

## Original Article

# Frequency of histopathological changes in gall bladder mucosa associated with gallstones



Vishram Singh<sup>a</sup>, Arvind Yadav<sup>a,\*</sup>, Surendra Pal Sharma<sup>b</sup>, Nidhi Verma<sup>b</sup>

<sup>a</sup> Department of Anatomy, Santosh Medical College, Ghaziabad, Delhi-NCR, India

<sup>b</sup> Department of Pathology, LLRM Medical College, Meerut, U. P., India

## ARTICLE INFO

## Article history:

Received 26 March 2018

Accepted 23 July 2018

Available online 30 July 2018

## Keywords:

Cholelithiasis  
Cholecystectomy  
Adenocarcinoma  
Histopathology

## ABSTRACT

**Introduction:** Aim and objective is to study the histopathological changes in gall bladder mucosa associated with gallstones and find out the important facts associated with carcinoma of gallbladder. Compare and correlate the study findings with similar studies done in the past in different part of India. **Material and method:** It is a cross-sectional hospital based study done in Santosh Medical College and Hospital Ghaziabad. The duration of this study is 2 years extending from January 2014 to January 2016. Study performed in total 131 open cholecistectomy specimens with complete gallstones. We included male and female patients of all the age group. Patient of gallstones diagnosed by radiology & recommended for cholecystectomy formed the study population. Autolysed cholecystectomy specimen & cholecystectomy specimen without gallstone were excluded from this study. It is the part of PhD thesis work done under the guidance of professor Dr. Vishram Singh.

**Result:** On the basis of microscopic finding maximum number of specimens had chronic cholecystitis 97.7%, followed by rokitansky aschoff sinuses 22.9%, muscular hyperplasia 15.3%, epithelial hyperplasia 8.4%, fibrosis & ulceration 3.8%, carcinoma 3.1%, antral metaplasia 2.3%, xanthogranulomatous cholecystitis 2.3%, eosinophilic cholecystitis and intestinal metaplasia each present with 0.8%. In this study carcinoma is usually present with pigment type gallstone.

**Discussion:** Most of the gall stones having rough surfaces which causing continuous irritation in the mucosa of gall bladder. Continuous presence for the long time period of gall stones ultimately causes the series of histopathological changes in gall bladder.

© 2018 Published by Elsevier, a division of RELX India, Pvt. Ltd on behalf of Anatomical Society of India.

## 1. Introduction

The gallbladder is a flask shaped blind-ending, hollow viscus. It is mainly serves as reservoir of bile with 30–50 ml in capacity.<sup>1</sup> The cholelithiasis is the most common biliary pathology making Cholecystectomy, the most common abdominal surgery throughout the world. Gallstones are hard pebble like deposits in the gallbladder. Gallstones generally form because the bile is saturated with either cholesterol or bilirubin then bile undergoes super saturation, nucleation and precipitation of cholesterol monohydrate crystals and growth to stone-size aggregation.<sup>2</sup>

## 2. Materials and method

It is a cross-sectional hospital based study done in Santosh Medical College and Hospital Ghaziabad and LLRM Medical College

and Hospital Meerut. The duration of this study is 2 years extending from January 2014 to January 2016. A total 131 open cholecystectomy specimens of cholelithiasis received from the department of pathology were studied. We included male and female patients of all the age groups. Patient of cholelithiasis were diagnosed by radiologists & recommended for cholecystectomy formed the study population. Autolysed cholecystectomy specimen & cholecystectomy specimen without gallstone were excluded from this study. For the detail microscopic examination of specimen routine histological technique were used.

## 3. Result

On the basis of microscopic findings, following histopathological changes were seen in the order of their frequency: chronic cholecystitis 97.7%, Rokitansky aschoff sinuses 22.9%, muscular hyperplasia 15.3%, epithelial hyperplasia 8.4%, fibrosis & ulceration 3.8%, carcinoma 3.1%, antral metaplasia 2.3%, xanthogranulomatous cholecystitis 2.3%, eosinophilic cholecystitis and intestinal metaplasia each present with 0.8%. It is important to note that the

\* Corresponding author.

E-mail address: [drarvindiyadav1982@gmail.com](mailto:drarvindiyadav1982@gmail.com) (A. Yadav).

