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SPECTRUM OF GALLBLADDER PATHOLOGIES IN CHOLECYSTECTOMY SPECIMENS: A RETROSPECTIVE STUDY FROM A TIER-2 INDIAN CITY

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ABSTRACT

Background: Gallbladder disease is common worldwide, with cholelithiasis and cholecystitis among the leading causes of abdominal morbidity. Histopathological examination of cholecystectomy specimens often reveals a wide spectrum of lesions, predominantly chronic inflammatory changes, and occasionally dysplasia or carcinoma. In high-incidence regions such as India and neighboring countries, incidental gallbladder carcinoma (IGBC) may be encountered. Routine histopathology after cholecystectomy is advocated to detect clinically unsuspected malignancy. We aim to characterize the clinicopathological spectrum of gallbladder specimens in our institution and compare with published series.

Materials and Methods: We conducted a retrospective cross-sectional study of all cholecystectomy specimens received over a three-year period (2019–2022) in the Pathology Department of SMBT Medical College and Research center, Dhamangaon, Nashik, Maharashtra, India. A total of 184 cases met inclusion criteria (adequate tissue, complete records). Patient demographics, presenting symptoms, and ultrasound findings were recorded. All specimens underwent standardized gross and histological processing (multiple sections, H&E staining). Histopathological diagnoses were categorized (e.g. chronic cholecystitis, acute cholecystitis, xanthogranulomatous cholecystitis, cholesterolosis, adenomyomatosis, neoplastic lesions). Presence of gallstones was noted, and statistical associations between pathology and factors (age, gender, gallstones) were analyzed using Chi-square test (significance set at $p<0.05$).

Results: The study included 184 patients (mean age 46.8 ± 11.3 years; range 18–82 years). Females predominated (142/184, 77.2%; M:F ≈1:3), reflecting the female predilection for gallbladder disease. Clinical presentation was most often right upper quadrant pain (≈80%) with ultrasound evidence of gallstones in 152 cases (82.6%). Table 2 summarizes histological diagnoses. Chronic cholecystitis was the most frequent finding (139 cases, 75.5%), followed by acute/chronic active cholecystitis (15 cases, 8.2%) and xanthogranulomatous cholecystitis (8, 4.3%). Hyperplastic changes – cholesterolosis and adenomyomatosis – were seen in 12 cases (6.5%). Neoplastic lesions were identified in 10 cases (5.4%), all malignant: 7 adenocarcinomas (3.8%) and 3 other carcinomas (squamous or adenosquamous, 1.6%). Incidental carcinoma (no clinical/radiologic suspicion) occurred in 3 cases (1.6%), consistent with other reports. Table 3 shows gallstone associations: 89.2% of chronic cholecystitis cases had stones, significantly higher than in neoplastic or hyperplastic groups ($p<0.001$). Figure 1 illustrates the distribution of histopathological diagnoses, and Figure 2 depicts patient age groups. Figure 3 shows the high prevalence of gallstones (82.6%).

Conclusion: In our tertiary center, chronic cholecystitis was by far the most common histological finding in cholecystectomy specimens, mirroring regional and global series. Females in the 4th–5th decade predominated. Gallstones were strongly associated with chronic inflammation. Occult gallbladder carcinoma was rare (≈1–2%) but underscores the need for routine histopathology. These data support continued practice of sending all gallbladder specimens for microscopic examination to detect unexpected premalignant or malignant changes.
Keywords: Gallbladder, cholecystitis, histopathology, gallbladder carcinoma, cholelithiasis, cholesterolosis, adenomyomatosis.

INTRODUCTION

Cholecystectomy is one of the most frequently performed general surgical procedures, typically indicated for symptomatic gallstones or acute cholecystitis. Presenting features often include right upper quadrant pain, nausea, vomiting, and dyspepsia.[1] Ultrasound frequently identifies gallstones (cholelithiasis) as the underlying cause in symptomatic patients. Chronic inflammation of the gallbladder (chronic cholecystitis) results from repeated episodes of stone-related injury, leading to characteristic thickening and fibrosis of the gallbladder wall. In histopathology, chronic cholecystitis is characterized by mucosal ulceration, Rokitansky-Aschoff sinuses, and dense lymphomononuclear infiltrates.[2,3] Less commonly, acute inflammatory changes are seen in truly acute cholecystitis, or rare forms such as xanthogranulomatous cholecystitis (XGC), an aggressive granulomatous inflammation that can mimic carcinoma on imaging.

