

**Original Research Article**

## Histopathological Patterns of Gall Bladder Diseases in Routine Cholecystectomy Specimens: A Hospital-Based Study from a Rural Medical College, Uttar Pradesh

Praneeta J. Singh<sup>1</sup>, Sheetal G. Gole<sup>2</sup>

<sup>1</sup>Associate Professor, Department of Pathology, K.D. Medical College Hospital and Research Center, Akbarpur, Mathura, Uttar Pradesh, 281406, India. <sup>2</sup>Professor & Head, Department of Pathology, Employee's State Insurance Corporation Medical College & Hospital, Faridabad, Haryana, 121001, India.

### Abstract

**Introduction:**Cholelithiasis is the most common disease affecting gallbladder. Gallstones cause several histological changes in gallbladder mucosa like acute and chronic inflammation, metaplasia, hyperplasia, calcification and dysplasia. Present study evaluates the incidence of various histopathological lesions observed in routine cholecystectomy specimen.

### Corresponding Author:

**Sheetal G. Gole,**  
Professor & Head, Department of Pathology, Employee's State Insurance Corporation Medical College & Hospital, Faridabad, Haryana, 121001, India.

**E-mail:**  
drsheelalgole@rediffmail.com

**(Received on 31.03.2018,  
Accepted on 23.04.2018)**

**Material and methods:**This was a hospital based prospective study conducted over a period of 1 year. Detailed gross examination was done in total 325 routine cholecystectomy specimens and microscopic examination was done on slides stained with hematoxylin and eosin stain.

**Results:** Maximum number of patients were in the age group of 21-40 years (49.85%). Number of female patients was 253 (77.85%) and that of male patients was 72 (22.15%). On gross examination, gallstones were found in 239 cases (73.54%). Maximum number of cases 216 (66.46%) and 166 (51.07%) showed normal wall thickness and normal mucosa respectively. Most common histopathological diagnosis was chronic non-specific cholecystitis in 270 (83.07%) cases followed by 8 (2.46%) cases each of follicular cholecystitis, cholesterolosis and adenomyomatosis. Epithelial changes like metaplasia seen in 28 (8.61%) cases, hyperplasia in 17 (5.23%) cases, reactive atypia in 6 (1.85%) cases and dysplasia in 3 (0.92%).

**Conclusion:** Chronic cholecystitis was the most common histopathological diagnosis and it was found to be associated with various changes in gallbladder mucosa like gastric and intestinal metaplasia, hyperplasia and dysplasia. Variants of cholecystitis like xanthogranulomatous cholecystitis, follicular cholecystitis and eosinophilic cholecystitis were also reported. The present study highlights the value of submitting all routine cholecystectomies for thorough histopathological examination.

**Keywords:** Chronic Cholecystitis; Gallstones; Acute Emphysematous Cholecystitis; Porcelain Gall Bladder; Dysplasia.

### Introduction

Cholelithiasis is most common disease affecting gallbladder. In India prevalence of gallstone disease is reported to be higher in North India [1].

Histopathological examination of cholecystectomy specimens reveals various lesions of gallbladder like acute

and chronic cholecystitis, xanthogranulomatous cholecystitis, cholesterolosis, adenomyomatosis, polyp, mucocele of gallbladder and most common histopathological lesion being non-specific cholecystitis. Changes in gallbladder mucosa associated with cholelithiasis like metaplasia, reactive atypia and dysplasia are postulated to be the precursors for

gallbladder carcinoma. Thus, histopathological examination of gallbladder specimen forms an important diagnostic tool [2].

Present study evaluates the incidence of various histopathological lesions observed in routine cholecystectomy specimen.

### Material and Methods

This was a hospital based prospective study conducted over a period of 1 year in the Department of Pathology at a rural tertiary care hospital in North India. All routine cholecystectomy specimens sent for histopathological examination during the study period were included in the study.

Cases with clinical suspicion of gall bladder carcinoma (GBC) were excluded from the study. Detailed gross examination of gallbladder was done and its size, external surface appearance, appearance of mucosa, thickness of the wall, presence of any suspicious lesion on cut surface and presence of any gallstones were noted. In some cases of cholelithiasis, already cut opened gall bladder specimens were received without gall stones. In such cases absence of gallstone was recorded in gross examination.

Three sections were taken from gallbladder each representing fundus, body and neck. Additional sections were taken from any suspicious areas. Histopathological sections were stained using hematoxylin and eosin (H&E) stain.

