

Original Research

A Retrospective Assessment of Different Histopathological Patterns as Diagnosed in Various Gall Bladder Lesions; An Original Study

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ABSTRACT:

Aim: This retrospective study was aimed to study different histopathological patterns as diagnosed in various gall bladder lesions.

Materials & Methods: This study was conducted during 2019 (Jan-Oct) in the department of pathology, career institute of medical science and hospital, Lucknow. Total 200 specimen of cholecystectomy were studied for histopathological changes and diagnosis. Study slides were prepared by routine methods utilizing standard protocols. This study included non neoplastic and neoplastic gall bladder lesions. Acalculous and calculous gall bladder both type of specimen were included in study.

Statistical Analysis and Results: Statistical analysis was done by statistical software Statistical Package for the Social Sciences (SPSS). The resultant data was sent to suitable statistical tests to achieve p values, mean, standard deviation, standard error and 95% CI. $P \leq 0.05$ was considered as statistically significant. All patients were further separated into three age groups. 20 specimens were noted with single stone while 120 specimens were identified with multiple stones. Total 60 specimens did not show any stone in their examinations. Maximum 85 specimens were confirmed for Chronic Cholecystitis with Cholelithiasis with multiple stones followed by Acalculous Chronic Cholecystitis.

Conclusion: Histopathological assessments confirmed that non neoplastic lesions are common in which chronic cholecystitis with cholelithiasis is commonest lesion. Moreover, neoplastic lesions are uncommon lesion in which adenocarcinoma are rare lesion. These data was only limited to the studied specimens of a particular territory therefore, author recommend other studies to be conducted on larger sample and on wider geographical area.

Key words: Cholecystitis, Histopathology, Gall Bladder, Cholecystectomy

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INTRODUCTION

Literature has well evidenced that gall bladder diseases (GBD) are very common in females than in males.¹ Particularly in India; the age range of patients distressing from gall bladder diseases is usually in between 12-78 years. As a proven fact, gall bladder diseases is more common in the Northern and North eastern states of Uttar Pradesh, Bihar, Orissa, West Bengal and Assam.² The different risk factors usually associated with these dilemmas are dietary pattern, life style, obesity and water intake. Gall bladder is a pear shaped structure lying on the visceral surface of right lobe of liver.³ Histologically, it is lined by the tall columnar epithelium bathed with mucus which

separates the mucosal cells from the bile.⁴ It has three layers namely mucosa, muscularis and adventitia.⁵ Cholelithiasis is the commonest etiology throughout the world. There is variation in the prevalence of cholelithiasis according to the age, sex and ethnicity.⁶ In India, the prevalence of cholelithiasis is between 2-29% while in Northern India, it is more prevalent that's why Northern India is known to be as stone belt. Cholelithiasis is a multifactorial disease⁷, more prevalent in fatty fertile females of forty years until menopause but can occur in children and males also. Additional factors include age, genetic susceptibility, obesity, insulin resistance, alcohol consumption, increased triglyceride level, pregnancy and various

drugs. Ascorbic acid and Calcium, consumption of unsaturated fats and dietary fibres have the protective effect.⁸ Gall stones are responsible for the irritation of the columnar epithelium and is the main underlying cause for a number of histopathological changes like acute and chronic cholecystitis, cholesterosis and pre-neoplastic conditions like metaplasia and dysplasia, ultimately culminating into the neoplasia.^{6,9,10} That's why, patients with cholelithiasis need proper surveillance as most of the carcinoma of gall bladder are found in association of the stones.^{11,12} As the most of the patients are asymptomatic, gall bladder carcinoma is often diagnosed late incidentally on histopathological examination accounting for the grave prognosis. Carcinoma gall bladder accounts for only 3% of all gastrointestinal malignancies. It is seen in patients of age more than 50 years and also more prevalent in females like other gall bladder pathologies. As it is diagnosed frequently in late stage, it has 5 year survival rate of only 1-5%. Most carcinomas are adenocarcinoma (approximately 84%), rest include adenosquamous, squamous and other rarer type of carcinoma.¹³ Such type of gallbladder wall has been identified in histopathological sections of 75-93% of calculus related cases. Cholelithiasis is a universal medical crisis, but the prevalence rates show substantial geographical variation, with the lowest rates reported in African populations.¹⁴ In most cases, they do not cause symptoms, and only 11% and 21% will eventually become symptomatic within 5 years and 20 years of diagnosis, respectively.¹⁵ Non-neoplastic lesions of gall bladder include acute or chronic cholecystitis, hydrops, cholesterosis (strawberry gallbladder), cholesterol polyps and porcelain gallbladder. Among the pre-malignant lesions the various entities included are polyp, adenoma, hyperplasia, metaplasia (antral or intestinal), dysplasia and xanthogranulomatous cholecystitis.^{16,17} This retrospective study was attempted to study different histopathological patterns as diagnosed in various gall bladder lesions.