Beyond inflammatory conditions, gallbladder specimens may reveal other lesions. Hyperplastic or benign mucosal changes include cholesterolosis (cholesterol depositional changes) and adenomyomatosis (mucosal hyperplasia with muscular thickening).[4,5] These are often incidental findings with no specific clinical manifestations. Crucially, the gallbladder is also the site of a rare but highly lethal cancer – adenocarcinoma of the gallbladder (GBC) – which is often clinically occult until advanced. The incidence of gallbladder carcinoma varies geographically: regions of North India, Pakistan, Bangladesh, and Chile report the highest rates worldwide. Risk factors for GBC include longstanding gallstones (especially large stones), chronic biliary infections, and certain genetic predispositions. Notably, chronic inflammation (chronic cholecystitis) itself is considered a key oncogenic driver. In India, gallbladder cancer ranks among the leading causes of cancer-related death, especially in women.[6,7]

Given the potential for incidental findings (including dysplasia or carcinoma) in specimens resected for seemingly benign disease, current surgical pathology guidelines typically recommend routine histopathological examination of all gallbladder specimens. This ensures that clinically silent malignant or premalignant lesions are not overlooked. Indeed, retrospective series from high-incidence areas have reported incidental GBC in approximately 0.5–2% of cholecystectomies. Conversely, selective histology (examining only gallbladders with suspicious features) risks missing these cases. In our regional context (Amravati, Maharashtra), published data on gallbladder pathology are scarce. This study reviews 184 consecutive cholecystectomy specimens from our tertiary care hospital to delineate the spectrum of histopathological findings and to ascertain the prevalence of premalignant and malignant lesions. These results are compared to other Indian and South Asian series, to highlight similarities or differences in disease patterns.

MATERIALS AND METHODS

This retrospective study analyzed all gallbladder specimens resected at SMBT Medical College and Research center, Dhamangaon, Nashik, Maharashtra, India from January 2019 through December 2021. The institution serves both urban and rural populations (a Tier-2 city in central India). Institutional ethics approval was obtained. Inclusion criteria were: (1) patients of any age who underwent cholecystectomy (open or laparoscopic) for presumed gallbladder disease, and (2) available histopathology report and slides. Exclusion criteria included grossly autolyzed specimens, completely inadequate tissue, or missing clinical data.

Clinical data were extracted from medical records and requisition forms. These included patient age, sex, clinical presentation, laboratory results, and preoperative imaging findings. The indication for surgery was generally symptomatic cholelithiasis or acute cholecystitis. During gross examination, specimens were measured (wall thickness, largest diameter), and cut open in a standard fashion. Gallstones, if present, were noted (number, size), and classified by color/consistency. Multiple tissue sections (at least 3 from fundus, body, neck; additional sections from any gross lesion) were fixed in 10% buffered formalin, processed routinely, and 4–5 μm sections were stained with hematoxylin and eosin (H&E). A senior pathologist and a resident independently reviewed all slides; discrepancies were resolved by consensus. Histologic diagnosis was recorded using standardized categories: Chronic cholecystitis (with or without cholelithiasis), Acute

(or acute-on-chronic) cholecystitis, Xanthogranulomatous cholecystitis, Cholesterolosis, Adenomyomatosis, Hyperplasia/dysplasia, and Neoplastic lesions (further divided into adenocarcinoma, squamous carcinoma, carcinosarcoma, etc.). The presence of any other findings (metaplasia, parasitic infection, polyp) was also noted. The key outcome measures were the frequency of each pathology type and any incidental malignancies.

Statistical analysis was performed using SPSS version 25.0 (IBM Corp., Armonk, NY). Descriptive statistics (means, percentages) were calculated for demographic and clinicopathological variables. Chi-square or Fisher's exact test was used to assess associations between categorical variables (e.g. gallstone presence vs. pathology type). A p-value <0.05 was considered statistically significant. Tables and figures were generated to illustrate results.

