Print ISSN: 2321-6379
Online ISSN: 2321-595X

Original Article

Spectrum of Histomorphological Lesions of Gallbladder in Cholecystectomy Specimens: A cross-sectional Study

Deepak Munjal[1], Nikhilesh Kumar[2], Monika Gupta[3], R K Shrivastava[4], Honey Bhasker Sharma[5]

[1]Post Graduate 3rd Year Junior Resident, Department of Pathology, TS Misra Medical College and Hospital, Lucknow, Uttar Pradesh, India, [2]Professor and Head, Department of Pathology, TS Misra Medical College and Hospital, Lucknow, Uttar Pradesh, India, [3]Professor, Department of Pathology, TS Misra Medical College and Hospital, Lucknow, Uttar Pradesh, India, [4]Professor, Department of Surgery, TS Misra Medical College and Hospital, Lucknow, Uttar Pradesh, India, [5]Associate Professor, Department of Pathology, TS Misra Medical College and Hospital, Lucknow, Uttar Pradesh, India

Abstract

Background: Gallbladder (GB) diseases are one of the most common digestive system diseases that include chronic cholecystitis, cholesterolosis, xanthogranulomatous cholecystitis (XGC), and malignant lesions as adenocarcinoma.

Aims and objectives: (1) The aim of the study was to study the range of histomorphological lesions in Cholecystectomy specimens, (2) to determine the age and sex distribution among patients with the lesions, (3) to ascertain the frequency of various histopathological benign and malignant lesions in cholecystectomy specimens, and (4) to evaluate the status of epidermal growth factor receptor expression in encountered adenocarcinoma GB cases.

Materials and Methods: In present study, we have studied total 170 cases of GB lesion during the period of 18-month study from January 2021 to June 2022 in the Department of Pathology at T.S. Misra Medical College and Hospital, Lucknow.

Results: GB lesions were more common in females as compared to male with a male: female ratio of 1:4.15. Among 61–70-year age group, males were more than females. In all other age groups, females were more than males. Majority of the subjects presented with Chronic Cholecystitis (48.8%) and Chronic Cholecystitis with cholelithiasis (20.6%) along with few cases of low-grade dysplasia, high-grade dysplasia, poorly differentiated adenocarcinoma GB, and XGC also seen in our study. EGFR was given a score of 2+ in a case of chronic acalculous cholecystitis with high-grade dysplasia. EGFR was given a score of 3+ in both cases of poorly differentiated adenocarcinoma GB staging.

Conclusion: There is thus an overarching need for routine histopathological examination of the resected GB specimens to exclude premalignant ailments such as intestinal metaplasia and dysplasia. These lesions may progress to GB adenocarcinoma.

Keywords: Adenocarcinoma, Cholecystitis, Gallbladder

INTRODUCTION

The prevalence of gallbladder (GB) diseases is variable within India and ranges from 2% to 29%.[1] The spectrum of ailments that afflict the GB can be inflammatory, congenital, or neoplastic in nature.[2,3] Inflammatory conditions of the GB are more common than other GB pathologies and encompass a spectrum of ailments including acute, chronic, follicular, or xanthogranulomatous cholecystitis (XGC).[4,5] Cholelithiasis is one of the common health problems encountered all over the world causing economic burden in developing countries.[6] Cholelithiasis affect 10–20% of adult population in developed countries.[7] The risk factors for the development of gall stone disease (GSD) can be categorized as non-modifiable and modifiable.

Gallstones appear to be the most important risk factor, being reported in 70–98% cases of GB carcinoma, a far higher prevalence than that in age-matched general population.[8] GSD helps to develop the pathology in GB

Access this article online

www.ijss-sn.com

Month of Submission : 04-2023
Month of Peer Review : 04-2023
Month of Acceptance : 05-2023
Month of Publishing : 05-2023

Corresponding Author: Dr. Deepak Munjal, Department of Pathology, TS Misra Medical College and Hospital, Lucknow, Uttar Pradesh, India.

cells or tissues where GB carcinoma (GBC) is most fatal transformation. Hyperplasia and metaplasia of the GB are the precursors of dysplasia and dysplasia itself is a potential condition of carcinoma.[9] GB cancer (GBC) is most common malignancy of the biliary tract.[10] GB carcinoma ranks 5th in the gastrointestinal malignant tumors, and due to non-specific clinical presentation, it is rarely diagnosed at an early stage.[11] GB carcinoma is a rare condition. It is not very uncommon as an incidental histological finding following cholecystectomy for gallstone diseases.[12]