### Results

Total 325 routine cholecystectomy specimens were studied over a period of 1 year. Age of the patients ranged from 9 years to 78 years. Maximum number of patients were in the age group of 21-40 years (49.85%) as shown in Table 1. Number of female patients was 253 (77.85%) and that of male patients was 72 (22.15%).

On gross examination, gallstones were found in 239 (73.54%) cases while it was absent in 86 (26.46%) cases. Cholesterol stones (yellow stones) were most common occurrence seen in 130 (54.39%) cases followed by pigmented stones in 93 (38.91%) cases and mixed stones in 16 (6.69%) cases. Out of total 325 cases, wall thickness was normal in 216 (66.46%) cases and it was > 0.3 cm in 109 (33.54%) cases. Mucosa was normal in 166 (51.07%), atrophied in 132 (40.61%), ulcerated in 7 cases (2.15%), strawberry like in 10 (3.07%), hyperplastic in 6 (1.85%), calcified in 2 (0.62%), necrotic in 1 (0.3%), and cystic in 1 (0.3%).

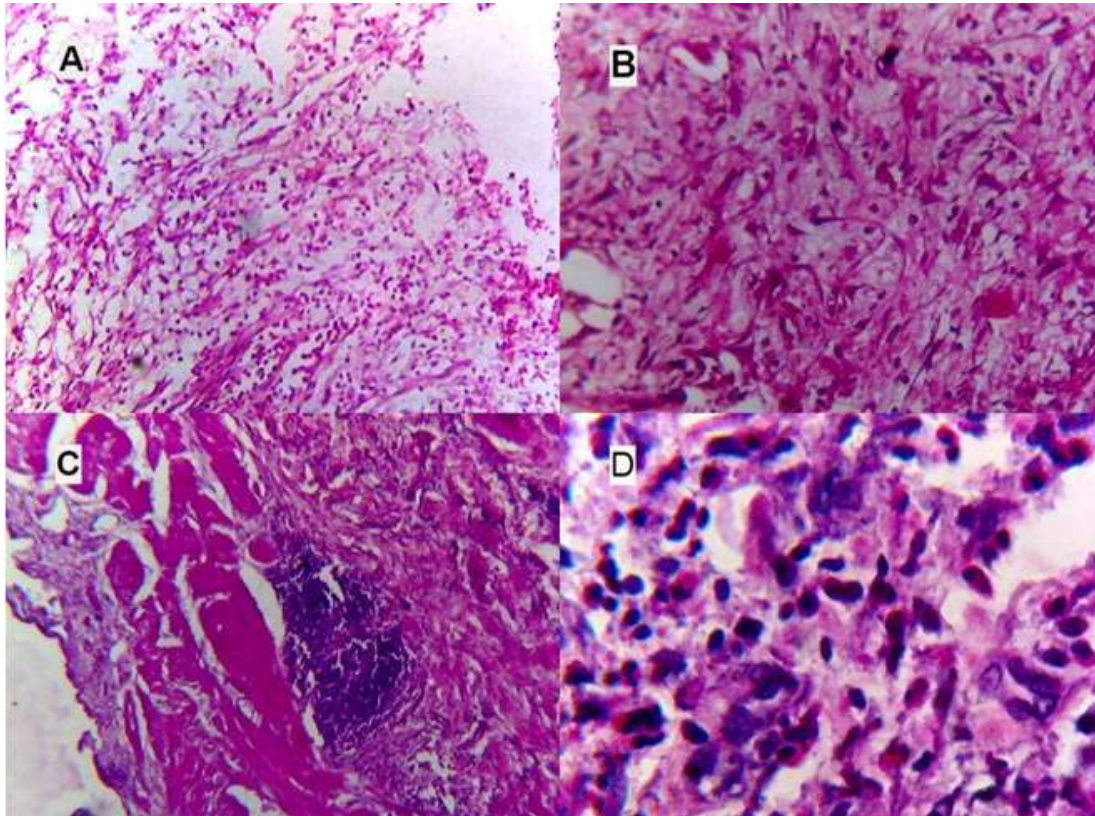
Most common histopathological diagnosis was chronic non-specific cholecystitis in 270 cases (83.07%), of which 200 (74.07%) cases were associated with gallstones and in 70 (25.93%) cases gallstone was absent as shown in Table 2. Eight cases (2.46%) each of follicular cholecystitis, cholesterolosis and adenomyomatosis were reported. Acute cholecystitis was reported in 5 cases (1.54%), of which gallstone was present in 1 case (20%) and absent in 4 cases (80%). One case (0.30%) of acute emphysematous cholecystitis was reported in adult female with no prior history of diabetes mellitus. Culture for organism

