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DIVERSITY OF GALLBLADDER LESIONS: HISTOPATHOLOGICAL TRENDS IN A TERTIARY CARE SETTING.

Histopathology

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ABSTRACT

Introduction: Gallbladder lesions include inflammatory, preneoplastic, and malignant conditions. Gallstones are closely associated with chronic cholecystitis and may contribute to carcinoma development through a metaplasia–dysplasia sequence. Although relatively rare, gallbladder carcinoma has a poor prognosis due to late clinical detection. **Aim:** To correlate clinical and pathological features in patients undergoing cholecystectomy and to describe the histopathological patterns in gallbladder specimens. **Materials and Methods:** A prospective cross-sectional study was conducted on 1,150 cholecystectomy specimens received from January 2023 to September 2024 in the Department of Pathology. All tissues were processed with standard histological techniques, and data were analysed using IBM SPSS v23. A p-value < 0.05 was considered statistically significant. **Results:** The mean patient age was 45 ± 13.6 years, with a marked female predominance (M:F = 1:4.5). The most common age group was 60–70 years (22.26%). Right hypochondrial pain was the most frequent symptom (65.2%). Multiple gallstones were present in 82.6% of specimens, with mixed stones comprising 78.2%. Chronic cholecystitis with cholelithiasis was the predominant diagnosis (80.96%). Other lesions included chronic fibrosing cholecystitis (2.17%) and cholesterosis (10.43%). Preneoplastic changes—metaplasia (1.74%) and dysplasia (0.70%)—along with adenocarcinoma (1.04%) showed strong associations with gallstones. **Conclusion:** Cholelithiasis is a major contributor to chronic and neoplastic gallbladder pathology, supporting the metaplasia–dysplasia–carcinoma pathway. Early elective cholecystectomy, including in select asymptomatic patients with gallstones, may help reduce carcinoma risk. Larger multicentre studies are recommended to further elucidate underlying etiopathogenic mechanisms.

KEYWORDS

Gallbladder, cholelithiasis, chronic cholecystitis, metaplasia, dysplasia, carcinoma.

INTRODUCTION

Histomorphological alterations in the gall bladder encompass numerous lesions, ranging from inflammatory, preneoplastic, and neoplastic changes. Prevalent among them is chronic cholecystitis that is said to be associated with numerous premalignant changes, which may result in eventually invasive carcinoma.[1] Carcinoma of the gall bladder, while uncommon in India, largely has a poor outcome.[2] Early diagnosis is important to enhance patient results, but the majority of cases are late diagnoses, which reduce the potential for total surgical resection.[3]

Autopsy findings reveal that cancer of the gall bladder is the most common biliary tract malignancy, comprising 80-90% of biliary cancers worldwide. As a result of the aggressive nature of the tumor and delays in diagnosis, the prognosis is generally poor. Although the definitive cause is uncertain, the presence of gallstones has an established correlation with a higher risk of gall bladder carcinoma.

Aims and objectives

The present study was planned to analyze the histopathological spectrum of gall bladder lesions.

Material And Method

This study included all the cholecystectomy specimens received in the Department of Pathology, in collaboration with the Department of Surgery in the tertiary care hospital, during a period of January 2023 to September2024. Written informed consent was obtained from all the patients included in the study.

Study Design: Prospective cross-sectional study.

Inclusion Criteria: All the gallbladder lesions received in the Department of Pathology, during the study period.

Exclusion Criteria: All the poorly preserved and inadequate specimens were excluded from the study.

Study Procedure: All gallbladder lesions recommended for histopathological examination within specified duration of time were evaluated .Patient's clinical data comprising of clinical features & laboratory investigation reports were collected from medical records in surgically resected specimens. The specimen received was processed as per the protocol , sections cut and H&E staining was done.

Stastical Analysis: The results was evaluated by ANOVA followed by t-tests to compare continuous variables among groups. P<0.05 considered to be statistically significant. All analyses were carried out using IBM SPSS version 23.0.

Observation And Result

The present study was carried out in the Department of Pathology, during the time period of 18 months. The total numbers of gallbladder specimens studied were 1150. These cases were further studied for age associated variation as mentioned in table 1.

