimens. In the present study also, the gall bladder specimens constituted for a minor component (1.59%) of total surgical pathology specimens However, Khan S *et al*. [11] and Medhi K *et al*. [12] has found the frequency of gall bladder specimens among total surgical pathology specimens as 19.4% and 34.13% respectively.

Age of patients in the present study ranged from 4 years to 89 years with a mean of 45.6 years. Highest number of cases were seen in 6th decade (78 cases, 17.5%) and 7th (80 cases, 22.2%). The results were similar to the results obtained by Navyashree N *et al* [13], Awasthi N [14], Beena D *et al* [15], Sharma I *et al* [6], Murmu S *et al*. [16], Mittal R *et al* [7] and Kumar H *et al* [17] where maximum number of cases were found in 5th to 7th decade of life.

In the literature, gall bladder diseases are seen predominantly affecting females as compared to males. Most of the cases (60%) included in the present study were female patients with male: female ratio being 1: 1.5. This value could be considered near to the results obtained from the study conducted by Thanigaimani G *et al* [18] (1:1.8), Navyashree *et al* [13] (1:1.8), Murmu S *et al* [16] (1: 2.3), Beena D *et al* [15] (1:1.2) and Mittal R *et al*[7] (1: 1.3). In our study, gall bladder lesions are seen predominantly affecting 216 females (60%) as compared to 144 males (40%) with male: female ratio of 1: 1.5. Our findings are comparable to studies done by these authors.

In the present study, all the patients presented with pain in right hypochondriac region which were accompanied by vomiting, fever or nausea in few cases. Selvi RT *et al* [19], Mahana S *et al* [20], also found pain in right hypochondriac region as the most common presenting symptom.

The normal histological structure of gall bladder consists of columnar epithelium with microvilli, lamina propria, muscular layer and serosa. The epithelium and lamina propria together are known as mucosa. The mucosal pattern needs to be studied very carefully so as to detect the high-risk cases for gall bladder malignancy since it is widely reported that long standing mucosal irritation by the stones cause atypical cellular changes and hyperplasia which may progress to metaplasia and carcinoma in situ.[21] The careful examination of mucosa may help in detection of gall bladder malignancy in its earliest phase. The findings in mucosal alterations are similar to few of the other studies, as outlined in Table 3.

Table 3: Comparison of mucosal alterations in gall bladder lesions

Mucosal alterations	Gaharwar A *et al*[21]	Khanna R *et al*[23]	Present study
Normal	0.00%	9.00%	5.50%
Hyperplastic	15.15%	69.00%	1.90%
Atrophic	12.21%	16.90%	19.10%
Atrophic mucosa with focal hyperplasia	63.64%	0.00%	0.00%
Ulcerated	0.00%	0.00%	66.30%
Antral metaplasia	25.98%	16.50%	0.80%

The term cholecystitis refers to a group of inflammatory disorders that vary in clinical, pathogenetic and pathological characteristics [22]. Cholecystitis can broadly be divided into acute or chronic, with various different patterns. There are similar such studies that have been undertaken to understand the spectrum of cholecystitis, as outlined in Table 4.

Table 4: Comparison of incidences of cholecystitis

Gall bladder lesions	Beena D *et al*[15] (2017)	Murmu S *et al*[16] (2017)	Damor NT *et al*[4] (2013)	Goyal *et al*[24] (2021)	Present study (2021)
Acute cholecystitis	21 (10.5%)	19 (17.92%)	17 (17.0%)	30 (9.58%)	25 (6.94%)
Acute cholecystitis with perforation	00 (0.00%)	00 (0.00%)	00 (0.00%)	00 (0.00%)	10 (2.77%)
Acute gangrenous cholecystitis	00 (0.00%)	03 (2.83%)	00 (0.00%)	01 (0.31%)	2 (0.50%)
Chronic cholecystitis	164 (82.0%)	79 (74.52%)	57 (57%)	181 (57.8%)	57 (15.8%)
Acute or Chronic Cholecystitis	06 (3.5%)	00 (0.00%)	01 (1.0%)	00 (0.00%)	08 (2.22%)
Xanthogranulomatous Cholecystitis	02 (1.0%)	01 (0.94%)	02 (2.0%)	08 (2.51%)	03 (0.80%)
Cholesterosis	05 (3.5%)	02 (1.88%)	01 (1.0%)	11 (3.50%)	01 (0.20%)