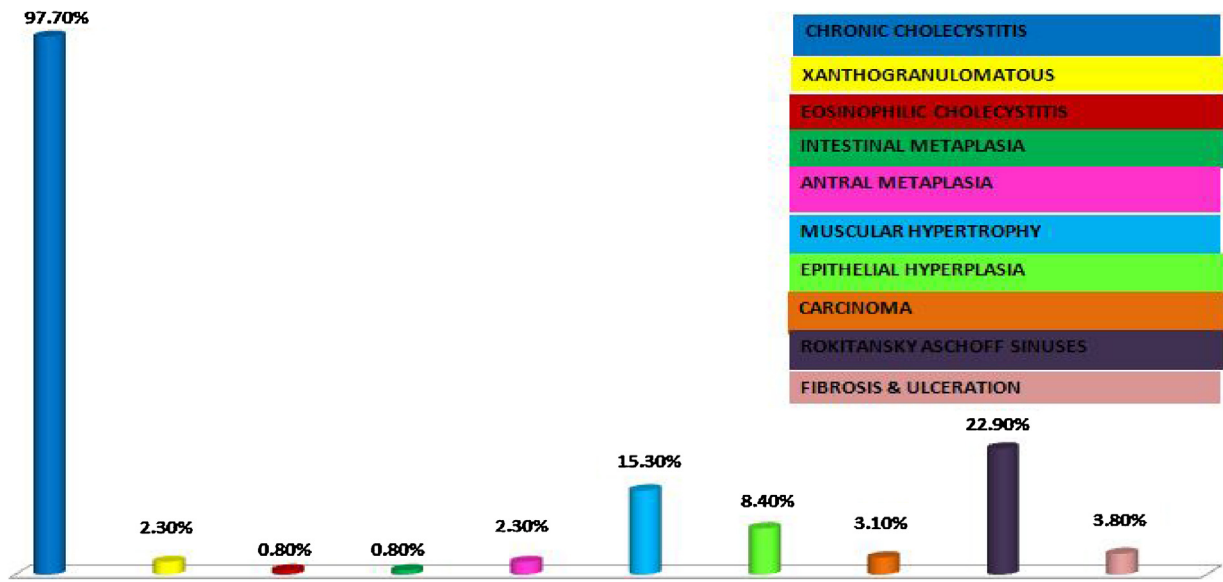


Fig. 1. Colour bar chart showing microscopic findings (mucosal changes) of cholecystectomy specimens in systematic order.

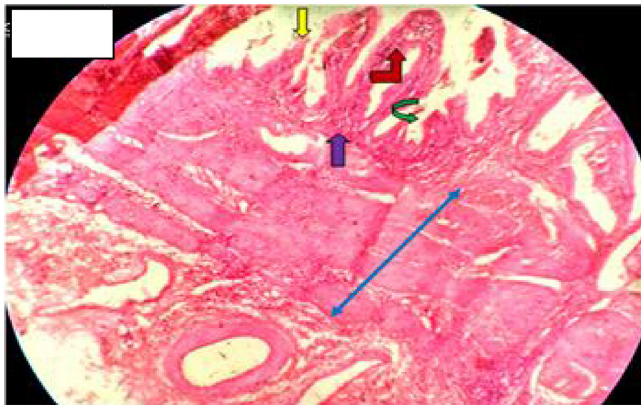


Fig. 2. Chronic cholecystitis of gall bladder as seen in H & E staining (10× power). Yellow arrow- disrupted epithelium, Red arrow- infiltrated lymphocytes & plasma cells, Purple arrow- lymphoid follicles, Green arrow- rokitansky aschoff sinuses, Blue arrow- hypertrophied fibro-muscular layer.