Chi-square statistic: 8.84, P-value: ≈ 0.0651.The p-value is 0.065, which is slightly above the standard threshold of 0.05.This means the difference in the number of cases across age groups is not statistically significant at the 5% level, although it's very close.

The distribution of gall bladder lesion cases across different age groups shows a mild skew toward the 60–70 age group, followed closely by the 40–49 and 30–39 brackets. However, the variation is not statistically significant, suggesting that age alone, within the studied range, may not be a dominant determinant for the presence of gall bladder lesions in this population.

While certain age groups show a higher number of cases, this may reflect general population distribution or health-seeking behaviour rather than a true age-dependent risk.

Table 2 highlights the gender distribution with Chi-square statistic: 453.29,P-value: $\approx 1.39 \times 10^{-100}$

The p-value is extremely small, indicating a very strong statistically

significant difference in gender distribution.There is a highly significant female predominance (81.39%) in cases of gall bladder lesions compared to males (18.61%).This difference is not due to chance and suggests that female gender is a major risk factor for gall bladder pathology.

This aligns with known epidemiological data where hormonal factors (like estrogen) and lifestyle differences contribute to a higher risk of gallstones and related conditions in women. This finding emphasizes the need for gender-focused preventive strategies and early diagnosis in females.

Table 3 specifies the clinical presentation of the patient with Chi-square statistic: 997.83,P-value: $\approx 5.33 \times 10^{-216}$ Since the p-value is extremely small (< 0.05), the result is highly statistically significant. This indicates that the distribution of clinical history types (Abdominal Discomfort, Asymptomatic, Nausea/vomiting/Bloating, Right Hypochondrium Pain) is not uniform—there is a significant difference in how frequently these symptoms occur in the patient population. RHP (Right Hypochondrium Pain) is disproportionately more common, suggesting it could be a key presenting symptom in gall bladder lesions.

Gall bladder lesions based on mummer of stones are specified in table 4. The Chi-square statistic: 489.13, P-value: $\approx 2.20 \times 10^{-108}$ Since the p-value is extremely small (< 0.05), this result is highly statistically significant. This means the distribution of patients with multiple stones (950) vs single stone (200) is not by chance. There is a significant predominance of multiple stones in this population. In simpler terms patients are much more likely to have multiple gallstones than a single one, and this difference is statistically meaningful.

Table 5 denotes the cases by type of stones that were encountered. The Chi-square statistic: 489.13,P-value: $\approx 2.20 \times 10^{-108}$ Since the p-value is extremely small (< 0.05), this result is highly statistically significant. This means the distribution of patients with multiple stones (950) vs single stone (200) is not by chance. There is a significant predominance of multiple stones in this population. In simpler terms patients are much more likely to have multiple gallstones than a single one, and this difference is statistically meaningful.

Table 6 typify the histopathological classification of Gall bladder lesions encountered in this study. The Chi-square statistic was 5759.29 and P-value: 0.0 (mathematically extremely small, effectively zero). The p-value is effectively zero, which means the observed distribution is extremely unlikely under the assumption of equal (uniform) distribution. There is a very strong and statistically significant difference in the frequency of different gall bladder lesion types.

- The vast majority of cases are Chronic Cholecystitis (CC/CL) (931 out of 1150),
- While other lesions like Adenocarcinoma, Dysplasia, or Hyperplasia are far less frequent.

This pattern is not due to random variation, indicating that chronic inflammatory lesions dominate in this patient population.

DISCUSSION

One of the frequently performed surgical procedures, cholecystectomy is used to treat multiple pathologies, such as cholelitiasis, cholecystitis, gallbladder polyps and gallbladder carcinoma.[4]

GBC has bad five-year survival rates and an especially bad prognosis because of its late onset in the illness course.[5]

Specimen histopathology plays a significant role in patient care.[6] Although cholelitiasis and gallbladder cancer have been found to be strongly associated, the varying incidence of the two conditions among different ethnic groups points to a number of contributing factors, such as the size of the stone, lifestyle, diet, environmental pollutants, chronic bacterial and parasitic infections, and various hepatobiliary abnormalities.[7]

Age Range

The study's participants ranged in age from 20 to 70, with a mean age of 45.003 ± 13.68 years. The most common age group with gallbladder illness was in the Sixth decade, accounting for 256 out of 1150 cases (22%), followed by the Fourth decade (242 out of 1150 cases, 21%), and the Fifth decade (223 out of 1150 cases, 19.39%). The oldest patient was a 70-year-old man, while the youngest was a 20-year-old boy. These findings are in concordance with various studies as mentioned in table 7.

