

## Study of histopathological spectrum of cholecystectomy specimens received in a government hospital

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### Abstract

**Introduction:** Gall bladder analysis for various lesions was conducted. Chronic cholecystitis is was most commonly encountered lesion. Cholelithiasis and incidentally diagnosed carcinoma constitutes more than 95% and 0.5-1.09% of gall bladder lesions respectively. So, every specimen should undergo histopathological examination.

**Aims and objectives:** i) To study various histopathological lesions of gall bladder ii) To evaluate the incidence of incidental gall bladder carcinoma.

**Materials and Methods:** A cross-sectional study of 430 cholecystectomy specimens was conducted at Pathology Department, GMERS Medical College and General Hospital, Sola, Ahmedabad from February 2017 to March 2019 (2 years). Specimens received in 10% Neutral Formalin were processed and Haematoxylin and Eosin sections were studied.

**Results:** We studied 430 cholecystectomy specimens. Females showed predominance (294 cases; 68.5%) with male-female ratio of 1:2.2. Most commonly affected age group was 21-40 years (154 cases, 35.8%), followed by 41-60 years (135 cases, 31.5%). The most common diagnosis was chronic calculous cholecystitis (279 cases, 65%). Others were chronic acalculous cholecystitis (114 cases, 26.4%), acute on chronic cholecystitis (13 cases, 3.1%), cholesterolosis (5 cases, 1.2%), acute cholecystitis (4 cases, 0.9%), xanthogranulomatous cholecystitis (4 cases, 0.9%) and acute suppurative cholecystitis (2 cases, 0.4%) with one case of adenomyomatosis (0.2%). Four cases of adenomas (ICPN- Intracholecystic Papillary-Tubular Neoplasms) and four cases of incidentally detected gall bladder carcinoma were obtained.

**Conclusion:** The microscopic examination of cholecystectomy specimens is required to study various lesions and to detect carcinomas which are difficult to diagnose grossly. Thus, histopathological examination is the gold standard diagnostic tool.

**Keywords:** Cholecystectomy, cholecystitis, cholelithiasis, Intracholecystic Papillary-tubular Neoplasms (ICPN), Signet ring adenocarcinoma

### Introduction

The gall bladder is one of the most commonly received specimens for histopathological examination. It presents with a huge spectrum of lesions ranging from congenital anomalies, inflammatory, non-inflammatory, non-neoplastic and neoplastic lesions.<sup>1</sup>

More than 95% of gall bladder lesions develop due to gall stones. Modifiable risk factors for the development of cholelithiasis are obesity, sedentary lifestyle and rapid weight loss; non-modifiable risk factors are female gender, increasing age group, oestrogen and family history.<sup>1</sup> Cholelithiasis can lead to lesions such as acute and chronic cholecystitis, mucocele, gangrene of gallbladder, perforation and carcinoma of gallbladder.<sup>2</sup>

Polypoid or papillary lesions which included adenomas, papillomatosis and non-invasive papillary neoplasms are currently considered under ICPN -Intracholecystic Papillary-tubular Neoplasms.<sup>3</sup> Flat (non-tumoral) dysplasia is not easy to be diagnosed grossly and also it comes as an incidental finding microscopically.<sup>3</sup> As it is associated with majority of invasive carcinoma and can present with or without some growth with various cell types, a thorough sampling and examination is required whenever dysplasia is found on initial microscopy.<sup>3</sup>

Adenocarcinoma of gall bladder constitutes 80-95% of cancers of biliary tract, is found in females and males with a ratio of 3-4:1.<sup>3</sup> Though 50% of the gall bladder cancers are

diagnosed incidentally, the most common clinical presentation is right upper quadrant abdominal pain and the laboratory finding found most commonly is increased level of alkaline phosphatase.<sup>3</sup> Gall bladder carcinomas is 5th among the gastrointestinal tract cancers and first among the cancers of the biliary tract. It is characterized by fast progression and a very highly lethal disease with 5 year survival rates of approximately 10%.<sup>4,5</sup> The highest incidences are reported in Indians, Pakistanis, Israelis and Americans.<sup>5</sup>