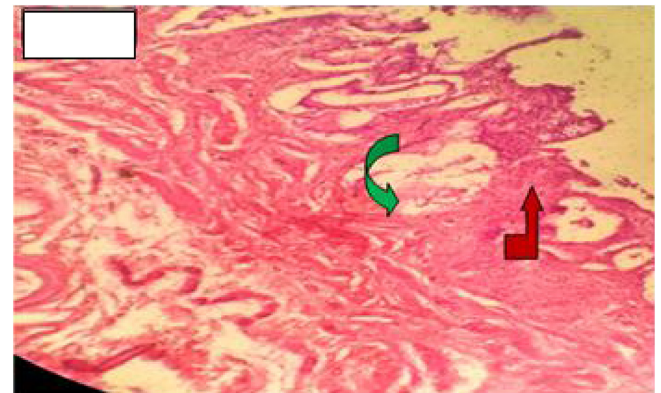


Fig. 3. Xanthogranulomatous cholecystitis of gall bladder as seen in H & E staining (10× power). Green arrow- occluded rokitansky aschoff sinuses. Red arrow- mixture of infiltrated foamy histiocytes, lymphocytes, fibroblast, giant cells and multinucleated foreign body.

carcinoma of gallbladder was found in (3.10%) cases which is higher ever reported in India. The results are tabulated in Table 1 and shown in Figs. 1–8.

#### 4. Discussion

Most of the gall stones have rough surfaces which causes continuous irritation in the mucosa of gall bladder. The presence of

Table 1  
Showing the incidence (in percentage) of mucosal changes in cholecystectomy specimens.

Sr. No.	Parameter	No. of cases	Percentage
1	Chronic Cholecystitis	128	97.7%
2	Xanthogranulomatous cholecystitis	3	2.3%
3	Eosinophilic Cholecystitis	1	0.8%
4	Intestinal metaplasia	1	0.8%
5	Antral metaplasia	3	2.3%
6	Muscular hyperplasia	20	15.3%
7	Epithelial hyperplasia	11	8.4%
8	Carcinoma	4	3.1%
9	Rokitansky-Aschoff Sinuses	30	22.9%
10	Fibrosis &Ulceration	5	3.8%

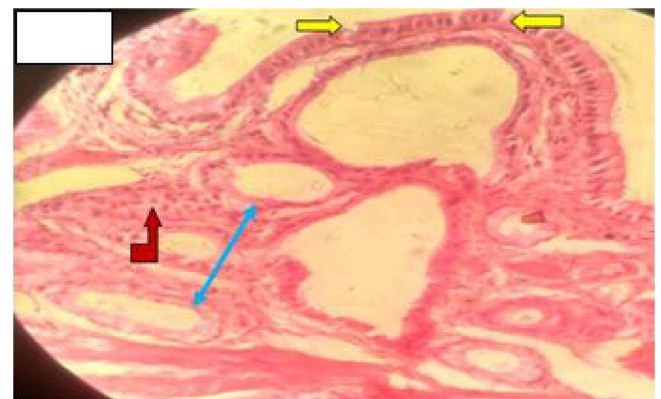
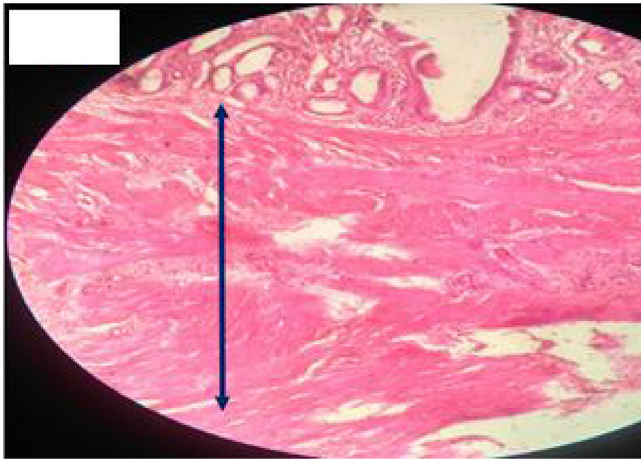
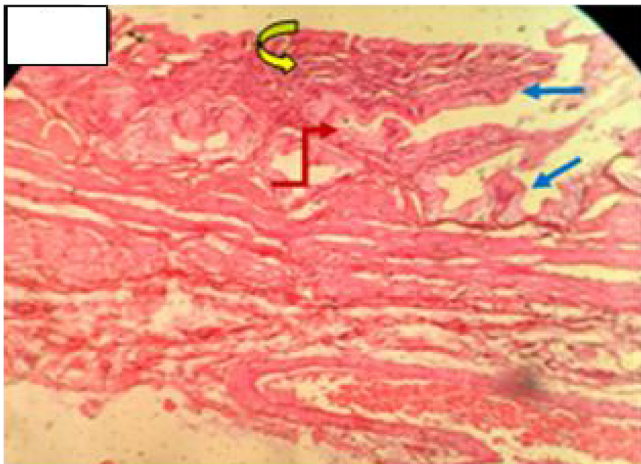