The incidence of GB carcinoma in India ranges 1.01/100,000 for males and 10.1/100,000 for females.[13] The biological behavior of carcinoma GB is based on certain well-established morphological features such as tumor size, site, grade, type, invasion, and metastatic state. Molecular markers, such as EGFR expressions along with other markers such as CEA, EMA, alpha fetoprotein, and CDX2, may also use to determine the behavior of tumor.[14] Thus, it is important to study histomorphological changes to determine the incidence, prevalence, and distribution of lesions. The present study was done to study the spectrum of histomorphological lesions of GB in cholecystectomy specimens.

MATERIALS AND METHODS

This cross-sectional observational study was conducted after clearance from the Board of Studies and Ethical committee in the Department of Pathology at T.S. Misra Medical College and Hospital, Lucknow. The total sample size was determined to be 170 patients. The study included all specimens of cholecystectomy-open and laparoscopic. The study excluded specimens without any clinical details, specimens too tiny or inadequate to evaluate, autolyzed specimens, and post-chemo/radiotherapy cases.

Patient's clinical data comprising clinical features and laboratory investigations reports were collected from medical records in surgically resected specimens. The specimen was fixed in 10% buffered formalin overnight. Gross findings of the outer surface of GB, mucosa, and any other gross lesions were noted. Mucosa was examined whether velvety, bile-stained, flattened with whitish streaks, any growth, ulceration, congestion, or polyp. Wall thickness was noted.

Sections were taken from the fundus, body-and-neck of the GB, additional sections were taken from abnormal appearing mucosa, thickened wall, ulcerated areas, or any growth if present. This were followed by processing with routine histopathological techniques for paraffin embedding and sectioning at 5-μ thickness. The tissue sections were placed on a slide warmer for deparaffiniation and further deparaffinization using xylene, followed by hematoxylin and eosin.

Inclusion Criteria

- All specimens of cholecystectomy-open and laparoscopic.

Exclusion Criteria

- Specimens without any clinical details
- Specimens too tiny or inadequate to evaluate
- Autolyzed Specimens
- Post-chemo/radiotherapy cases.

The following IHC protocol was used

- Score 0 = No staining is observed
- Score 1+ = Faint membrane staining in more than 1% of tumor cells in part of the cell membrane
- Score 2+ = Weak-to- moderate complete membrane staining in over 1% of tumor cells
- Score 3+ = Strong complete membrane staining in over 1% of tumor cells

The statistical tests were applied as follows: quantitative variables in any two groups were compared using independent t-test. Qualitative variables were correlated using Chi-square test/Fisher exact test.

RESULTS

Among study population, there were 27.6% of subjects from 18 to 30 years, 29.4% from 31 to 40 years, 20.6% from 41 to 50 years, 17.1% from 51 to 60 years, 4.1% from 61 to 70 years, and 1.2% from above 70 years. The mean age of the study population was 40.17 ± 12.52 (18–77) years [Table 1].

There were 33 (19.4%) males and 137 (80.6%) females with a male: female ratio of 1:4.15 [Table 2].

Among 61–70-year age group, males were more than females. In all other age groups, females were more than males [Table 3].

Table 1: Distribution of study population according to age groups

Age groups	Frequency	Percent
18–30 years	47	27.6
31–40 years	50	29.4
41–50 years	35	20.6
51–60 years	29	17.1
61–70 years	7	4.1
Above 70 years	2	1.2
Mean±SD	40.17±12.52 (18–77)	

Majority of the subjects presented with chronic acalculous cholecystitis (48.8%) and chronic cholecystitis with cholelithiasis (20.6%). There were 14 cases of low-grade dysplasia, 1 case of papillary hyperplasia with chronic acalculous cholecystitis and cholesterolosis and high-grade dysplasia and 2 cases of poorly differentiated adenocarcinoma GB each and 3 cases of XGC [Table 4 and Figures 1-3].