MATERIALS & METHODS

This retrospective study was planned, outlined and executed during 2019 (Jan-Oct) in the department of pathology, career institute of medical science and hospital, Lucknow. Initially, two hundred twenty new specimens were selected from the department. All specimens were related to different gall bladder pathologies. Pure randomized sampling procedure was used in the selection procedure. Depending upon specimen's quality and specifications of slides, total 200 specimen of cholecystectomy were studied for histopathological changes and diagnosis. Study slides were prepared by routine methods utilizing standard protocols. This study included non neoplastic and neoplastic gall bladder lesions. Acalculous and calculous gall bladder both type of specimen were included in the study. Non neoplastic lesions were with acute cholecystitis, chronic cholecystitis,

eosinophilic cholecystitis, cholesterosis, xanthogranulomatous cholecystitis, lymphoplasmacytic cholecystitis and porcelain gall bladder. Neoplastic lesion included hyperplastic gall bladder, adenocarcinoma gall bladder (stage-1), adenocarcinoma gall bladder with clear cell changes. All types of gall bladder diseases were studied comprehensively for their incidence, frequency and other related parameters. Allocation of specimens as per gall bladder calculus also attempted. Figure 1 is showing chronic cholecystitis with Rokitansky Aschoff Sinus. Figure 2 is showing acute cholecystitis with edematous, haemorrhagic and sloughed out mucosa. Figure 3 is showing cholesterol clefts with bile deposition with foamy macrophages- chronic cholecystitis with cholesterosis. Figure 4 is showing porcelain gall bladder with atrophied mucosa, calcium deposition and eosinophilic hyalinized wall. Figure 5 is showing Papillary Adenocarcinoma of gall bladder infiltrating upto serosa. (stage-I). Figure 6 is showing Adenocarcinoma of gall bladder with clear cell changes. Results thus received was compiled in table and subjected to basic statistical analysis. P value less than 0.05 was considered significant ($p < 0.05$).

STATISTICAL ANALYSIS AND RESULTS

In the current study, all obvious findings and data were gathered in logical manner. Compiled data was sent for statistical analysis using statistical software Statistical Package for the Social Sciences version 21 (IBM Inc., Armonk, New York, USA). The processed data was subjected to suitable statistical tests to obtain p values, mean, standard deviation, chi-square test, standard error and 95% CI. Table 1 and Graph 1 showed that out of 200 specimens, males were 42 and females were 158. All patients were further separated into three age groups. 90 specimens were found in the age range of 20-40 years. P value was not significant here. 95 specimens were noticed in the age range of 40-60 years. P value was significant for this age group; also this age range is most common for gall bladder diseases. Accordingly, it can be presumed that roughly 92 percent of the studied specimens were in first and second age groups. Table 2 illustrated allocation of specimens as per gall bladder calculus. 20 specimens were noted with single stone while 120 specimens were identified with multiple stones. Total 60 specimens did not show any stone in their examinations. Table 3 is explaining about diagnosis of different gall bladder lesions as confirmed by histopathological assessment (with their incidence in the studied specimens). Maximum 85 specimens were confirmed for Chronic Cholecystitis with Cholelithiasis with multiple stones followed by Acalculous Chronic Cholecystitis (33) and Chronic cholecystitis with cholesterosis (20). Table 4 showing the fundamental statistical description with level of significance evaluation using pearson chi-square test. P value was significant for specimen id 1, 3, 4 and 6.