**Table 1:** Age wise distribution of cases

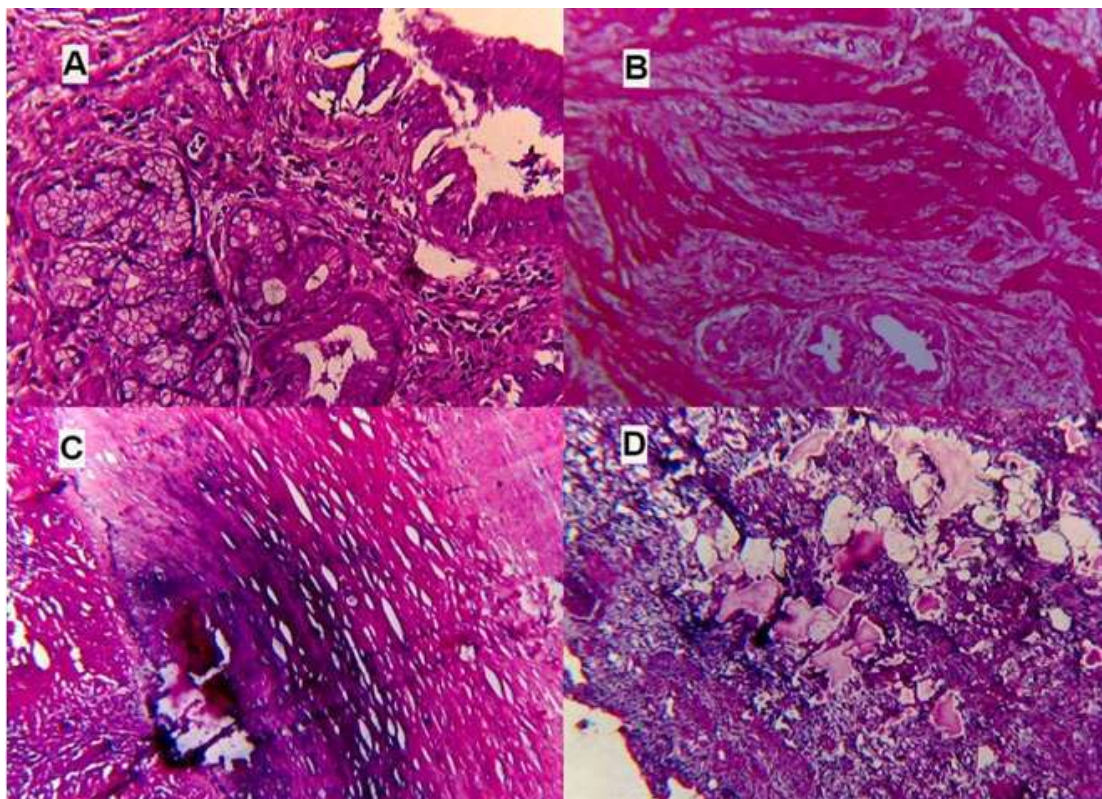
Age group	Total number (%)
0-20	11 (3.38)
21-40	162 (49.85)
41-60	114 (35.07)
61-80	38 (11.70)

**Table 2:** Distribution of cases according to histopathological diagnoses and type of gallstone

Histopathological Diagnoses	Total no. of cases N (%)	Distribution of cases according to gallstones				Gallstone absent
		Yellow	Pigment	Mixed	Total	
Chronic non-specific cholecystitis	270 (83.07)	106	80	14	200 (74.07)	70 (25.93)
Chronic cholecystitis with dysplasia	03 (0.92)	02	01	-	03 (100)	-
Acute cholecystitis	05 (1.54)	-	01	-	01 (20)	04 (80)
Acute on chronic cholecystitis	04 (1.23)	03	-	-	03 (75)	01 (25)
Acute emphysematous cholecystitis	01 (0.30)	01	-	-	01 (100)	-
Follicular cholecystitis	08 (2.46)	04	03	-	07 (87.5)	01 (12.5)
Eosinophilic cholecystitis	02 (0.62)	-	-	-	-	02 (100)
Lympho eosinophilic cholecystitis	07 (2.15)	02	04	-	06 (85.71)	01 (14.29)
Cholesterolosis	08 (2.46)	06	-	01	07 (87.5)	01 (12.5)
Xanthogranulomatous cholecystitis	06 (1.85)	04	01	01	06 (100)	-
Porcelain gallbladder	02 (0.62)	-	01	-	01 (50)	01 (50)
Mucocele of gallbladder	01 (0.30)	-	-	-	-	01 (100)
Adenomyomatosis	08 (2.46)	02	02	-	04 (50)	04 (50)