Table 2: Distribution of study population according to gender

Gender	Frequency	Percent
Male	33	19.4
Female	137	80.6
Total	170	100.0
Male: Female ratio	1:4.15	

Table 3: Distribution of study population according to age group

Age groups	Male	Female
18–30 years	5	42
	10.6%	89.4%
31–40 years	8	42
	16.0%	84.0%
41–50 years	9	26
	25.7%	74.3%
51–60 years	5	24
	17.2%	82.8%
61–70 years	5	2
	71.4%	28.6%
Above 70 years	1	1
	50.0%	50.0%

Table 4: Distribution of study population according to diagnosis

Diagnosis	Frequency	Percent
Chronic acalculous cholecystitis	83	48.8
Chronic cholecystitis with cholelithiasis	35	20.6
Chronic cholecystitis with cholelithiasis and cholesterolosis	30	17.7
Eosinophilic cholecystitis	1	0.6
Xanthogranulomatous cholecystitis	3	1.8
Papillary hyperplasia with chronic acalculous cholecystitis and cholesterolosis	1	0.6
Chronic cholecystitis with cholelithiasis and low-grade dysplasia	11	6.6
Chronic acalculous cholecystitis with xanthogranulomatous reaction with low-grade dysplasia	1	0.6
Acute on chronic cholecystitis with cholelithiasis and low-grade dysplasia	1	0.6
Eosinophilic cholecystitis with low-grade dysplasia and cholelithiasis	1	0.6
Chronic acalculous cholecystitis with high-grade dysplasia	1	0.6
Poorly differentiated adenocarcinoma gallbladder Staging - T3 N0 Mx	2	1.2

Chronic cholecystitis with cholelithiasis and low-grade dysplasia was significantly more among 41–50-year age group [Table 5].

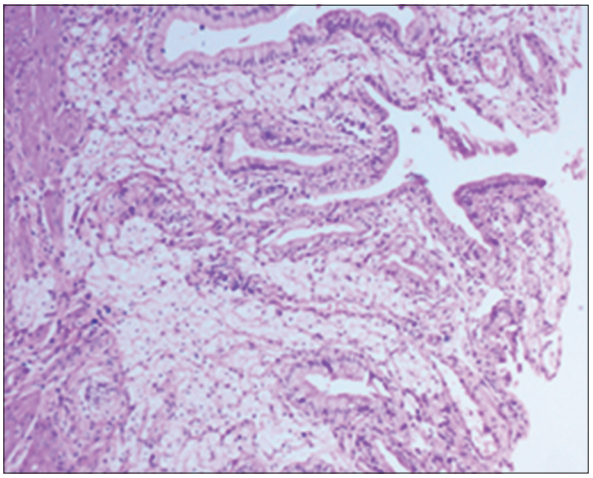

Figure 1: Cholesterolosis (×10)

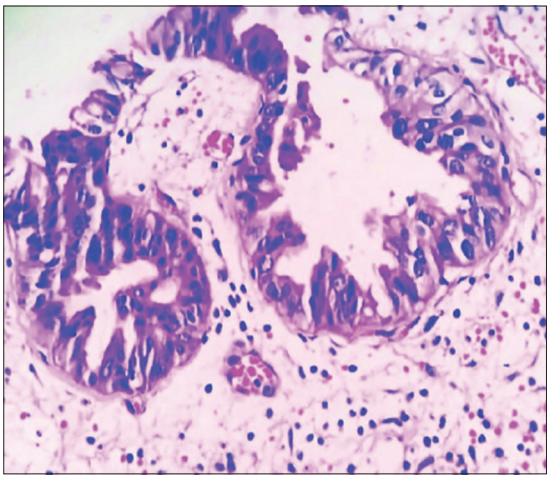

Figure 2: Chronic acalculous cholecystitis with high-grade dysplasia (×40)

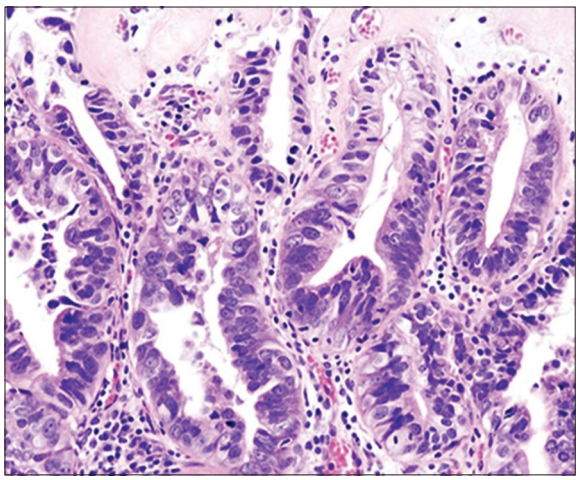

Figure 3: Adenocarcinoma gall bladder (×40)