Figure 1; Photomicrograph showing chronic cholecystitis with Rokitansky Aschoff Sinus

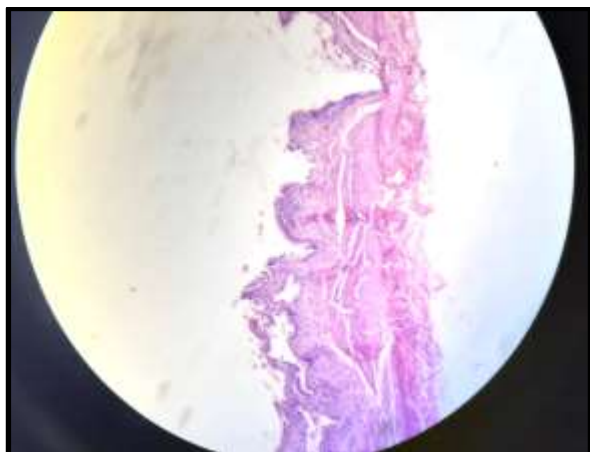


Figure 4; Photomicrograph showing porcelain gall bladder with atrophied mucosa, calcium deposition and eosinophilic hyalinized wall

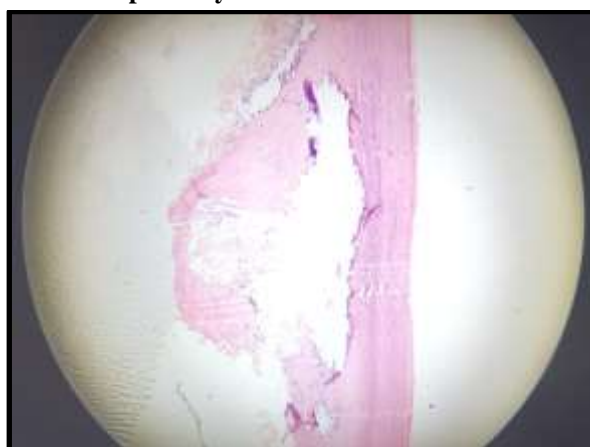


Figure 2; Photomicrograph showing acute cholecystitis with edematous, hemorrhagic and sloughed out mucosa

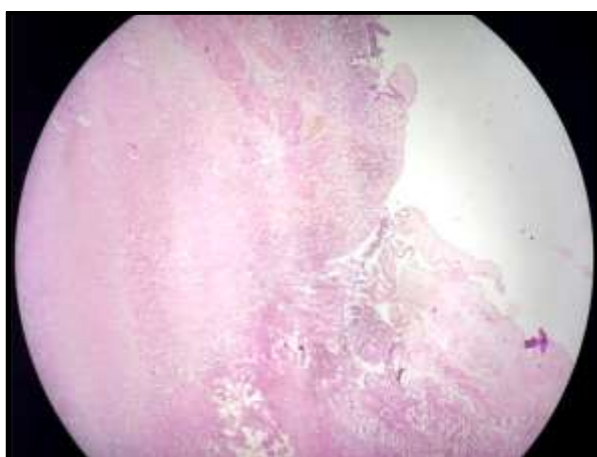


Figure 5; Photomicrograph showing Papillary Adenocarcinoma of gall bladder infiltrating up to serosa. (Stage; I)

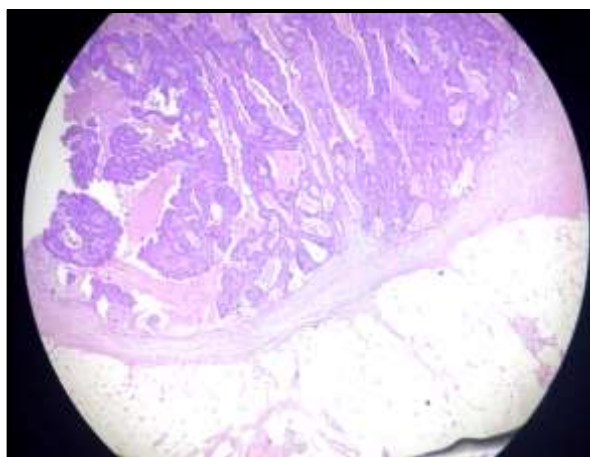


Figure 3; Photomicrograph showing cholesterol clefts with bile deposition with foamy macrophages- chronic cholecystitis with cholesterosis

