Histopathological Study of Gallbladder Disease in Tertiary Care Centre

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Abstract: <u>Background</u>: Disorder of gallbladder affect significant population in world. Gallbladder is affected by inflammation, infection, benign and malignant conditions. Most of are due to cholelithiasis where females are affected more than male. The present study aim to delineate the occurrence of various gallbladder histopathology. <u>Aim</u>: To study the histopathological lesions of gallbladder in cholecystectomy specimens. To determine the age and sex distribution among patients with lesions. <u>Materials and Methods</u>: A study was conducted from may 2021 to october 2021 in department of pathology. Total 200 cases of cholecystectomy specimens were preserved in 10% neutral buffered formalin, surgically dissected, processed, stained using hematoxylin & eosin stain and evaluated. <u>Results</u>: The most common histopathological diagnosis was chronic cholecystitis followed by acute cholecystitis. Female preponderance was observed in all gallbladder diseases. The present study carried out in our institution showed gall bladder malignancy was uncommon. <u>Conclusions</u>: Almost all cases of gallbladder lesions are inflammatory in origin and of which the most common cause causing diseases was chronic calculous cholecystitis. Malignancy is uncommon and presents late in the course with the nonspecific symptoms, which can misguide the clinicians. Diagnosis of malignancy was made only by Histopathological examinations.

Keywords: Cholecystitis, Chronic inflammation, Gall stones

1. Introduction

Gall bladder is small pear-shaped sac located underneath the liver. It stores and concentrates the bile which helps in digestion of fat. ^(1,2,3) It also secrets the mucus-approximately 20 ml is produced per day. ^(4,5) The wall of gall bladder is composed of three layers, namely mucosa, muscular and peri muscular layers. Unlike other parts of gastrointestinal tract, the gall bladder does not have a muscularis mucosa and submucosa. ⁽⁶⁾





Disease of gallbladder is one the common gastrointestinal manifestation encountered worldwide. Because of westernization of lifestyle, incidence of gall stones is increasing in India. Hence, gallbladder is the frequent surgical specimen in most of the histopathology laboratories. Gall bladder disease is more common in females than in males. $^{\left(7\right)}$

The gall bladder is affected by a variety of pathological processes ranging from congenital anomalies, all too familiar cholelithiasis and its complications, inflammatory lesions and the rare neoplastic ones. ^(8,9,10)

Gall stone disease is one of the major gastrointestinal disorders, which is mainly due to metabolic problems of hepato-biliary system.⁽¹¹⁾

Risk factors involved in occurrence of gallbladder stones diseases can be classified as modifiable and nonmodifiable. Sedentary lifestyle, obesity, metabolic syndrome, parity and pregnancy, high fat & low fiber diet can be included in modifiable causes, where nonmodifiable risk factors include age, female sex preponderance, hereditary and ethnicity.

Lesions of gallbladder can be divided into two broad categories which include non-neoplastic & neoplastic lesions. Histopathological study of gallbladder is important diagnostic modality for differentiation of nonmalignant from malignant tumors. The Rare and most fearsome complication of gallstone disease is carcinoma, since it carries the worst prognosis notably when diagnosed at a later course of the disease.

Histopathological study of gall bladder is important diagnostic modality for differentiation of non-malignant

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from malignant tumors.

2. Aims and Objectives

- To study the Histopathological lesions of gallbladder in cholecystectomy specimens.
- To determine the age and sex distribution among patients with the lesions.

3. Materials and Methods

3.1 Sources of data

The present study is a observational study consists of 200 cases of gallbladder lesions conducted at B.J medical College, civil hospital, Ahmadabad, Gujarat state of India during the periods of may 2021 to October 2021.In each cases details history regarding age, sex, clinical history and radiological findings were taken. Every specimen of gallbladder received in our institute is properly preserved in 10% neutral buffered formalin, surgically dissected, processed & staining was done by hematoxylin and eosin and slide were prepared. During microscopic examination, light microscope was used for the diagnosis of various lesions.

3.2 Inclusion criteria

All cholecystectomy specimens received in the department of pathology in our institute during may 2021 to October 2021.

3.3 Exclusion criteria

Fully or partially autolyzed organs not taken for this study.

4. Observations and Results

 Table 1: Distribution of gallbladder lesions according to clinical features:

Symptoms	Number of cases	Percentage
Pain in abdomen	182	91 %
Nausea	11	5.5 %
Vomiting	30	15 %
Weight loss	2	1 %
Anorexia	2	1 %
Fever	7	3.5 %
Jaundice	13	6.5 %

In our study patients presented with varied symptoms like pain in abdomen, nausea/vomiting, jaundice, fever, weight loss and anorexia. Majority of the patients presented with pain abdomen and nausea/vomiting. Out of 200 cases 91% (182 cases) patients were complaining of pain in abdomen, followed by vomiting in 15 % (30 cases) of cases. (Table 1).