Table 5: Distribution of study population according to age groups

Diagnosis	Age groups					
	18–30 years	31–40 years	41–50 years	51–60 years	61–70 years	Above 70 years
Chronic acalculous cholecystitis	28	19	15	17	3	0
	59.6%	36.0%	45.7%	58.6%	28.6%	0.0%
Chronic cholecystitis with cholelithiasis	9	12	10	3	1	0
	19.1%	24.0%	28.6%	10.3%	14.3%	0.0%
Chronic cholecystitis with	8	14	4	5	1	0
cholelithiasis and cholesterolosis	12.8%	20.0%	2.9%	10.3%	0.0%	0.0%
Acute on chronic cholecystitis	0	0	0	1	0	0
with cholelithiasis and low-grade dysplasia	0.0%	0.0%	0.0%	3.4%	0.0%	0.0%
Chronic cholecystitis with	1	1	5	1	1	1
cholelithiasis and low-grade dysplasia	0.0%	2.0%	2.9%	0.0%	0.0%	50.0%
Chronic acalculous cholecystitis	0	0	0	1	0	0
with high-grade dysplasia	0.0%	0.0%	0.0%	3.4%	0.0%	0.0%
Chronic acalculous cholecystitis with	0	1	0	0	0	0
xanthogranulomatous reaction with low-grade dysplasia	0.0%	2.0%	0.0%	0.0%	0.0%	0.0%
Eosinophilic cholecystitis	0	1	0	0	0	0
	0.0%	2.0%	0.0%	0.0%	0.0%	0.0%
Eosinophilic cholecystitis with	0	0	1	0	0	0
low-grade dysplasia and cholelithiasis	0.0%	0.0%	2.9%	0.0%	0.0%	0.0%
Papillary hyperplasia with chronic	0	1	0	0	0	0
acalculous cholecystitis and cholesterolosis	0.0%	2.0%	0.0%	0.0%	0.0%	0.0%
Poorly differentiated adenocarcinoma	0	0	1	0	0	1
gall bladder Staging - T3 N0 Mx	0.0%	0.0%	2.9%	0.0%	0.0%	50.0%
Xanthogranulomatous cholecystitis	1	1	0	0	1	0
	2.1%	2.0%	0.0%	0.0%	14.3%	0.0%

χ^2 value=12.780, *P*=0.044*

Chronic cholecystitis with cholelithiasis and low-grade dysplasia was significantly more among females [Table 6].

EGFR was given a score of 0 in a case of chronic cholecystitis with cholelithiasis and low-grade dysplasia.

EGFR was given a score of 1+ in a case of chronic acalculous cholecystitis with high-grade dysplasia

EGFR was given a score of 3+ in both cases of poorly differentiated adenocarcinoma GB staging [Table 7 and Figure 4].

DISCUSSION

In current study, there were 27.6% of subjects from 18 to 30 years, 29.4% from 31 to 40 years, 20.6% from 41 to 50 years, 17.1% from 51 to 60 years, 4.1% from 61 to 70 years, and 1.2% from above 70 years. The mean age of the study population was 40.17 ± 12.52 (1877) years. In concurrence to our study, Mondal *et al*.[9] found that mean ages for patients with chronic cholecystitis, hyperplasia, metaplasia, dysplasia, and carcinoma were 34.5, 37.2, 42.9, 43.9, and 53 years, respectively. Talreja *et al*.[15] reported the average age of patients was 41.30 ± 8.43 years (range: 26–68 years). Sailabala and Kalyani[16] reported that the incidence of non-neoplastic lesions was peak in the age group of 41–60 years and Khan and Abilsh[17] reported that the most common age group affected was 4th–5th decade.