As per Indian Cancer Registry data, the incidence of gall bladder carcinoma is 0.8-1.0%. While New Delhi and Bhopal are leading states, the lowest incidence is seen in Chennai.<sup>5</sup>

Shukla et al. has shown that the gangetic belt of northern India has high incidence of gall bladder carcinoma may be because of presence of heavy metals such as lead, cadmium and mercury in gall bladder specimens.<sup>6</sup>

IGC (Incidental Gall bladder Carcinoma) is defined as gall bladder carcinoma diagnosed by histopathological examination incidentally. It is otherwise called inapparent/occult/missed gall bladder carcinoma.<sup>5</sup> Gallbladder carcinoma is the leading cause of mortality from biliary tract malignancies.<sup>7</sup>

Royal College of Pathologists mandates to submit all cholecystectomy specimens for histopathology as many

important gall bladder pathologies can mimic normal morphology.<sup>8</sup>

Simple cholecystectomy is an adequate treatment for all benign lesions and early stage of gallbladder carcinoma. Therefore, no other intervention is required.<sup>9</sup>

## Materials and Methods

This is a cross-sectional study of 430 gall bladder specimens conducted at Pathology Department, GMERS Medical College and General Hospital, Sola, Ahmedabad over a period of two years (from February 2017 to March 2019). For retrospective cases (from February 2017 to June 2018), the clinical details and histopathology data was obtained from histopathology registers and records. For prospective cases (from June 2018 to March 2019), both laparoscopic and open cholecystectomy specimens were received in 10% Neutral Buffered Formalin. Fixation of the gall bladder specimens was done promptly as the epithelium is quite susceptible to bile-related autolysis. Grossing was done as per the standard protocol. For the routine cases, standard three sections including fundus, body and neck were taken. In cases of any growth, irregular mucosa, thickened wall, calcification, necrosis, etc. more sections were taken. Lymph nodes, whenever present were also submitted for histopathology. These sections were subjected to routine processing and stained by Haematoxylin & Eosin stain.

## Results

The gall bladder is one of the most commonly resected specimens to be received in histopathology. We received 430 specimens for histopathological examination in Pathology Department, Sola, Ahmedabad during the period of two years (February 2017 to March 2019).

Out of 430 cases, the maximum number of cases received were of chronic calculous cholecystitis (279 cases, 65%) followed by chronic acalculous cholecystitis (114 cases, 26.4%). Other non-neoplastic lesions received were acute cholecystitis (4 cases -0.9%), acute on chronic cholecystitis (13 cases - 3.1%), xanthogranulomatous cholecystitis (4 cases - 0.9%) and acute suppurative cholecystitis (2 cases -0.4%). Four cases grossly examined as polyps were diagnosed as adenomas on histopathological examination – three as tubular adenoma and one as papillary adenoma. They are currently classified as ICPN (Intracholecystic Papillary-Tubular Neoplasms).

Among the malignant lesions, three cases of conventional adenocarcinoma and one case of signet ring type of adenocarcinoma of gall bladder were received. All four were incidental findings on microscopy. (Table 1)

Among age criteria, the youngest case was of 15-year-old female and eldest case was seen in 90-year-old female. Most cases were seen between 21-40 years age followed by 41-60 years. (Table 2) Cholelithiasis was found in 297 cases (60%) out of 430 cases studied in total – which is depicted in the following table according to the histopathological diagnosis. (Table 3) The gall bladder diseases seen were commonly in females with a ratio of 2.2:1 (Chart 1)

## Discussion

In the present study, the distribution of lesions of gall bladder according to age was in the range of 15-90 years, most common age group being 21-40 years (154 cases, 35.8%) followed by 41-60 years (135 cases, 31.5%) which is similar to studies by Bharathi IV et al<sup>10</sup> and Sharma JD et al.<sup>11</sup> Sangwan MK et al.<sup>2</sup> found majority of cases belonging to 31-40 years age group.