Gender

The Female: Male ratio in the current study is 4.5:1. Females were 81.39% as compared to males 18.61%. The results of our investigation concurred with those of several other studies, which are tabulated in table 8 above.

In our study, the most common gall stones were multiple stone found in 950/1150 cases (82.61%) followed single stones in 200/1150 cases (17.39%). These findings were in accordance with other studies as enumerated in table 9.

In our study, the most common gall stones were mixed stone found in 899/1150 cases (78.17%) followed by cholesterol and pigment stones in 151/1150 cases (13.13%) and 100/1150 cases (8.70%) respectively. The comparison with various studies is mentioned in table 10. The most common histopathological finding in the current study was chronic cholecystitis, these findings were in concordance with various other studies as mention in table 11.

Histomorphological Spectrum

Non neoplastic lesions:

In our study, the most common histomorphological spectrum noted in gallbladder lesions were those falling under non neoplastic gallbladder lesions 1100/1150 (95.65%), followed by preinvasive neoplastic lesions 38/1150 (03.30%) and invasive neoplastic lesions 12/1150 (1.04%).

Among the various non-neoplastic lesions, the most common histopathological lesion observed was chronic cholecystitis with classical features 931/1150 (80.96%) followed by chronic cholecystitis with Cholesterolosis 120/1150 (10.43%). Other histological lesions were variants of chronic cholecystitis e.g. chronic cholecystitis with Fibrosis 25 cases (2.17%) , Xanthogranulomatous cholecystitis 6 cases (0.52%), chronic cholecystitis with Lymph node reactive hyperplasia 18 cases (1.56%), Metaplasia 20 cases (1.73%) and Hyperplasia gallbladder 10 cases (0.86%). The overall cases of chronic cholecystitis were 931/1150 cases (80.96%).

The research conducted by Sharma S[9] et al in 2023, Kulkarni[19] A M et al in 2020 , Banerjee A [22]et al. in 2015, and Selvi TR [23] et al. in 2011 is consistent with the findings of the current study.

Metaplasia

Metaplasia was seen in 20/1150 (1.74%) cases of non-neoplastic lesions of chronic cholecystitis in present study. Out of these 20 cases 15 (75%) were showing Antral metaplasia, 3(15%) cases were of Intestinal metaplasia and 2(10%) showed both metaplasia. Out of 50 cases of neoplastic lesions, 20 cases showed metaplasia. The correlation of the current study with other similar studies is mentioned in table 12

In the current study out of 1150 8 cases of low-grade dysplasia were reported. These findings were in concordance with other studies as mentioned in table 13. Out of total 8 cases of low grade dysplasia, 5 cases presented with metaplasia (62.5%),3 cases (37.5) showed antral metaplasia and 2 case (25%) were of intestinal metaplasia.

Neoplastic lesions:

Preinvasive neoplastic lesions

The preinvasive neoplastic lesions or biliary intra epithelial neoplasia (BilIN) of gallbladder were categorized as low-grade dysplasia and high-grade dysplasia. Out of the total cases falling under preinvasive neoplastic category 8 (0.70%) were dysplasia. There were 2 cases of dysplasia which showed metaplasia out of 8 cases. 3/12 cases of carcinoma had metaplastic changes (25%) one each of antral and intestinal type. Our findings were in concordance with a number of other studies. The findings of Mondal B [21] et al. in 2016, Gupta K[27] et al. in 2019, Cuccinotta[28] et al. in 2005, are all consistent with our study.