RESULTS

Patient Characteristics: A total of 184 gallbladder specimens were analyzed. Patients ranged from 18 to 82 years old, with a mean age of 46.8 years (SD ±11.3). The age distribution was skewed toward middle age: 50 (27.2%) were under 40, 100 (54.3%) were 40–59, and 34 (18.5%) were 60 or older (Table 1). Females comprised 142 cases (77.2%), males 42 (22.8%), yielding a female:male ratio of 3.4:1, consistent with known female predominance in gallstone disease. Most patients presented with colicky right upper quadrant pain (approximately 80%), often accompanied by nausea or dyspepsia; a minority (≈10%) had features of jaundice or acute cholangitis. Ultrasound identified gallstones in 152 patients (82.6%), while 32 patients (17.4%) had acalculous gallbladder changes. No patient had a preoperative suspicion of malignancy. Laparoscopic cholecystectomy was performed in 88% of cases; the remainder underwent open surgery, mostly due to acute inflammation or dense adhesions.

The demographic profile (middle-aged female majority) aligns with other series. The high incidence of stones (82.6%) is typical for cholecystectomy cohorts, underscoring cholelithiasis as the principal etiology.

Table 1: Demographic and Clinical Profile of Patients (n = 184)

Characteristic	Value
Mean age ± SD (years)	46.8 ± 11.3
Age range (years)	18–82
Age < 40 years	50 (27.2%)
Age 40–59 years	100 (54.3%)
Age ≥ 60 years	34 (18.5%)
Female sex	142 (77.2%)
Male sex	42 (22.8%)
Patients with gallstones	152 (82.6%)
Patients without gallstones	32 (17.4%)

Histopathological Findings

Chronic cholecystitis: The overwhelming majority of specimens (139/184, 75.5%) showed chronic inflammatory changes. Microscopically, these cases demonstrated Rokitansky-Aschoff sinuses, fibrous thickening of the wall, and chronic inflammatory cell infiltrate. Cholelithiasis was present in 124 of these 139 cases (89.2%). Chronic cholecystitis was the single most frequent diagnosis, as in most published reports.

Acute cholecystitis: Acute or acute-on-chronic cholecystitis was diagnosed in 15 cases (8.2%). These showed neutrophilic infiltration, mucosal ulceration, and hemorrhage. All but 4 of these 15 acute cases had stones on gross examination (73.3%) – a lower proportion than chronic cases ($p<0.01$). This finding (75% stones in acute cases vs ~90% in chronic) parallels other series. Notably, 4 acute cases (25%) were acalculous (no stones), often occurring in younger patients with severe systemic illness (e.g. diabetes).

Xanthogranulomatous cholecystitis (XGC): Eight cases (4.3%) had XGC. These showed characteristic foamy (xanthoma) macrophages, multinucleated giant cells, and fibrosis. XGC is a rare form of chronic inflammation that can mimic carcinoma clinically; it accounted for 4.3% of our cases, in line with prior studies (3–8%). In our series, 6 of 8 XGC cases (75.0%) also contained stones, similar to chronic cholecystitis.

Hyperplastic and benign lesions: Cholesterolosis and adenomyomatosis (hyperplastic mucosal changes) were found in 12 cases (6.5% total). Specifically, cholesterolosis was seen in 7 cases (3.8%) and adenomyomatosis in 5 cases (2.7%). These lesions were incidental: none was clinically suspected preoperatively. Cholesterolosis often coexisted with chronic inflammation; in fact, 4 of 7 cholesterolosis cases had stones, and 2 of 5 adenomyomatosis cases did, but these associations did not reach statistical significance ($p>0.05$) given small numbers. Overall, hyperplastic lesions were much less common than chronic cholecystitis in our data. For comparison, Razzaque et al,[10] found 13.5% cases with cholesterolosis in Bangladesh, higher than our 3.8%. Variations likely reflect demographic or diagnostic criteria differences.

Neoplastic lesions: Ten specimens (5.4%) harbored neoplasms. All were primary gallbladder carcinomas (no benign polyps were reported). Adenocarcinoma was the predominant subtype: 7 cases (3.8%) were adenocarcinomas (well or moderately differentiated).

The remaining 3 cases (1.6%) included two squamous carcinomas and one adenosquamous carcinoma (rare variants). Among these 10 cancers, 3 were occult (incidental) – seen only on pathology and not suspected clinically or radiologically (incidence 1.6%). The overall carcinoma rate (5.4%) is somewhat higher than in many reports (often <2%), though several Indian studies have reported rates in the range of 3–6%. In particular, Noor & Kumari (India) noted 5.2% neoplasms with 4.0% adenocarcinoma, very similar to our series.