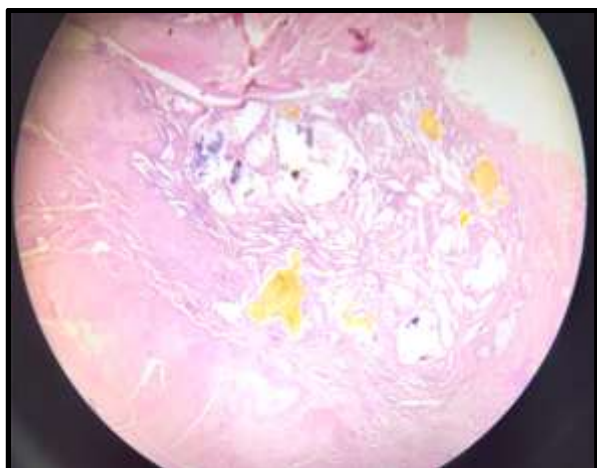
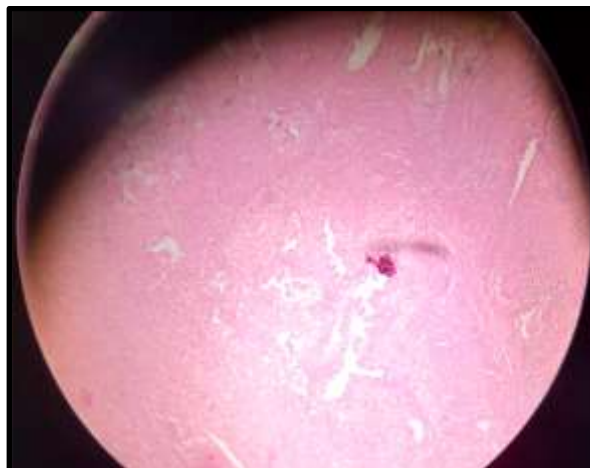


Figure 6: Photomicrograph showing Adenocarcinoma of gall bladder with clear cell changes



Graph 1: Age & gender wise distribution of specimens

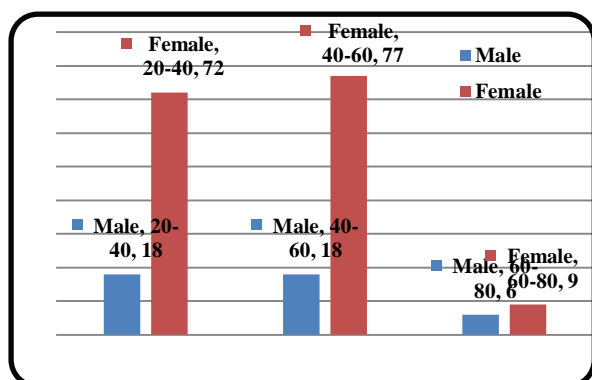


Table 1: Age & gender wise allocation of specimens

Age Group (Yrs)	Male	Female	Total	P value
20-40	18	72	90	0.70
40-60	18	77	95	0.01*
60-80	6	9	15	0.08
Total	42	158	200	*Significant

Table 2: Allocation of specimens as per gall bladder calculus

Gall Bladder Calculus	Specimens (n)
Single stones	20
Multiple Stones	120
No Stones	60
Total	200

DISCUSSION

Researchers across the globe have stated that gall stones are one of the main causes of morbidity and mortality affecting 11% of all adult people. Different epithelial pathological changes in the gall bladder mucosa can be ruled out with the help of clinico-radiological examination and extensive histological evaluation to prevent cancer related morbidity and mortality.¹⁸ According to the study conducted by Srivastav et al, gall bladder disease was commonest lesion and was seen in 77.9% of all cholecystectomy specimens in the present study. These finding were in accordance with our outcomes.¹⁹ Bansal and colleagues stated that gall bladder diseases are associated with varied histopathological lesions in cholecystectomy specimens. Non-neoplastic (inflammatory) lesions of GB are far more common than neoplastic lesions. The histopathological findings seen in chronic cholecystitis were lymphocytic