Adenomyoma is a non-neoplastic, probably development lesion. Goyal S *et al*. [24] found adenomyomatous changes in four cases (1.2%) while the present study found adenomyomatous changes in four cases (1.1%).

Adenomas of the biliary tract are uncommon. The present study found a single case of tubulovillous adenoma, presented with pain and tenderness on systemic examination.

Gallbladder carcinoma is the 20th most common carcinoma worldwide with 17th most commonly occurring cancer in men and the 18th most commonly occurring cancer in women. The overwhelming majority of patients are diagnosed at an advanced, surgically unresectable stage. In present study, out of 360 specimens, 24 cases (6.6%) of adenocarcinoma were seen, in which there were 11 cases (48.0%) of poorly differentiated carcinoma, 9 cases (39.0%) of moderately differentiated adenocarcinoma and 3 cases (13.0%) well differentiated adenocarcinoma in 3 cases (13%). Kumbhakar D *et al*. [26], Mohan H *et al* [25] and Damor NT *et al*. [4] found incidence of malignant lesions of gall bladder as 1.25%, 1.09% and 2% respectively.

7. Conclusion

The present study revealed a few pertinent socio-demographic, clinical and histomorphological patterns in gall bladder lesions. Cholecystectomies had to be done most commonly in the 7th decade (bulk of disease in 41-80 years) with a female preponderance. Laparoscopic approach (82.50%) is the preferred approach for gall bladder removal. Majority of the lesions are inflammatory in origin, out of which the most common lesion on histopathological diagnosis being chronic cholecystitis with cholelithiasis. Pigmented gall stones were found to be the most common etiology of chronic cholecystitis. Though malignant lesions (6.6%) of the gall bladder are a rare occurrence in the current setting, however; a few of these lesions had unremarkable pre-operative radiological findings and minimal gross abnormalities. Hence, the present study strongly supports the dictum a prompt detailed histopathological analysis of all cholecystectomy specimens should be done.

In addition to the direct conclusions from the study, it must be noted that at present, laparoscopic cholecystectomy forms the common surgical option to remove gall bladder, and its analysis would help to confirm the benign nature of the disease or to detect any precursors of malignancy. With greater availability of ultrasonography, all the patients with pain in abdomen should undergo the same; and patients with gall stones must be advised laparoscopic cholecystectomy. This may help in early diagnosis of gall bladder lesions. Additionally, care must be taken to ensure adequate and immediate fixation of specimen accompanied by meticulous macroscopic and microscopic evaluation by the pathologist; this will be decisive in the management and prognostication of the patient.