The distribution of gall bladder lesions based on gender showed female to male ratio as higher indicating gall bladder lesions are much commoner in females as compared to males. This was found to have correlation with studies by Awasthi et al,<sup>1</sup> Sangwan MK et al,<sup>2</sup> Jha et al,<sup>5</sup> Bharathi IV et al,<sup>10</sup> Sharma JD et al<sup>11</sup> and Dipti Kalita et al.<sup>12</sup>

In the current study, the most common lesion was found to be chronic calculous cholecystitis which constitutes 65% i.e. 279 cases which correlates well with studies by Awasthi et al,<sup>1</sup> Sangwan MK et al,<sup>2</sup> Bharathi IV et al<sup>10</sup> and Kini H et al.<sup>13</sup> Grossly, chronic cholecystitis shows thickened wall and microscopically, it shows mononuclear infiltration in the mucosa, hypertrophied and fibrosed wall with presence of irregular Rokitansky -Aschoff sinuses.<sup>3</sup> (Figure 1a) The second most common diagnosis was chronic acalculous cholecystitis 114 cases (26.51%). Chronic acalculous cholecystitis occurs as a result of repeated attacks of acute cholecystitis.<sup>10</sup>

Genetic susceptibility increases the risk for gall stone formation to 5 times.<sup>2</sup> Cholelithiasis (gallstones) is responsible for more than 95% of gall bladder disease.<sup>14</sup> The patients may remain asymptomatic for decades and if symptomatic, they present with biliary colic usually after a fatty meal.<sup>14</sup> But in our study, out of 430 cases, only 297 cases (60%) were found to be associated with cholelithiasis which is similar to study done by Bharathi IV et al<sup>10</sup> and lesser as compared to other studies done by Awasthi et al,<sup>1</sup> Sangwan MK et al<sup>2</sup> and Kini H et al.<sup>13</sup>

4 cases of acute cholecystitis were received. Acute cholecystitis grossly shows markedly oedematous wall and angry red coloured mucosa with focal/extensive ulceration which were our similar findings in 3 specimens. On microscopy, it shows hyperaemia, oedema and extravasated red blood cells.<sup>3</sup> (Fig. 1b)

Amongst cholecystitis and its types, a special mention of xanthogranulomatous cholecystitis is given. It is characterised by inflammation of gall bladder, seen microscopically by marked fibrosis, infiltration of wall by macrophages and foam cells. It is important because few reports of xanthogranulomatous cholecystitis presenting with aggressive pattern have been found. In our study, its prevalence was 0.9% and none of them mimicked a malignant lesion. It was similar to a study done by Sharma JD et al.<sup>11</sup> (Fig. 2a)

We received 5 cases of cholesterosis. Its microscopic picture reveals presence of lipid laden foamy cells in the tips of villi along with insignificant inflammatory changes similar to our findings. It is also called strawberry gall bladder due to presence of linear yellow streaks in the ridges with surrounding congested mucosa.<sup>3</sup> (Fig. 2b)

Adenomyomatosis is an example of diverticulosis of gall bladder associated with muscular hypertrophy and is a common finding, seen in 5% cases. It consists of cystically dilated glands, which depict extended Rokitansky-Aschoff sinuses within the smooth muscle which is hypertrophied; the glands may lie in vicinity of nerves simulating neural invasive component.<sup>3</sup>

Polypoid or papillary lesions which included adenomas, non-invasive papillary neoplasms and papillomatosis are currently considered under ICPN -Intracholecystic Papillary-tubular Neoplasms.<sup>3</sup> Grossly, ICPNs are papillary and/or papillary and may enlarge over 5 cm; are friable enough to detach and can be mistaken for any necrotic tissue. Microscopically, these are papillary, tubular or tubulopapillary. High grade dysplasia and invasiveness are common to occur in papillary and tubulopapillary lesions.<sup>3</sup> Four cases of polyps were diagnosed as adenomas on histopathological examination – three tubular and one papillary adenoma. (Fig. 3)