Table 6: Distribution of study population according to gender

Diagnosis	Gender	
	Female	Male
Chronic acalculous cholecystitis	68	15
	49.6%	45.5%
Chronic cholecystitis with cholelithiasis	30	5
	21.9%	15.2%
Chronic cholecystitis with	25	5
cholelithiasis and cholesterolosis	18.2%	15.2%
Eosinophilic cholesystitis	1	0
	0.7%	0.0%
Acute on chronic cholesystitis with	0	1
cholelithiasis and low-grade dysplasia	0.0%	3.0%
Chronic cholecystitis with cholelithiasis	10	1
and low-grade dysplasia	7.3%	3.0%
Chronic acalculous cholecystitis	0	1
with high grade dysplasia	0.0%	3.0%
Chronic acalculous cholecystitis with	1	0
xanthogranulomatous reaction	0.7%	0.0%
with low-grade dysplasia		
Eosinophilic cholecystitis with	0	1
low-grade dysplasia and cholelithiasis	0.0%	3.0%
Papillary hyperplasia with chronic	1	0
acalculous cholecystitis and cholesterolosis	0.7%	0.0%
Poorly differentiated adenocarcinoma	1	1
gall bladder staging - T3 N0 Mx	0.7%	1.0%
Xanthogranulomatous cholecystitis	0	3
	0.0%	9.1%

χ^2 value=8.920, *P*=0.046*

In present study, there were 19.4% males and 80.6% females with a male: female ratio of 1:4.15. Our study

Table 7: Distribution of study population according to EGFR

Diagnosis	EGFR			
	Score 0	Score 1+	Score 2+	Score 3+
Chronic cholecystitis with cholelithiasis and low-grade dysplasia	1	-	-	-
Chronic acalculous cholecystitis with high-grade dysplasia	-	1	-	-
Poorly differentiated adenocarcinoma gallbladder staging	-	-	-	2

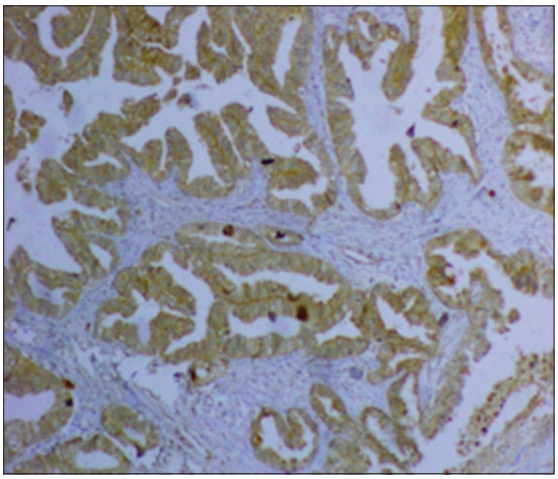

Figure 4: Immunohistochemistry of adenocarcinoma gallbladder (×20)

findings agreed with Talreja *et al*.[15] reported that most of them were females 70.29%. Almas *et al*.[18] found a female predominance among the patient population was observed.

In the current study, majority of the subjects presented with chronic acalculous cholecystitis (48.8%) and chronic cholecystitis with cholelithiasis (20.6%). There were 14 cases of low-grade dysplasia, one case of papillary hyperplasia with chronic acalculous cholecystitis and cholesterolosis, 1 case of high-grade dysplasia, 3 cases of XGC, and two cases of poorly differentiated adenocarcinoma GB.

Kulkarni *et al*.[19] reported that chronic calculous cholecystitis (57.76%), followed by chronic acalculous cholecystitis (22.36%). Remaining cases were of acute on chronic cholecystitis (6.21%), acute on chronic cholecystitis with cholelithiasis (4.96%), acute on chronic cholecystitis with perforation peritonitis (1.24%), acute suppurative cholecystitis with perforation peritonitis (0.62%), and biliary atresia (1.24%). In the current study, EGFR was given a score of 0 in a case of chronic cholecystitis with cholelithiasis and low-grade dysplasia. EGFR was given a score of 1+ in a case of chronic acalculous cholecystitis with high-grade dysplasia. EGFR was given a score of 3+ in both cases of poorly differentiated adenocarcinoma GB staging.

Gomes *et al*.[20] studied the expression of EGFR in relation to the variables of interest in the 35 cholangiocarcinoma cases. There was significant EGFR expression in ten (28.6%) of the 35 lesions, being score 3+ in eight patients and 2+ in two patients. In 25 patients (71.4%), EGFR expression was negative, being 1+ in five patients and 0 in 20 patients.

CONCLUSION

GB disease remains a major indication for cholecystectomy. Postoperative histopathological evaluation of the excised GB specimens divulges a vast spectrum of underlying pathologies. Of these, chronic cholecystitis with or without cholelithiasis/cholesterolosis remain the most prevalent. Furthermore, a macroscopic absence of remarkable features does not preclude the presence of an underlying premalignant or malignant lesion. There is thus an overarching need for routine histopathological examination of the resected GB specimens to exclude premalignant ailments such as intestinal metaplasia and dysplasia. These lesions may progress to GB adenocarcinoma.