Fig. 4. Antral metaplasia of gall bladder as seen in H & E staining (40× power). Yellow arrow- goblet cells. Red arrow- lymphocytes. Blue arrow- Glandular epithelium.

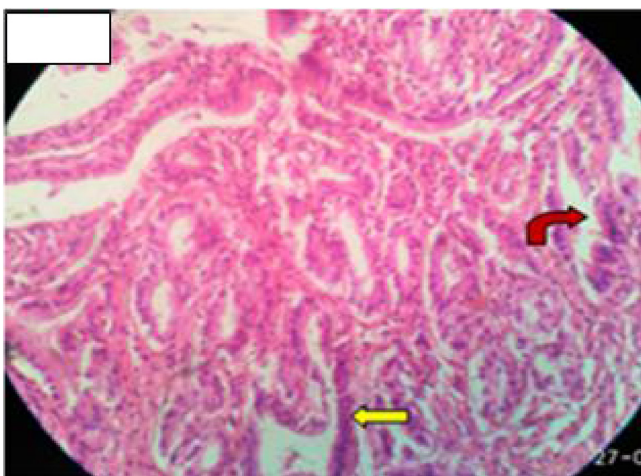




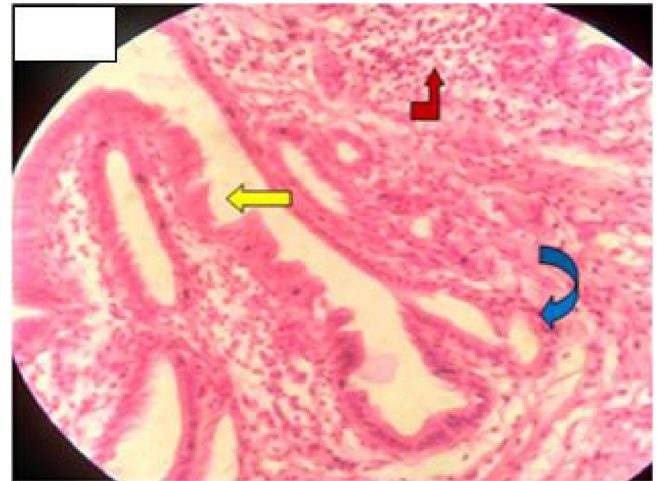
**Fig. 5.** Muscular hyperplasia of gall bladder as seen in H & E staining (10× power). Blue arrow- thickness of fibro-muscular layer.



**Fig. 6.** Epithelial hyperplasia of gall bladder as seen in H & E staining (10× power). Yellow arrow- lymphocytes. Blue arrow- hyperplastic epithelium. Red arrow- Rokitansky aschoff sinuses.



**Fig. 7.** Carcinoma of gall bladder as seen in H & E staining (40× power). Section from the growth of gallbladder shows abnormally form glandular structure (red arrow) lined by malignant epithelial cells (yellow arrow- hyperchromatid nuclei with variable shape and size of cell), infiltrated into stroma, tumor tissue is moderately differentiated.



**Fig. 8.** Rokitansky Aschoff Sinuses as seen in H & E staining in Cholecystectomy specimen (40× power). Yellow arrow- disrupted epithelium. Red arrow- lymphocytes. Blue arrow- rokitanski aschoff sinuses.

gallstones for the long period causes the series of histopathological changes in gall bladder. These are:

#### 4.1. Chronic cholecystitis

In the present study the most common finding was chronic cholecystitis, reported in 97.7% cases (Table 1 and Fig. 2). This fact is supported by the previous studies done by other researchers,<sup>3–5</sup> but it is contradiction to the other studies.<sup>6–8</sup> Maximum percentage of incidence of chronic cholecystitis was reported by Zahrani et al.<sup>9</sup> to be 97%, where as minimum by Jain et al.<sup>10</sup> who reported it to be 30.50%.