Table 2: Age & Sex wise distribution in gallbladder

diseases						
Age(years)	Percentages					
0-10	1	3	2 %			
11-20	3	5	4 %			
21-30	9	19	14 %			

31-40	13	30	21.5 %
41-50	14	30	22 %
51-60	13	26	19.5 %
61-70	10	26	18 %
71-80	2	5	3.5%
81-90	1	2	1.5 %
Total	66(33%)	134(67%)	200(100%)

Age of the patients in the present study ranged from 0 year to 85 years with a mean age of 44.67 years. Most common age group affected was 5th decade and 4th decade with 44 cases (22 %) in 5th decade and 43 cases (21.5%) in 4th decade, followed by 6th decade with 39 cases (19.5%). (Table 2).

Age	Gallbladder without calculi	Gallbladder with calculi
0-10	4	0
11-20	3	5
21-30	5	23
31-40	10	33
41-50	11	33
51-60	14	25
61-70	8	16
71-80	3	4
81-90	1	2
Total	59	141

Among the patients with gallbladder showing calculi in the present study, patients of 4^{th} and 5^{th} decade (each had 33 cases, 16.5%) were commonly affected, followed by 6th decade (16 cases, 8%) and least was in 9th decade (2 cases, 1%). Patients of first decade had no calculi. (Table 3).

Table 4: Distribution of various lesions of Gallbladder:

Histonathological lesions	Number	Percentage
Thistopathological resions	of cases	of cases
1)Congenital anomalies		
Biliary atresia	1	0.5%
Choledochal cyst	3	1.5%
2)Inflammatory-non infectious		
Acute cholecystitis	12	6%
Acute on chronic cholecystitis	13	6.5%
Chronic cholecystitis	152	76%
Gangrenous cholecystitis	1	0.5%
Nonspecific inflammation	2	1%
Xantho granulomatous cholecystitis	1	0.5%
Lymphoplasmacytic cholecystitis	1	0.5%
3)Inflammatory-infectious		
Empyema of gallbladder	2	1%
4)Non-neoplastic		
Spongioid hyperplasia	1	0.5%
Adenomyomatous hyperplasia	1	0.5%
5)Neoplastic		
1)Premalignant lesion		
Biliary intraepithelial neoplasm	2	1%
Intracholecystic papillary neoplasm	1	0.5%
2)Primary malignant lesions	5	2.5%
Adenocarcinoma	1	0.5%
Adeno squamous Carcinoma		
3)Secondary malignant lesions (Metastatic	1	0.5%
carcinoma)		
Total	200	100%

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Out of total 200 cases, majority of the study population were having chronic cholecystitis (152 cases, 76 %), followed by acute on chronic cholecystitis (13 cases, 6.5%), acute cholecystitis (12 cases, 6%), congenital anomalies (choledochal cyst 3 cases, 1.5 %; biliary atresia 1 cases, 0.5%), xanthogranulomatous cholecystitis(1 cases, 0.5%), non-neoplastic tumor like conditions spongioid hyperplasia (1 cases,0.5%), adenomyomatosis 1 case(0.5%), nonspecific inflammation (2 cases, 0.5%), gangrenous cholecystitis (1 cases, 0.5 %), empyema of gallbladder (2 cases, 1%)(Table 4).



Figure 1: Microscopy of Acute cholecystitis (4x)



Figure 2: Microscopy of Chronic cholecystitis (4x)



Figure 3: Microscopy of Xanthogranulomatous Cholecystitis (4x)



Figure 4: Microscopy of Well differentiated Adenocarcinoma (4x)



Figure 5: Microscopy of Moderately differentiated Adenocarcinoma (4x)



Figure 6: Microscopy of Adeno-squamous carcinoma (4x)

5. Discussion

The observations and results of the patients in present study were compared with various similar studies and findings were discussed below.

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Table 5: Comparison of most common clinical symptoms of the present study with various study:						
Various study	Chitra Singh et $al^{(12)}$ (2018)	Kanetkar et al ⁽¹³⁾ (2020)	Mahajan et al ⁽¹⁴⁾ (2018)	Percentage		
Pain in abdomen	32.69	100%	98.93%	91 %		
Nausea	5.8	-	-	5.5%		
Vomiting	17.3	78%	23.93%	15 %		
Weight loss	10.6	-	-	1%		
Anorexia	8.65	0.8%	-	1%		
Fever	19.2	8.5%	14.78%	3.5%		
Jaundice	2.9	3.8%	13.87%	6.5%		

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In present study most common symptoms of the patients were pain in abdomen (91%) which is correlated with other studies done by Chitra et al, Kanetkar et al, Mahajan et al.

Second most clinical feature is vomiting which is also second most common features in other studies. (Table 5).