REFERENCES

1. Lack EE. Pathology of the Pancreas, Gallbladder, Extrahepatic Biliary Tract, and Ampullary Region. United Kingdom: Oxford University Press; 2003. p. 20.
2. Gupta K, Faiz A, Thakral RK, Mohan A, Sharma VK. The spectrum of histopathological lesions in gallbladder in cholecystectomy specimens. Int J Clin Diagn Pathol 2019;2:146-51.
3. Singh A, Singh G, Kaur K, Goyal G, Saini G, Sharma D. Histopathological changes in gallbladder mucosa associated with cholelithiasis: A prospective study. Niger J Surg 2019;25:21-5.
4. Gupta OP, Khan S. Incidents and complications in laparoscopic cholecystectomy: A retrospective analysis of 336 cases. Int J Contemporary Med Surg Radiol 2019;4:1-5.
5. Thukral S, Roychoudhury AK, Bansal N, Rani E. Histopathological spectrum of gall bladder lesions in a tertiary care hospital in the Malwa belt a hospital based study. Ann Pathol Lab Med 2018;5:878-81.
6. Terada T. Histopathologic features and frequency of gall bladder lesions in consecutive 540 cholecystectomies. Int J Clin Exp Pathol 2013;6:91-6.
7. Carter D, Greenson JK. Gallbladder, extrahepatic biliary tree and ampulla. In: Sternberg's Diagnostic Surgical Pathology. 5th ed., Vol. 2. Netherlands: Wolters Kluwer; 2010. p. 1600-51.
8. Kumar H, Kini H, Tiwari A. Histological evaluation of 400 cholecystectomy specimens. J Pathol Nepal 2015;5:834-40.
9. Mondal B, Maulik D, Biswas BK, Sarkar GN, Ghosh D. Histopathological spectrum of gallstone disease from cholecystectomy specimen in rural areas of West Bengal, India-an approach of association between gallstone disease and gallbladder carcinoma. Int J Community Med Public Health 2016;3:3229-35.
10. Randi G, Franceschi S, La Vecchia C. Gallbladder cancer worldwide: Geographical distribution and risk factors. Int J Cancer 2006;118:1591-602.
11. Byars JP, Pursnani K. An alternative approach to sending all gallbladders for histology following cholecystectomy? Surg Sci 2012;3:15-20.

12. Lobo L, Prasad HL, Satoskar RR. Carcinoma of the gall bladder: A prospective study in a tertiary hospital of Bombay, India. J Clinic Diagn Res 2012;6:692-95.
13. Phadke PR, Mhatre SS, Budukh AM, Dikshit RP. Trends in gallbladder cancer incidence in the high-and low-risk regions of India. Indian J Med Paediatr Oncol 2019;40:90-3.
14. Lazardis KN, Gores GJ. Cholangiocarcinoma. Gastroenterology 2005;128:1655-67.
15. 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;2016:9319147.
16. Sailabala G, Kalyani D. Spectrum of gall bladder lesions in cholecystectomy specimens-a hospital based study. IOSR J Dent Med Sci 2019;18:70-80.
17. Khan DM, Abilsh SC. Histopathological spectrum of gallbladder diseases in a tertiary care centre. Arch Cytol Histopathol Res 2018;3:206-9.
18. Almas T, Murad MF, Khan MK, Ullah M, Nadeem F, Ehtesham M, *et al*. The spectrum of gallbladder histopathology at a tertiary hospital in a developing country: A retrospective study. Cureus 2020;12:e9627.
19. Kulkarni AM, Jadhav ED, Ramteke RV. Histopathological spectrum of gall bladder lesions. Int J Res Med Sci 2020;8:1056-60.
20. Gomes RV, Rodrigues MÂ, Rodrigues JB, Vidigal PT, Damasceno KA, Lima HA, *et al*. Expression of epidermal growth factor receptor (EGFR) in cholangiocarcinomas: Predictive factors and survival. Rev Col Bras Cir 2018;45:e1826.

How to cite this article: Munjal D, Kumar N, Gupta M, Shrivastava RK, Sharma HB. Spectrum of Histomorphological Lesions of Gall Bladder in Cholecystectomy Specimens: A Cross-sectional Study. Int J Sci Stud 2023;11(2):24-29.

Source of Support: Nil, **Conflicts of Interest:** None declared.