8. References

1. Frierson HF, Jr. The gross anatomy and histology of the gallbladder, extrahepatic bile ducts, Vaterian system, and minor papilla. Am J Surg Pathol 1989;13(2):146-162.
2. Stinton LM, Shaffer EA. Epidemiology of gallbladder disease: Cholelithiasis and cancer. Gut Liver 2012;6:17287.
3. Shah H, Khan MA, Shah W. Histopathological pattern of 400 cholecystectomy specimens. J Postgrad Med Inst 2016;30(3):250-3.
4. Damor NT, Chauhan DH, Jadav DH. Histological study of human gallbladder. International Journal of Biomedical and Advance Research 2013;4(9):597-601.
5. Sharma H, Sharma MK, Gupta G. Evaluation of histological changes in chronic cholecystitis and cholelithiasis of human gallbladder. Int J Anat Res 2014;2(4):752-756.
6. Sharma I, Choudhury D. Histopathological patterns of gall bladder diseases with special reference to incidental cases-a hospital-based study. Int J Res Med Sci 2015;3:3553-7.
7. Mittal R, Jesudason MR, Nayak S. Selective histopathology in cholecystectomy for gallstone disease. Indian J Gastroenterol 2010;29(1):32-36.
8. Awasthi N. A retrospective histopathological study of cholecystectomies. Int J Health Allied Sci 2015;4:203-6.
9. Mills SE. Sternberg's diagnostic surgical pathology. 6th ed. China: Wolters Kluwer 2015, 1770-1832.
10. Rashmi HK, Shivamurthy YL, Suresh KK, Chatura KR. Gross and macroscopic features of gallbladder in cholecystectomy specimen. MedPulse International Journal of Pathology. February 2018;5(2):52-55.
11. Khan S, Jetley S, Husain M. Spectrum of histopathological lesions in cholecystectomy specimens: A study of 360 cases at a teaching hospital in South Delhi. Arch Int Surg 2013;3:102-578.

12. Medhi KB, Goswami RR, Daimary M. Histopathological profile of cholecystectomy biopsies in a tertiary care teaching hospital – a retrospective study. Paripex-Indian Journal of Research 2016;5(5):129-132.
13. Navyashree N, Sujata S Giriyan, Incidence and clinical profile of gallbladder disease in south Indian population: Four years study in a tertiary hospital, MedPulse International Journal of Pathology, Print ISSN: 2550-7605, Online ISSN: 2636-4697, 2020;13(2):50-54.
14. Awasthi N. A retrospective histopathological study of cholecystectomies. Int J Health Allied Sci 2015;4:203-6.
15. Beena D, Shetty J, Jose V. Histopathological spectrum of diseases in gallbladder. National Journal of Laboratory Medicine 2017;6(4): PO06-PO096.
16. Murmu S, Topno VJ, Baitha B. Histopathological study of gallbladder lesions in East Singhbhum, Jharkhand. IOSR Journal of Dental and Medical Sciences 2017;16:01-03.
17. Kumar H, Dundy G, Kini H, Tiwari A, Bhardwaj M. Spectrum of gallbladder diseases- A comparative study in North Vs South Indian population. Indian Journal of Pathology and Oncology 2018;5(2):273-6.
18. Thanigaimani GD, Ganapathy H. Retrospective Study of Cholecystectomy Specimens. Saudi J. Pathol. Microbiol, April 2018;3(4):105-108.
19. Selvi RT, Sinha P, Subramaniam PM, Konapur PG, Prabha CV A clinicopathological study of cholecystitis with special reference to analysis of cholelithiasis. International journal of basic medical science, Jul 2011;4:68-72.
20. Mahana S, Poflee V, Shrikandae AV. Morphological spectrum of gallbladder lesions presenting as biliary colic. J Biosci Tech 2013;4(3):519-24.
21. Gaharwar A, Mishra SR, Kumar V. A study on cholecystectomy specimens. J. Anat. Sciences, 2016;24(1):7-12.
22. Beena D, Shetty J, Jose V. Histopathological spectrum of diseases in gallbladder. National Journal of Laboratory Medicine, Oct 2017;6(4): PO06-PO096.
23. Khanna R, Chansuria R, Kumar M, Shukla HS. Histological changes in gallbladder due to stone disease. Indian J Surg 2006; 68:2014.
24. Goyal S, Singla S, Duhan A. Correlation between gallstones characteristics and gallbladder mucosal changes: A retrospective study of 313 patients. Clin Cancer Investig J. 2014; 3:157-61.
25. Mohan H, Punia RPS, Dhawab SB, Ahal S, Sekhon MS. Morphological spectrum of gallstone disease in 1100 cholecystectomies in North India. Indian J surg 2005;67:140-2.
26. Kumbhakar D. A Histopathological Study of Cholecystectomy Specimens. JMSCR 2016;4(7):11234-11238.