**Fig. 1A:** Xanthogranulomatous cholecystitis (H&E,10X) **B:** Xanthogranulomatous cholecystitis (H&E,40X) **C:** Follicular cholecystitis (H&E,10X), **D:** Eosinophilic cholecystitis (H&E,40X)



**Fig. 2A:** Gastric metaplasia in case of chronic cholecystitis (H&E,40X), **B:** Segmental adenomyosis (H&E,40X), **C:** Porcelain gall bladder showing calcification (H&E,40X), **D:** Acute emphysematous cholecystitis (H&E,40X)

identification was not done in this case. In both cases (0.62%) of eosinophilic cholecystitis, gallstone was absent. Out of 7 cases (2.15%) of lymphoeosinophilic cholecystitis, gallstones were present in 6 cases (85.71%) and absent in 1 case (14.29%). All 6 cases (1.85%) of xanthogranulomatous cholecystitis were associated with gallstones. Porcelain gallbladder was reported in 2 cases (0.62%) out of which one was associated with gallstone while in 1 case gallstone was absent. Mucocele of gallbladder was reported in 1 case (0.30%). In 3 cases (0.92%) dysplasia was seen in association with chronic cholecystitis associated with gallstones as shown in Table 2.

On microscopic examination following epithelial changes were noted: metaplasia in 28 cases (8.61%) out of which gastric antral metaplasia seen in 16 cases (4.92%) and intestinal metaplasia in 12 cases (3.69%), hyperplasia in 17 cases (5.23%), reactive atypia in 6 cases (1.85%) and dysplasia in 3 cases (0.92%).

## Discussion

In India gallstone disease affects younger age group as compared to the western population with a female predominance [11]. In present study also maximum number of patients 162 (49.85%) belonged to the younger age group of 21-40 years with sex wise distribution showing female predominance (77.85%). Similar findings were reported by Khan S et al [3].

In the present study, gallstones were present in 239 cases (73.54%). In retrospective study by Khan S et al [3], it was observed that though clinical data given on histopathology form by surgeons showed presence of gallstones in 99.2% patients but all of it was not received in the laboratory since in many cases the stones were handed over to the patients' relatives after the surgery. Similar practice of handing over gallstones to patients' relatives was carried out at our hospital. Present study was a prospective study so cases where cholelithiasis was mentioned on histopathology form but no stone was received in histopathology laboratory, absence of gallstone was recorded in gross examination. This may have led to less number of cholelithiasis cases in present study.

In North India cholesterol gall stones (>80%) are common while pigment gallstones are more common in South India [4]. Present study was conducted in North India and most common gallstone was cholesterol gallstone 130 (54.39%) cases.

In present study, wall thickness was normal in maximum number of cases 216 (66.46%) and increased in 109 cases (33.54%). Similar findings were reported by Khanna R et al [5]. (57.5% normal thickness and 42.5% thickened wall) and Baidya R et al [6]. from Nepal (normal

in 53.4). Mathur SK et al [7]<sup>1</sup> reported thickened gallbladder wall in 53.6% cases and normal thickness in 46.4% cases.

In present study, on gross examination mucosa was normal in maximum number of cases 166 (51.07%). Similar finding was reported by Baidya R et al [6] while Khanna R et al [5] reported equal number of cases with normal and atrophic mucosa.

## Metaplasia

The review of literature shows that cholelithiasis and inflammation leads to gastric or intestinal type of metaplasia in gallbladder mucosa which in turn can be associated with dysplasia and carcinoma [8,9]. Studies have reported that gastric metaplasia was the most common type of metaplasia in cases of chronic cholecystitis or cholelithiasis [8].