#### 4.2. Xanthogranulomatous cholecystitis

In the present work the incidence of xanthogranulomatous cholecystitis was found in 3 (2.29%) cases (Fig. 3). Xanthogranulomatous cholecystitis was usually associated with chronic cholecystitis in 66.66% cases. It usually occurs when occluded rokitansky aschoff sinus rupture. This fact were supported by the other studies also,<sup>1,19</sup> but Kaur et al.<sup>12</sup> 2012 reported very low 1.04% incidence where as Khan et al.<sup>5</sup> 2014 reported highest 3.6% incidence of xanthogranulomatous cholecystitis.

#### 4.3. Eosinophilic cholecystitis

It was observed in only 1 (0.76%) case of all cholecystectomy specimens (Table 1). Incidence of eosinophilic cholecystitis supports the study done by others.<sup>4,5,19</sup>

#### 4.4. Metaplastic changes

The Metaplastic changes were present in total 4 cases (3.05%), among these, the antral metaplasia was more frequently seen in 3 (2.29%) cases, followed by intestinal metaplasia which was observed in only 1 (0.76%) case (Table 1 and Fig. 4). Incidence of intestinal metaplasia is very less in present study in comparison to other studies, but it is in agreement with the study done by Jain et al.<sup>10</sup> who has reported (2.5%) incidence but contradicts the other studies.<sup>12,17,18</sup> Incidence of antral metaplasia is also very less in present study in compare to previous studies, which contradict the studies done by others.<sup>10,12,16</sup>

#### 4.5. Muscular hyperplasia

The incidence of muscular hyperplasia is found in 20 (15.30%) cases (Table 1 and Fig. 5). This fact is supported by the previous study,<sup>14</sup> but contradicts by the studies.<sup>9,15,16</sup>

#### 4.6. Epithelial hyperplasia

In present study the epithelial hyperplasia occurred in 11 (8.40%) cases (Table 1 and Fig. 6). Epithelial hyperplasia was also reported by other researcher although much higher.<sup>11,16–18</sup>

#### 4.7. Carcinoma of gallbladder

In present research work carcinoma of gallbladder was found in 4 (3.05%) cases (Table 1 and Fig. 7). Gallstones appear to be the most important risk factor, being reported in 70–98% cases of gallbladder cancer, a far higher prevalence than that in age-matched general population.<sup>9</sup> Gallstones are responsible for generating a series of epithelial histopathological changes which may act as precursor of lesions of gallbladder cancer. The incidence of carcinoma gallbladder found in present study was supported by the most of previous studies,<sup>3,4,20</sup> however it is contradicted by the study done by Khanna et al.<sup>16</sup> who reported very lowest incidence (0.7%), Zahrani et al.<sup>9</sup> reported 1% incidence. The work of previous workers including present study shows that during last two decades the incidence of gallbladder carcinoma is gradually increased.<sup>4–9,11,13,17</sup> The trend of diseases has changed in the last decades. It may be due to migration of large number of people to cities because of urbanization. So the people have change their food habits, culture and environment. Excessive use of junk food, increase amount of fat, refined carbohydrates, decrease dietary fibres and physical exercise is also an important risk factor for formation of gallstone.

#### 4.8. Rokitansky aschoff sinuses

In the present research work the second most common finding is the presence of Rokitansky aschoff sinuses, which was present in 30 (22.90%) cases (Table 1 and Fig. 8). The presences of Rokitanski aschoff sinuses have been also reported by previous studies done in different part of world in different time period. In 2011 Zuhair et al.<sup>11</sup> reported 33.2% cases, Kaur et al.<sup>12</sup> reported 44.80% cases and Terada et al.<sup>13</sup> reported 65% cases in their studies.

#### 4.9. Fibrosis

In pre research work it was found that the fibrosis occurred in 5 (3.82%) cases (Table 1). Fibrosis of gall bladder has been reported by other studies also but the prevalence is very high in these studies,<sup>7,16</sup> in comparison to present study.