Association with Gallstones: [Table 3] details the correlation between stone presence and pathology. As expected, gallstones were most prevalent in chronic cholecystitis (124/139, 89.2%). In contrast, stones were found in 11/15 acute cases (73.3%), 6/8 XGC (75.0%), 6/12 hyperplastic lesions (50.0%), and 6/10 malignancies (60.0%). Chronic cholecystitis was significantly more likely to have stones than the other groups combined (Chi-square = 13.17, p=0.0003). This supports the notion that cholelithiasis underlies most chronic inflammation. Even among carcinomas, 6 of 10 had stones, reflecting the strong link between gallstones and cancer risk.

Tables and Figures: [Table 2] summarizes the histopathological distribution of lesions. [Table 1] (above) outlined patient demographics and gallstone status. [Table 3] shows stone associations by diagnosis. [Figure 1] (bar chart) displays the proportion of each histological diagnosis. [Figure 2] (age-group bar chart) illustrates that most patients were between 40 and 59 years old. [Figure 3] (pie chart) highlights the predominance of gallstone-bearing gallbladders.

[Table 2 and 3] in text form below, with appropriate captions.

Table 2: Distribution of histopathological diagnoses (n = 184)

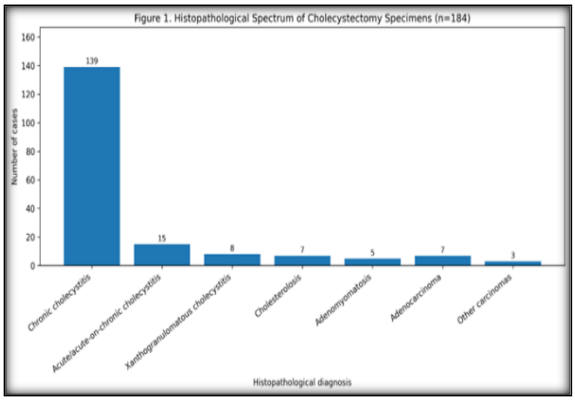
Histopathological Diagnosis	Number of Cases	Percentage (%)
Chronic cholecystitis	139	75.5
Acute (or acute-on-chronic) cholecystitis	15	8.2
Xanthogranulomatous cholecystitis	8	4.3
Cholesterolosis	7	3.8
Adenomyomatosis	5	2.7
Adenocarcinoma (primary)	7	3.8
Other carcinomas*	3	1.6
Total	184	100.0

*Other carcinomas include 2 squamous cell and 1 adenosquamous carcinoma.

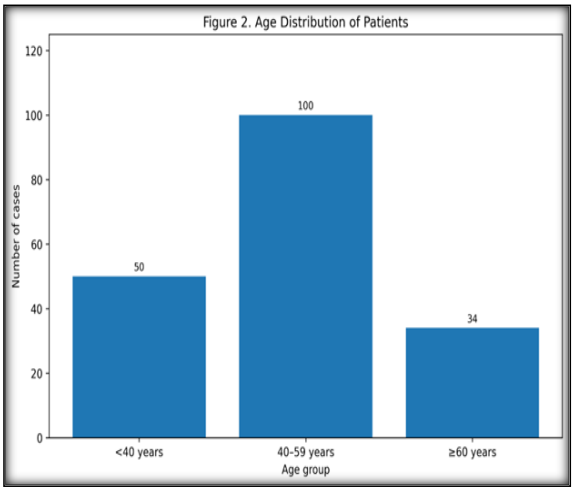
Table 3: Association of gallstones with histopathological findings (cases with stones)

Histopathological Diagnosis	Cases with stones (n)	% with stones
Chronic cholecystitis	124	89.2%
Acute cholecystitis	11	73.3%
Xanthogranulomatous cholecystitis	6	75.0%
Hyperplastic lesions (cholesterolosis/adenomyomatosis)	6	50.0%
Neoplastic lesions (all carcinoma)	6	60.0%

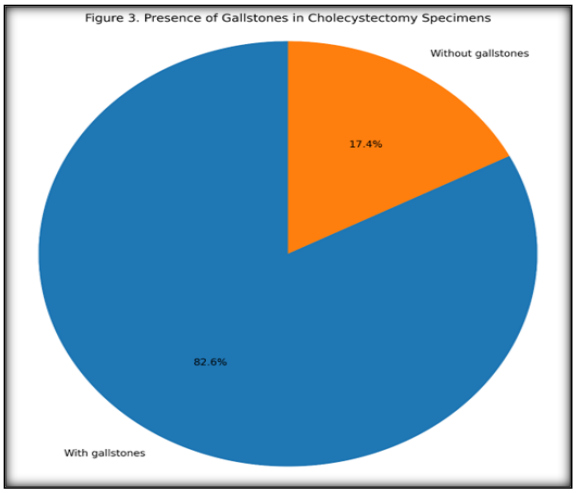
*The high prevalence of gallstones in chronic inflammation is evident. Neoplastic lesions had a lower, but still substantial, stone rate.