In present study metaplasia was reported in 28 cases (8.61%) which is higher as compared to study by Zahrani IH et al. [10] (3%) and Stancu M et al. [11] (5%) and lower as compared to study by Arathi NA et al. [12] (18.6%). On dividing metaplasia into two categories as gastric and intestinal metaplasia, occurrence of gastric antral metaplasia was slightly higher than intestinal metaplasia [4.92% and 3.69% respectively] in present study. (Figure 2A) Significantly higher percentage of gastric metaplasia was reported by Zahrani IH et al. [10] (88%) Stancu M et al. [11] (83.7%) and Arathi NA et al. [12] (79.5%). While studies by Mathur SK et al. [7] (pyloric metaplasia in 10% cases and intestinal metaplasia in 8%) and Khanna R et al. [5] (antral metaplasia in 16.5%, intestinal metaplasia in 15.5%) reported no significant difference in occurrence of gastric and intestinal metaplasia.

## Hyperplasia

Studies have suggested hyperplasia of gallbladder mucosa could be a precursor lesion of carcinoma gallbladder [13].

In present study epithelial hyperplasia was seen in 17 cases. Higher percentage of epithelial hyperplasia (69%) was reported by Khanna R et al. [5], Baidya R et al. [6] (46.2%), Kaur A et al. [14] (25.02%) and Stancu M et al. [11] (7.8%).

In present study dysplasia associated with cholelithiasis was seen in 3 (0.92%) cases. In all 3 cases of dysplasia, whole gallbladder was submitted for histopathological examination to rule out any associated carcinoma. Dysplasia was distinguished from reactive metaplasia on basis of nuclear features like chromatin pattern, presence or absence of prominent nucleoli and loss of polarity and presence or absence of intraepithelial neutrophils. Studies by Sharma I et al. [15] (1.3%) and Baidya R et al. [6] (1.3%) reported similar percentage of dysplasia while higher

percentage dysplasia was reported by Khanna R *et al.*[5](8.5%) and lower percentage of dysplasia (0.4%) was reported by Stancu M *et al* [11].

In present study most, common histopathological diagnosis was chronic non-specific cholecystitis in 270 (83.07%) which is comparable to other studies [3,15,16].

Five cases (1.72%) of acute cholecystitis were seen in present study. Similar finding was reported by Khan S *et al.*[3] (2.7%) while Talreja V *et al.*[16]reported higher incidence of acute cholecystitis (6.32%) cases.

In present study acute on chronic cholecystitis was reported in 4 cases (1.38%)while Mathur SK *et al.*[7]reported higher percentage of such cases (12%).

In present study 7 cases (2.41%) of Xanthogranulomatous cholecystitis (Figure 1AB) and 2 cases (0.69%) of Eosinophilic cholecystitis (Figure 1D) were reported. Similar findings were reported that Khan S *et al.*[3]and Sharma I *et al* [15].

In present study 7 cases (2.41%) of Follicular cholecystitis(Figure 1C) were reported. Higher percentage of cases (5%) was reported by Mathur SK *et al.*[7]while Khan S *et al.*[3]reported lower percentage of cases (0.25%).

Cholesterosis was reported in 5 cases (1.72%)in present study, while higher percentage of cases were reported by Khan S *et al.*[3] (10%), Mathur SK *et al.*[7] (6%), Sharma I *et al.*[15] (4.4%) and Talreja V *et al.*[16](12.31%).

Adenomyomatosis of gallbladder is a tumor like lesion but some studies have suggested that it may have malignant potential and may act as precursor for developing carcinoma [19].

In present study adenomyomatosis (Figure 2B) was reported in 6 cases (2.07%), which is less as compared to study done by Mathur SK *et al* [7] and higher as compared to study done by Khan S *et al* [3].

In present study one case of porcelain gallbladder (Figure 2C) was seen in which full thickness of gallbladder wall was involved and it was replaced by calcified fibrosis and mucosa was completely denuded.

Previously many studies reported that absence of mucosa in cases of porcelain gallbladder with extensive calcification reduces the risk of subsequent development of carcinoma [17]. However recent studies suggested that pattern or the depth of calcification should not be considered while predicting the risk of developing carcinoma in the future [17].

Acute emphysematous cholecystitis is a form of acute cholecystitis reported to be more common in older patients with history of diabetes mellitus and Clostridium is the most common causative agent [18]. Khare S *et al.*[18] reported a case of acute emphysematous cholecystitis in young nondiabetic patient caused by Escherichia coli.