### 5. Conclusion

In the present study it was observed that the most common histopathological changes in mucosa of gallbladder associated

with cholelithiasis is chronic cholecystitis followed by rokitansky aschoff sinuses, muscular hyperplasia, epithelial hyperplasia, fibrosis & ulceration, carcinoma, antral metaplasia, xanthogranulomatous cholecystitis, eosinophilic cholecystitis and intestinal metaplasia.

This study also brings light on the fact that 3.05% of specimens showed the carcinomatous changes. There for it is deduced from this study that all cholecystomic specimens removed for gallstones should be subjected to biopsy to rule out any carcinoma, if a carcinoma is detected the radical surgery must be done for better prognosis of the patients.

### Conflict of interest

None.

### References

1. Susan Standring in gray's anatomy-the anatomical basis of clinical practice, gallbladder and biliary tree. 41st ed. Churchill livingstone elsevier; 2016.
2. Smith BF, LaMont JT. The sequence of events in gallstone formation. *Lab Invest.* 1987;56:125–126.
3. Laitio M, Nevalainen T. Gland ultrastructure in human gallbladder. *J Anat.* 1975;120:105–112.
4. Siddiqui FG, Memon AA, Abro AH, Sasoli NS, Ahmad L. Routine histopathology of gallbladder after elective cholecystectomy for gallstones: waste of resources or a justified act? *BMC Surg.* 2013;13(26):13–26.
5. Narang S, Goyal P, Bal MS, Bandlish U, Goyal S. Gall stones size, number, biochemical analysis and lipidogram-an association with gall bladder cancer: a study of 200 cases. *Int J Cancer Ther Oncol.* 2014;2:1–6.
6. 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;3:102–105.
7. Baig SJ, Biswas S, Das S, Basu K, Chattopadhyay G. Histopathological changes in gallbladder mucosa in cholelithiasis: correlation with chemical composition of gallstones. *Trop Gastroenterol.* 2002;23:25–27.
8. Mathur SK, Duhan A, Singh S, et al. Correlation of gallstone characteristics with mucosal changes in gallbladder. *Trop Gastroenterol.* 2012;33(1):39–44.
9. 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;3:157–161.
10. Zahrani Ibrahim H, Mansoor Ibrahim. Gallbladder pathologies and cholelithiasis. *Saudi Med J.* 2001;22(10):885–889.
11. Jain BB, Biswas RR, Sarkar S, Basu AK. Histopathological spectrum of metaplasia, dysplasia and malignancy in gall bladder and association with gall stones. *JIMSA.* 2010;23(April–June (2)):81–83.
12. Zuhair M, Mumtaz R. Histological changes of gall bladder mucosa: correlation with various types of cholelithiasis. *Iraqi J Community Med.* 2011;24(July (3)):234–240.
13. Kaur A, Dubey VK, Mehta KS. Gallbladder mucosal changes associated with chronic cholecystitis and their relationship with carcinoma gallbladder. *JKS.* 2012;14:89–92.
14. Terada Tadashi. Histopathologic features and frequency of gall bladder lesions in consecutive 540 cholecystectomies. *Int J Clin Exp Pathol.* 2013;6(1):91–96.
15. Hamdani NS, Qadri SK, Aggarwalla R, et al. Clinicopathological study of gall bladder carcinoma with special reference to gallstones: our 8-year experience from Eastern India. *Asian Pac J Cancer Prev.* 2012;13(11):5613–5617.
16. Baidya R, Sigdel B, Baidya NL. Histopathological changes in gallbladder mucosa associated with cholelithiasis. *J Pathol Nepal.* 2012;2:224–225.
17. Khanna R, Chansuria R, Kumar M, Shukla HS. Histological changes in gallbladder due to stone disease. *Indian J Surg.* 2006;68:201–204.
18. Byna SS. Epidemiological and pathological study of resected gall bladders due to cholelithiasis. *Int J Chem Life Sci.* 2013;02(07):1195–1198.
19. Giri S. Histopathological changes in gallbladder mucosa associated with cholelithiasis. *IJCRR.* 2013;05:126–129.
20. Al-Hadeedi SY, Moorhead RI, Leaper DJ, Wong J. Carcinoma of the gallbladder: A diagnostic challenge. *J Coll Surg Edin.* 1991;36:174–177.