Flat (nontumoral) dysplasia is not easy to be diagnosed grossly, is an incidental finding microscopically.<sup>3</sup> As it is associated with majority of invasive carcinoma and presents with or without some growth with various cell types, a thorough sampling and examination is required whenever dysplasia is found on initial microscopy.<sup>3</sup>

Gall bladders presenting with cancers in 80-90% cases usually have calculi and have marked fibrotic wall.<sup>3</sup> Among four malignant cases, 2 cases (50%) showed association with gall stones which is lesser as compared to Jha et al,<sup>5</sup> Bharathi IV et al<sup>10</sup> and Kini H et al.<sup>13</sup> Gallbladder carcinoma appears to develop from dysplasia then to carcinoma in situ followed by invasive carcinoma.<sup>7</sup>

Only 4 cases of gall bladder carcinoma were obtained which were diagnosed incidentally without any clinical suspicion. Three were diagnosed as conventional adenocarcinoma (the most common histological type) (75%), similar to a study by Dipti Kalita et al<sup>12</sup> and one as signet ring type of adenocarcinoma. Other types are: adenosquamous, intestinal, mucinous, clear cell, pure squamous, neuroendocrine, hepatoid.<sup>3</sup>

Grossly, gall bladder cancers can present as diffuse growth (70%) or nodular/polypoid/papillary mass (30%). The majority arise in fundus (70-80%), 10-20% in body and rest in neck.<sup>3</sup> Carcinoma of the gallbladder is the most common malignancy of the extrahepatic biliary tract.<sup>2</sup> Out of 4 cases of adenocarcinoma of gall bladder, one presented with a cauliflower-like solid nodular growth (Fig. 4a) and with other polypoid lesion at fundus with lymph node metastasis seen microscopically. The tumour cells didn't invade the lymphovascular and perineural areas. Another specimen had a diffusely thickened wall of 0.7 cm Both microscopically, showed well-formed irregular and widely spaced infiltrative glands with wide lumina by anaplastic epithelial cells having hyperchromatic pleomorphic vesicular nuclei and prominent nucleoli.(Fig. 4b) Foci of intraneural and perineural invasion was seen in another specimen. One case was diagnosed with signet ring type of adenocarcinoma showing dysplastic glands and necrotic eroded mucosa with many cells having mucin with nuclei pushed to the periphery- signet ring appearance. (Fig. 5)

Table 4 shows comparison of incidence of adenocarcinoma of gall bladder of the present study and other studies which have been mentioned in this article.

**Table 1:** Histopathological diagnosis of total 430 specimens received

S. No.	Histopathological diagnosis	No. of cases	Percentage of cases (%)
1	Chronic calculous cholecystitis	279	65
2	Chronic acalculous cholecystitis	114	26.4
3	Acute cholecystitis	04	0.9
4	Xanthogranulomatous cholecystitis	04	0.9
5	Acute on chronic cholecystitis	13	3.1
6	Acute suppurative cholecystitis	02	0.4
7	Cholesterosis	05	1.2
9	Adenomyomatosis	01	0.2
8	Adenoma (ICPN)	04	0.9
10	Adenocarcinoma	04	0.9
	Total	430	100%