Similarly, in present study an isolated case of acute emphysematous cholecystitis (Figure 2D) was reported in young female with no prior history of diabetes mellitus. As culture was not done in this case causative organism could not be identified.

## Conclusion

Cholelithiasis was common in younger age group with a female predominance. Chronic cholecystitis was most common histopathological diagnosis and it was found to be associated with various changes in gallbladder mucosa like gastric and intestinal metaplasia, hyperplasia and dysplasia. In few cases variants of cholecystitis like xanthogranulomatous cholecystitis, follicular cholecystitis, eosinophilic cholecystitis was also reported. The present study highlights the value of submitting all routine cholecystectomies for thorough histopathological examination.

## References

1. Kapoor VK, McMichael AJ. Gallbladder cancer: an 'Indian' disease. *Natl Med J India* 2003;16(4):209-13.
2. Taha MM Hassan, Anil Mohan Rao. S. Benign Mimickers of Gall Bladder Carcinoma in Cholecystectomy Specimens: Histopathological Study. *International Journal of Scientific Research*. 2015;4(7).
3. 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 IntSurg* 2013; 3(2):102-5.
4. Choudhuri G, Agarwal DK, Negi TS. Polarizing microscopy of partially dissolved gallstone powder: A simple technique for studying gallstone composition. *J Gastroenterol Hepatol* 1995;10(3):241-5.
5. Khanna R, Chansuria R, Kumar M, Shukla HS. Histological changes in gallbladder due to stone disease. *Indian J Surg* 2006;68(4):201-4.
6. Baidya R, Sigdel B, Baidya NL. Histopathological changes in gallbladder mucosa associated with cholelithiasis. *Journal of Pathology of Nepal* 2012;2(3):224-5.
7. Mathur SK, Duhan A, Singh S, Aggarwal M, Aggarwal G, Sen R, et al. Correlation of gallstone characteristics with mucosal changes in gall bladder. *Trop Gastroenterol* 2012; 33(1):39-44.
8. Mukhopadhyay S, Landas SK. Putative precursors of gallbladder dysplasia: A review of 400 routinely resected specimens. *Arch Pathol Lab Med* 2005;129(3):386-90.
9. Nora Katabi. Neoplasia of Gallbladder and Biliary Epithelium. *Archives of Pathology & Laboratory Medicine* 2010;134(11):1621-7.

10. Zahrani IH, Mansoor I. Gallbladder pathologies and cholelithiasis. *Saudi Med J* 2001;22(10):885-9.
  11. Caruntu ID, Giuca S, Dobrescu G. Hyperplasia, metaplasia, dysplasia and neoplasia lesions in chronic cholecystitis – a morphologic study. *Romanian J of Morphol Embryol* 2007;48(4):335-42.
  12. Arathi NA, Awasthi S, Kumar A. Pathological profile of cholecystectomies in a tertiary centre. *National Journal of Medical and Dental Research* 2013;2(1):28-38.
  13. Albores-Saavedra J, Molberg K, Henson DE. Unusual malignant epithelial tumors of the gallbladder. *Semin Diagn Pathol* 1996;13(4):326-38.
  14. Kaur A, Dubey VK, Mehta KS. Gallbladder mucosal changes associated with chronic cholecystitis and their relationship with carcinoma gallbladder. *Surgery ASCOMS, JK Science*. 2011;14(2):89-92.
  15. Sharma I, Choudhary D. Histopathological patterns of gall bladder diseases with special reference to incidental cases: a hospital-based study. *International Journal of Research in Medical Sciences*. 2015;3(12):3553-7.
  16. Talreja V, Ali A, Khawaja R, Rani K, Samnani SS, Farid FN. Surgically resected gall bladder: Is histopathology needed for all? *Surg Res Pract*. 2016; Article ID 9319147.
  17. Machado NO. Porcelain Gallbladder Decoding the malignant truth. *Sultan Qaboos University Med J* 2016;16(4):416-21.
  18. Khare S and Pujahari AK. A Rare Case of Emphysematous Cholecystitis. *J Clin Diagn Res* 2015;9(9):13-14.
  19. Ozgonul A, Bitiren M, Guldur ME, Sogut O, Yilmaz LE. Fundal Variant Adenomyomatosis of the Gallbladder: Report of Three Cases and Review of the Literature. *J Clin Med Res* 2010;2(3):150-3.
-