Table 6: Comparison of mean age and sex ratio of the present study with other studies:

Study by	Navyashree et al ⁽¹⁵⁾ (2018)	Kanetker et al $^{(13)}$ (2020)	Chitra Singh et al ⁽¹²⁾ (2018)	Taneja et al $^{(16)}(2018)$	Talal et al ⁽¹⁷⁾ (2020)	Present study
Mean age (years)	47.5	50	42.41	45	45.77	44.67
Male	36.07%	47%	24.04%	24.5%	25.34%	33%
Female	63.93%	53%	75.96%	75.5%	74.66%	67%
Male:Female ratio	1:1.8	1:13	1:3.16	1:08	1:2.95	1:2.03

The mean age of the patients in our study was 44.67 years which was synonymous with other studies done by Navyashree et al, Chitra Singh et al, Taneja et al and Talal et al. Most of the cases included in the present study were female patients (67%) with Male: Female ratio being 1: 2.03. (Table 6)

Table 7: Comparison of status of gall stone and wall thickness of the present study with various study:

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Various study	Awasthi et al (18) (2015)	Kumari et al ⁽²⁾ (2018)	Pannaga et al ⁽¹⁹⁾ ((2018)	Present study		
Gall stone absent	4.8%	12.6%	22.5%	29.5%		
Gall stone present	95.2%	87.4%	77.5%	70.5%		

70.5% of the gall bladder have gall stone and 29.5% had not gall stone in present study which is similar to study done by

Pannaga et al, Awasthi et al and Kumari et al. (Table 7).

Table 8: Comparison of incidence of the Non-infectious inflammatory lesions of the present study with various study

Verious study	Kumari et al	Jokhi et al	Prithal G et	Chitra Singh et	Faran Khan et	Ahadi M et al ⁽⁶⁾	Present
v arious study	⁽²⁾ (2018)	⁽²⁰⁾ (2019)	al ⁽⁸⁾ (2020)	al ⁽¹²⁾ (20 18)	al ⁽²¹⁾ (2014)	(2020)	study
Acute cholecystitis	0.36 %	9.2%	1.45%	9.61%	0.31 %	16.22 %	6%
Acute on chronic cholecystitis	3.82 %	-	1.3%	2.88%	4.25 %	9.37 %	6.5%
Chronic cholecystitis	89.09 %	82.30 %	92%	69.23 %	89.1 5%	64.9 %	76%
Gangraneous cholecystitis	-	0.8%	0.8%	-	-	9.57 %	0.5%
Xanthogranulomatous cholecystitis	1.64 %	2.3%	3.7%	0.96%	0.1 %	0.4%	1%
Lymphoplasmacytic cholecystitis	0.18 %	-	-	-	-	-	0.5%

In present study 6 % cases of acute cholecystitis of gall bladder which was higher than studies done by Kumar et al, Talal et al Prithal G et al and Faran Khan et al. Most of the

cases were chronic cholecystitis (76%) in present study which was correlate with other studies. (Table 8).

Table 9: Comparison of incidence of the premalignant lesions of the gall bladder in present study with various study

Various study	PrithalG et al ⁽⁸⁾ (2019)	Tekeşin K et al (22) (2018)	Jaswant Singh etal ⁽²³⁾ (2018)	Present study
Biliary intraepithelial neoplasm	-	0.13%	1.03%	1%
Intracholecystic papillary neoplasm	0.25%	-	-	0.5%

Total 1 % of cases had biliary intraepithelial lesions in present study. 0.13% of cases have BiIIN in study done by Tekesin et al and 1.03% in study done by Jaswant Singh et al. Intracholecystic papillary neoplasm was seen in 0.5 % of cases in present study and 0.25% in study done by Prithal G et al. No cases of ICPN in study done by byTekesin et al and Jaswant Singh. (Table 9)

Table 10: Comparison of incidence of the primary malignant lesions of the gall bladder in present study with various study:

Various study	Chitra Singh et al $^{(12)}(2018)$	Alok Mohan et $al^{(24)}(2018)$	Faran Khan et al $^{(21)}$ (2014)	Agrawal et al ⁽⁷⁾ (2018)	Present study
Adenocarcinoma	6.73%	1.36%	0.21%	9.8%	2.5%
Adenosquamous carcinoma	0.96%	0.07%	-	0.2%	0.5%

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In present study 2.5 % of the cholecystectomy specimens had adenocarcinoma, which is correlate with study done by Alok Mohan et al. Adenosquamous carcinoma was seen in 0.5 % of cases in our study which was correlate with study done by Chitra Singh et al, Alok Mohan et al and Agrawal et al. Study done by Faran khan et al, there was no case of adenosquamous carcinoma. (Table 10).

Secondary metastatic malignancy: 0.18% Secondary malignancy seen in study done by Kumari et al² which is correlate with our study (0.51%).

6. Conclusion

Gall bladder disease demonstrated diverse spectrum of histopathological changes in cholecystectomy specimens. In agreement with other studies, the current study affirmed that it showed female Preponderance. The study wishes to emphasize that chronic cholecystitis should always be considered as one of the first line diagnosis whenever middle-aged females presenting with abdominal pain. Majority of the gallbladder lesions were non-neoplastic, of which chronic cholecystitis formed the major bulk.

Hence, the present study emphasized the need to examine all the cholecystectomy specimens and thorough sampling of thickened portion as well as any suspicious area in the gallbladder specimen should be done, in order to avoid missing gallbladder carcinoma cases.

Conflict of interest: None

Source of funding: self

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