ICPN-Intracholecystic Papillary-tubular Neoplasms

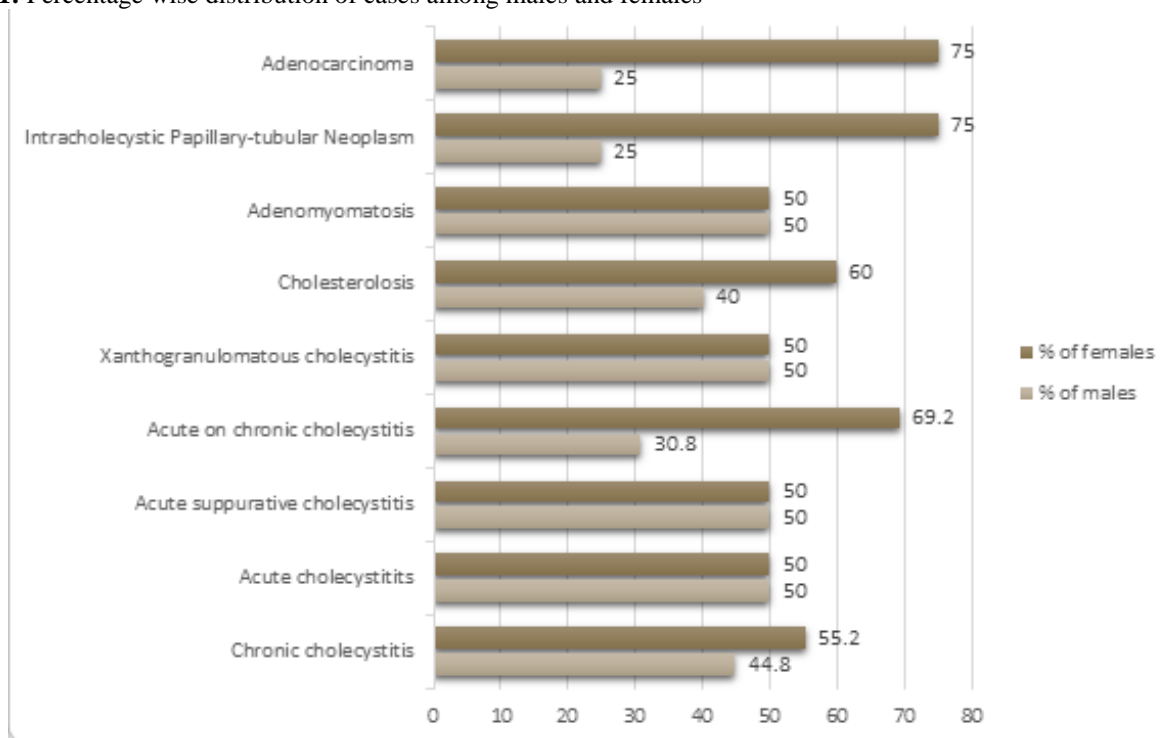
**Table 2:** Age and gender distribution

Age group (In Years)	No. of males (%)	No. of females (%)	Total (%)
0-20	23(5.3%)	18 (4.2%)	41 (9.5%)
21-40	34(7.9%)	120 (27.9%)	154 (35.8%)
41-60	30(7%)	105 (24.5%)	135 (31.5%)
61-80	28(6.5%)	30 (7%)	58 (13.5%)
81-100	21(4.9%)	21 (4.9%)	42 (9.7%)
Total	136(31.5%)	294 (68.5%)	430 (100%)

**Table 3:** Gall bladder lesions and their association with cholelithiasis

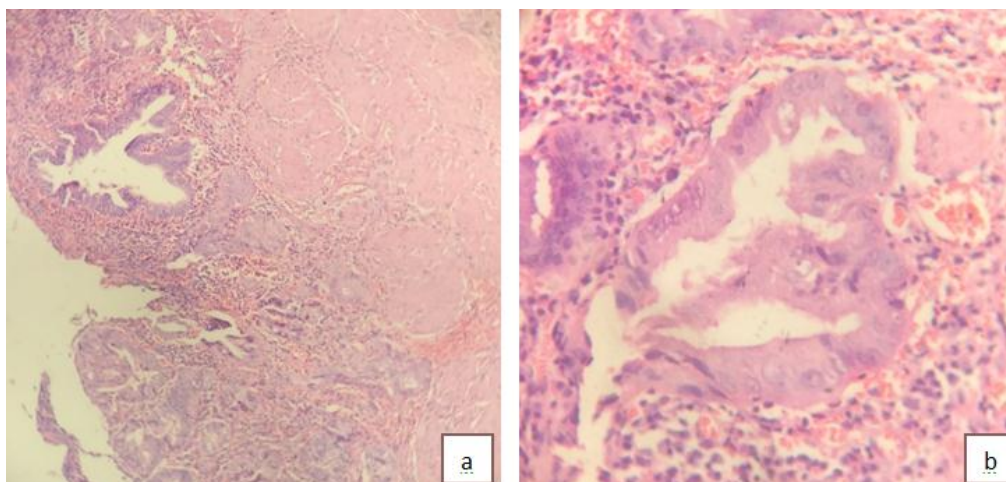
Histopathological diagnosis	No. of cases with stones (%)	Total no. of cases
Chronic cholecystitis	279(71%)	393
Cholesterolosis	02(40%)	05
Acute on chronic cholecystitis	11(84.6%)	13
Xanthogranulomatous cholecystitis	03(75%)	04
Adenocarcinoma of gall bladder	02(50%)	04