Table 3: Diagnosis of different gall bladder lesions as confirmed by histopathological assessment (with their incidence in the studied specimens)

Specimen Group ID	Diagnosis	n=200
1	Chronic Cholecystitis with Cholelithiasis with single stone	9
2	Chronic Cholecystitis with Cholelithiasis with multiple stones	85
3	Acalculous Chronic Cholecystitis	33
4	Chronic cholecystitis with cholesterosis	20
5	Chronic Follicular Cholecystitis	6
6	Xanthogranulomatous Cholecystitis	12
7	Acute Cholecystitis	18
8	Acute Eosinophilic Cholecystitis	5
9	Porcelain Gall Bladder	6
10	Adenocarcinoma	3
11	Mucinous Adenocarcinoma	1
12	Adenocarcinoma with clear cell changes	1
13	Lymphoplasmacytic Cholecystitis	1

infiltration and fibrosis with thickening of GB wall; few showed denuded mucosa with atrophy. Other histopathological findings accompanying chronic cholecystitis were cholesterosis, Xanthogranulomatous cholecystitis.²⁰ Similar inferences were put forwarded by Devi and co workers in 2017.²¹ However, Carey has already described that gall bladder disease appeared to be increasing in incidence over past couple of decades in India and western world due to increased intake of fatty and high calorie diet and sedentary lifestyle.²² According to Khan et al, in non-neoplastic lesions, chronic cholecystitis with cholelithiasis contributed the majority of the cases, (75%) in the present study which was similar to the studies conducted in Chennai, (61.92%), whereas the study from Punjab showed 49.6%.²³ Gallbladder cancer continues to be a very rare entity. Even though some evidence suggests the possibility of diagnosing this malignant disease before pathology analysis, most centres continue to send every extracted gallbladder to the pathology department for its routine analysis.^{24,25} Singh and Lowenfels stated that this is mainly because of the lack of large and prospective studies that can give solid evidence to support the hypothesis that sending

every gallbladder to the pathologist is not always necessary.^{26,27}

Table 4: Fundamental statistical description with level of significance evaluation using pearson chi-square test

ID	Mean	SD	SE	95 % CI	PCS Value	df	p value
1	3.32	0.87	0.63	2.52	1.93	2.0	0.00 *
2	3.98	0.53	0.25	1.69	1.29	1.0	0.06
3	3.23	1.03	0.59	1.82	2.44	1.0	0.02 *
4	3.62	0.63	0.43	1.02	1.74	2.0	0.00 *
5	3.98	1.95	0.73	1.96	2.03	1.0	0.08
6	3.27	1.93	0.54	1.91	1.93	1.0	0.00 *
7	2.32	0.87	0.63	1.52	1.93	2.0	0.09
8	1.98	0.83	0.53	1.69	1.29	1.0	0.06
9	1.21	1.00	0.74	1.02	2.82	1.0	0.10
10	1.66	0.67	0.35	1.26	1.74	2.0	0.09
11	1.95	1.39	0.64	1.96	2.51	1.0	0.08
12	1.24	1.03	0.52	1.09	1.90	1.0	0.50
13	1.33	0.83	0.02	1.32	1.82	2.0	0.20

CONCLUSION

Within the limitations of the study, author has presented very significant facts. Histopathological assessments confirmed that non neoplastic lesions are common in which chronic cholecystitis with cholelithiasis is commonest lesion. Moreover, neoplastic lesions are uncommon lesion in which adenocarcinoma are rare lesion. These data was only limited to the studied specimens of a particular territory therefore, author recommend other studies to be conducted on larger sample and on wider geographical area. Inferences of this study could be judiciously utilized for clinical decision making and surgical planning. Chronic cholecystitis with cholelithiasis is very common lesion amongst gall bladder lesion. This lesion is associated with stones and stones are formed with the stasis of bile. So, life style changes could also prevent stasis of bile and

formation of stone. Long term stasis of stone could also change gall bladder mucosa and may cause neoplastic lesion. So, better to avoid fatty saturated food to prevent cholecystitis. Nevertheless, authors expect few other genuine studies wider parameters so as to establish concrete guidelines in these regards.

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