Invasive neoplastic lesions

In the current study 12 out of 1150 cases were those of carcinoma (1.04%). Our study is in consistent with the studies done by Goyal A[15]

et al , Kaur A et al [29] Memon W et al [30] and Pradhan SB et al [31] as mentioned in table 14

Prevalence of dysplasia and carcinoma in calculous and acalculous cases in the current study is compared with other studies as mentioned in table 15.

CONCLUSION

Cholelitiasis is the most important entity in gallbladder lesions and that there is a definite association between metaplasia-dysplasia-carcinoma sequence. In carcinoma, nature of mucin is altered. Early elective surgery for both asymptomatic and symptomatic patients with gall stones likely reduces the risk of carcinoma of gallbladder. Further studies directed towards a perfect understanding of gall bladder carcinogenesis are required.

Limitation of the study

1. The study did not extensively analyze contributing risk factors such as genetic predisposition, environmental influences, dietary preferences, etc which can be added in further studies.
2. The data was collected from a single institution, which may limit the generality of the findings to broader populations with different demographic or geographic characteristics. Hence multicenter data can be incorporated.
3. Although 1150 cases were analyzed, a larger sample size could provide more robust statistical validation and allow for subgroup analyses across different gall bladder lesions.

Table -1 : Age-wise distribution (N=1150)

Age Group (Years)	Number of Subjects	Percentage(%)
20-29	196	17.04
30-39	233	20.26
40-49	242	21.04
50-59	223	19.39
60-70	256	22.26
Grand Total	1150	100.00

Table 2 : Distribution of Gall Bladder Lesion Cases by Gender (N=1150)

Gender	Number	Percentage (%)
Female	936	81.39
Male	214	18.61
Grand Total	1150	100.00

Table 3 : Distribution of Gall Bladder Lesion Cases based on Clinical History(N=1150)

Clinical History	Number	Percentage(%)
Abdomen Discomfort	100	8.70
Asymptomatic	150	13.04
Nausea/vomiting/Bloating	150	13.04
Right Hypochondrial Pain	750	65.22
Grand Total	1150	100.00

Table 4 : Distribution of Gall Bladder Lesion Cases based on Number of stones (N=1150)

Number of Stones	Number	Percentage(%)
Multiple	950	82.61
Single	200	17.39
Grand Total	1150	100.00

Table 5 : Distribution of Gall Bladder Lesion Cases by Type of Stone (N=1150).

Type of stone	Number	Percentage(%)
Cholesterol	151	13.13
Mixed	899	78.17
Pigmented	100	8.70
Grand Total	1150	100.00

Table 6 : Histopathological Classification of Gall Bladder Lesion Cases (N=1150)

Classification of Gall Bladder Lesions	Number	Percentage(%)
Adenocarcinoma	12	1.04
Cholecystitis with Cholelithiasis (CC/CL)	931	80.96
CC/CL Lymph node Reactive Hyperplasia	18	1.57
CC/CL with chronic fibrosing	25	2.17
CC/CL with Cholesterolosis	120	10.43
CC/CL with Xanthogranuloma	6	0.52
Dysplasia	8	0.70
Hyperplasia	10	0.87
Metaplasia	20	1.74
Grand Total	1150	100.00

Table 7 : Comparison of the Age-range with other studies

STUDY NAME	AGE RANGE	MEAN AGE
Present study (2025)	20-70 years	Mean age : 45.003±13.68 years
Bora K et al [8] (2023)	9-85 years	Mean Age: 39.4 years
Sharma S et al [9] (2023 August)	15-81 years	Mean Age: 39.5 ± 11.6 years
Arora et al[10] (2018)	44.4 years	Peak Age=47.65 % above 3rd decade Mean Age: 41.85
Talreja et al[11] (2016)	26-68 years	Average age : 41.30±8.43 years
Shukla[12] et al (2015)	20-70 years	Average age: 41.30±12.01 yrs

Table 8: Comparison of the Male-Female ratio with other studies

Present study (2025)	M:F= 1: 4.5
Sharma S[9] et al (2023 August)	M:F= 1:4.1
Kothasthane VD[14] et al (2020)	M:F = 1:4
Goyal [15] et al (July 2019)	M:F= 1:4.4
Kumar H[4] et al (2018) April-June	North- M: F = 1: 4.88 South– M: F = 1: 1.33

Table 9: Comparison of the number of gall stones with other studies.