**Chart 1:** Percentage wise distribution of cases among males and females

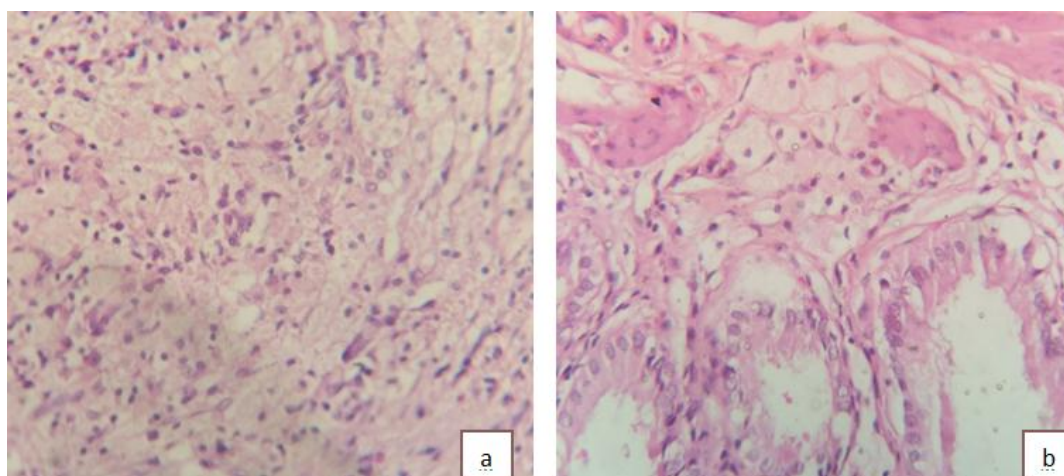


**Table 4:** Comparison between the present study and the articles quoted in the study

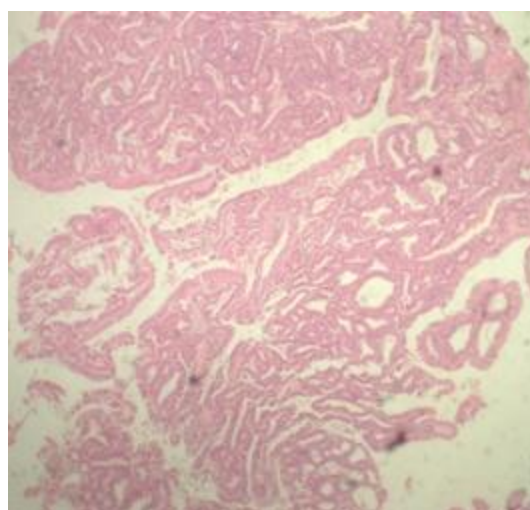
Study	Year	Sample size	Male to female ratio	Incidence of carcinoma (%)
Awasthi et al. <sup>1</sup>	2014	732	1:2.6	-
Sangwan MK et al. <sup>2</sup>	2015	530	1:6.07	1.9
Jha et al <sup>5</sup>	2016	4800	1:2.3	0.41
Tiwari A. et al <sup>6</sup>	2016	800	1:9	1.25
Sharma I et al <sup>7</sup>	2015	348	1:2.8	0.94
Vikash Talreja et al <sup>8</sup>	2015	973	-	1.14
Dincel, et al <sup>9</sup>	2016	1294	1:3.7	0.4
Bharathi et al <sup>10</sup>	2016	252	1:2.2	1.6
Sharma et al <sup>11</sup>	2008	863	1:2.2	1.97
Dipti Kalita et al <sup>12</sup>	2012	4115	0.87:1	0.44
Kini H et al <sup>13</sup>	2007	400	1:1.33	1.25
Present study	2019	430	2:2.2	0.9



**Fig. 1:** (1a, 1b); Chronic cholecystitis: Microscopically, it shows infiltration of mononuclear cells, fibrosis with smooth muscle hypertrophy. (H&E 400X) Acute cholecystitis: Microscopically, there is hyperaemia, oedema, and extravasation of red blood cells.(H&E 400X)

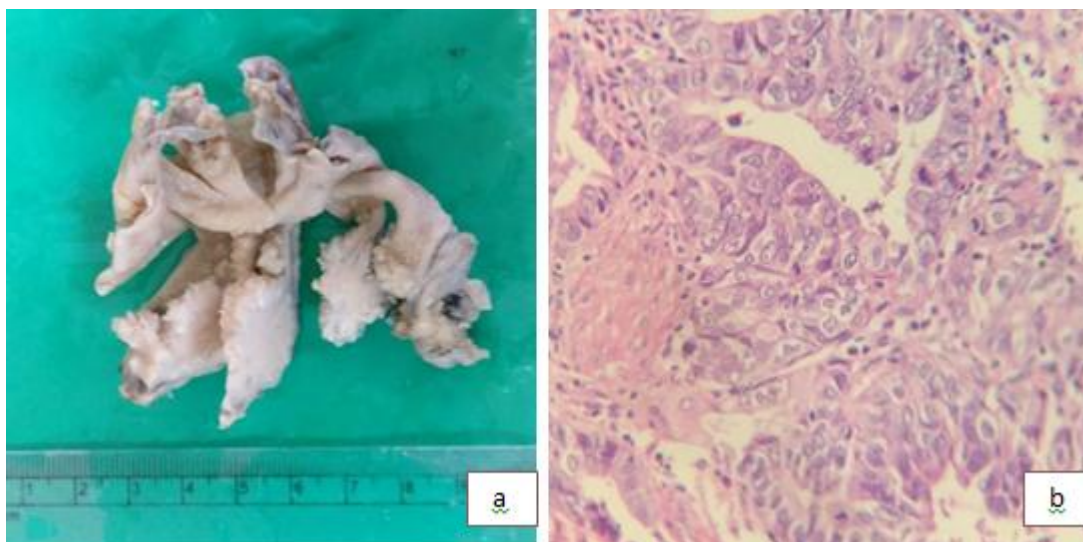


**Fig. 2:** (2a,2b)- Xanthogranulomatous cholecystitis: Microscopically shows diffuse collection of foamy macrophages mixed with chronic inflammatory cells. (H & E 400X). Cholesterolosis: Microscopically, showing presence of lipid laden foamy cells in the tips of villi with insignificant inflammation. (H & E 400X)

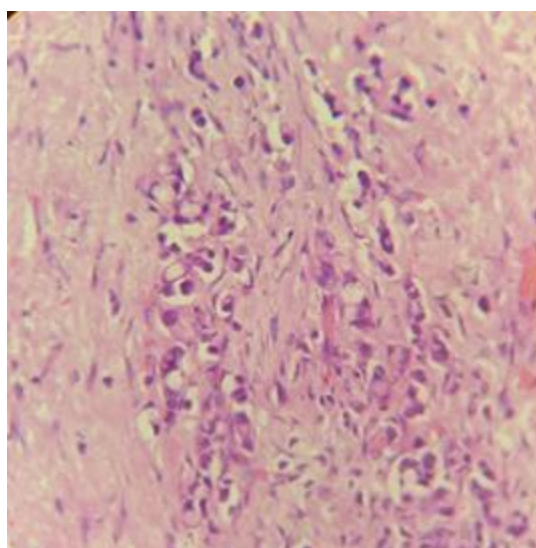


**Fig. 3:** Tubular Adenoma: Microscopically shows glandular epithelial proliferation forming tubules. (H & E 400X)





**Fig. 4:** (4a,4b); Gall bladder adenocarcinoma showing irregular greyish white growth with diffusely thickened wall. Adenocarcinoma of gall bladder: well-formed irregular infiltrative glands with wide lumina by anaplastic epithelial cells having hyperchromatic pleomorphic vesicular nuclei and prominent nucleoli. (H & E 400X)