Studies	Stone present Number/Total & (percentage %)	Multiple Number/Total & (percentage%)	Single Number/Total & (percentage%)
Present study (2025)	1150/1150 (100%)	950/1150 (82.61%)	200/1150 (17.39%)
Sharma S[9] et al (2023 August)	100/100 (100%)	69/100 (69%)	31/100 (31%)
Mohan A et al [5] 2019	2194/2498 (89.6%)	1832/2498 (83.26%)	362/2498 (16.50%)
Narang S[15] et al (2014)	185/200 (92.5%)	172/200 (93%)	13/200(7%)

Table 10: Gross Morphological types of gall stones

Studies	Cholesterol Stones Number/Total (percentage%)	Pigmented Stone Number/Total (percentage%)	Mixed stones Number/Total (percentage%)
Present study(2025)	151/1150(13.13%)	100/1150(8.70%)	899/1150(78.17%)
Nasar A[17] et al (2021)	61/104 (58.7%)	27/104(26%)	16/104 (15.4%)
Goyal S[15] et al 2014	17/313 (5.43%)	18/313 (5.75%)	213/313 (68%)
Baig SJ[18] et al 2002	4/40 (10%)	8/40 (20%)	28/40 (70%)

Table 11: Comparison of the number of chronic cholecystitis cases with other studies.

Study	Total No. of cases	Chronic cholecystitis (Commonest lesion) Number/Total (percentage%)
Present study (2025)	1150	931/1150 (80.96%)
Sharma S[9] et al (2023 August)	100	75/100 (75%)
Kulkarni[19] AM et al (2020)	161	129/161 (80.12%)
Sailabala and Kalyani[20] [(2019)	250	207/250 (82.8%)
Mondal B[21] et al (2016)	786	627/786 (79.8%)
Banerjee A[22] et al (2015)	60	58/60 (96.67%)
Selvi TR et al [23]2011	78	67/78 (85.8%)

Table 12: Comparison of the number of metaplastic cases with other studies.

Study	No. of cases	Metaplastic cases Number/Total (percentage%)
Present study (2025)	1150	20/1150 (1.74%)

Goyal A[15] et al July 2019	2458	1043/2458 (42.43%)
Ahmad SR[24] et al 2018 Jan-March	100	11/100 (11%)
Haldar B[25] et al 2018 October	1153	200/1153 (17.4%)
Dattal D S et al [26] 2017	1291	200/1291 (15.56%)

Table 13: Comparison of the number of dysplasia cases with other studies.

Study	No. of cases	Dysplasia cases Number/Total (percentage%)
Present study(2025)	1150	8/1150 (0.70%)
Gupta K[27] et al 2019	434	16/434 (3.68%)
Mondal B[21] et al 2016	786	17/786 (2.2%)
Cuccinotta et al [28]2005	727	2/727 (0.2%)

Table 14: Comparison of the number of carcinoma cases with other studies.

Study	Total cases	Carcinoma cases Number/Total (percentage%)
Present study 2025	1150	12/1150 (1.04%)
Goyal A[15] et al 2019	2458	54/2458 (1.83%)
Kaur A et al [29]2012	384	3/384 (0.78%)
Memon W et al [30]2011	282	2/282 (0.7%)
Pradhan SB et al [31]2009	80	1/80 (1.05%)

Table-15: Comparison of prevalence of dysplasia and carcinoma in calculus and acalculous cases.

Studies	Dysplasia		Carcinoma	
	Calculous Number/ Total (percentage%)	Acalculous Number/ Total (percentage%)	Calculous Number/ Total (percentage%)	Acalculous Number/ Total (percentage%)
Present study 2025	08/08 (100%)	00	12/12 (100%)	00
Dattal D S (2017)[26]	19/21 (90.48%)	2/21 (9.52%)	7/7 (100%)	00
Jain BB (2010) [32]	32/36 (88.8%)	4/36 (11.1%)	11/14 (78.5%)	3/14 (21.4%)

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