**Fig. 5:** Signet ring type of adenocarcinoma: Microscopically, shows many cells having intracellular mucin with nuclei pushed to the periphery. (H & E 400X)

### Conclusion

Present study included 430 cases of cholecystectomy specimens which showed female predominance (68.5%) and majority cases (35.8%) belonged to 3<sup>rd</sup> and 4<sup>th</sup> decades of life.

Cholelithiasis was contributory to majority (60%) of lesions of gall bladder. Non-neoplastic lesions were commoner, in which chronic cholecystitis was the most common diagnosis; whereas the neoplastic lesions consisted of adenomas and incidentally detected adenocarcinomas.

Therefore, thorough sampling and meticulous microscopic examination of every cholecystectomy specimen is essential to detect flat dysplasia or incidental invasive carcinoma for better management and prognosis of the patient.

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**Conflicts of interest:** None.

### References

1. Awasthi N. A retrospective histopathological study of cholecystectomies. *Int J Health Allied Sci* 2015;4(3):203.
2. Sangwan MK, Sangwan V, Garg MK, Singla D, Malik P, Duhan A et al. Incidental carcinoma of gallbladder in north India: is routine histopathology of all cholecystectomy specimens justified?. *Int Surg J* 2016;2(4):465-70.
3. Rosai J, Ackerman S. Surgical pathology. Eleventh edition, Mosby. 2018.
4. Jamal K, Ratansingham K, Siddique M, Nehra D. Routine histological analysis of a macroscopically normal gallbladder— A review of the literature. *Int J Surg* 2014;12(9):958-62.
5. Jha V, Sharma P, Mandal KA. Incidental gallbladder carcinoma: Utility of histopathological evaluation of routine

- cholecystectomy specimens. *South Asian J Cancer* 2018;7(1):21.
6. Tiwari A, Rai R, Jain SK. Importance of Routine Histopathological Examination of Gallbladder Specimen in Detecting Incidental Malignancies. *J Lumbini Med Coll* 2016;30;4(1):15-9.
  7. 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* 2014;3:3553-7.
  8. Talreja V, Ali A, Khawaja R, Rani K, Samnani SS, Farid FN et al. Surgically resected gall bladder: is histopathology needed for all?. *Surg Res Pract* 2016;2016.
  9. Dincel O, Goksu M, Hatipoglu HS. Importance of routine histopathological examination of a gallbladder surgical specimen: Unexpected gallbladder cancer. *J Cancer Res Ther* 2018;14(6):1325.
  10. Bharathi IV, Devi PU, Lakshmi AB. Study of cholecystectomy specimens over a period of one year in tertiary care centre. *Int J Res Med Sci* 2017;5: 916-21.
  11. Sharma JD, Kalita I, Das T, Goswami P, Krishnatreya M. A retrospective study of post-operative gall bladder pathology with special reference to incidental carcinoma of the gall bladder. *Int J Res Med Sci* 2014;2(3):1050-3.
  12. Kalita D, Pant L, Singh S, Jain G, Kudesia M, Gupta K et al. Impact of routine histopathological examination of gall bladder specimens on early detection of malignancy-a study of 4,115 cholecystectomy specimens. *Asian Pac J Cancer Prev* 2013;14(5):3314-8.
  13. Kumar H, Kini H, Tiwari A. Histological evaluation of 400 cholecystectomy specimens. *J Pathol Nepal* 2015;14;5(10):834-40.
  14. Kumar V, Abbas AK, Aster JC. Robbins basic pathology book. Elsevier Health Sciences; 9<sup>th</sup> edition, 2017 Mar 8.

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