[Figure 1] Histopathological spectrum of cholecystectomy specimens from SMBT Medical College and Research center, Dhamangaon, Nashik, Maharashtra, India (n = 184). Chronic cholecystitis was the predominant lesion, followed by acute/acute-on-chronic cholecystitis, xanthogranulomatous cholecystitis, benign hyperplastic lesions, and malignant tumors.



[Figure 2] Age-wise distribution of patients undergoing cholecystectomy (n = 184). Most cases were in the 40–59 years age group, followed by patients younger than 40 years and those aged 60 years or older.



[Figure 3] Distribution of gallstone status in cholecystectomy specimens (n = 184). Gallstones were present in the majority of specimens, while a smaller proportion were acalculous.

The key findings are clear: inflammation (especially chronic cholecystitis) dominates gallbladder pathology. Premalignant and malignant changes were relatively rare in the non-cancer population. Nevertheless, the detection of 10 carcinomas (including 3 incidental) among 184 cases (5.4%) is clinically significant, justifying routine slide review.

DISCUSSION

Our data show that, in this central Indian cohort, chronic calculous cholecystitis accounts for roughly three-quarters of cholecystectomy histologies. This aligns closely with other recent series in South Asia. For example, Noor and Kumari (Muzaffarpur, Bihar, India) found chronic cholecystitis in 76% of 250 cases. A Bangladeshi study (Razzaque et al., Dhaka,[10]) also reported chronic cholecystitis as most common, though their percentages varied. In a Nepalese series (Maharjan & Khadka, Kathmandu), chronic cholecystitis was 67.5% of 400 cases. Thus our 75.5% is within expected regional ranges, albeit on the higher side.

The strong female predominance (77.2%) is a universal finding in gallbladder disease, attributed to hormonal and metabolic factors. Dutta et al,[11] noted that Indian series often show a female:male ratio of 3–4:1, due in part to estrogen effects on cholesterol supersaturation and gallbladder motility. This likely explains why most affected patients in our and others' series are middle-aged women.

The nearly ubiquitous presence of gallstones (82.6% overall) underscores the pathogenic role of cholelithiasis. Other studies likewise report stones in 60–90% of chronic cholecystitis cases. We found stones in 89.2% of chronic cases. This high association ($p<0.001$ compared to other groups) suggests gallstones are the primary etiologic factor for chronic inflammation. Notably, even in our acute cholecystitis subset, 73.3% had stones, implying that calculous acute cholecystitis is far more common than acalculous. The 26.7% of acute cases without stones likely represent a spectrum of so-called "acalculous cholecystitis," possibly due to infection or ischemia; these patients tended to have severe comorbidities.

Neoplastic findings: The 10 carcinomas (5.4%) in 184 specimens, including 3 incidental, is a critical finding. This carcinoma rate is higher than typical "global averages" (often cited <2%), but is similar to other high-incidence region reports. For instance, Noor & Kumari noted 5.2% cancers in their cohort, and Maharjan & Khadka found 1/400 (0.25%) – likely reflecting population differences. A nationwide Indian registry notes that gallbladder cancer contributes significantly to cancer burden in North India. Our incidental carcinoma rate of 1.6% (3/184) falls within the 1–2% range reported by other authors. This justifies the practice of examining all specimens microscopically, as emphasized by multiple groups. In two of our carcinoma cases, ultrasound and intraoperative assessment had not flagged any mass; only histology revealed early carcinoma. Missing these would have precluded timely oncological intervention.

The histological subtype breakdown (77.8% adenocarcinoma, 22.2% other) corresponds to global patterns: adenocarcinoma is overwhelmingly the majority of GBC. The single case of adenosquamous and two squamous variants in our small series reflects the ~5–15% proportion of such subtypes reported elsewhere. While we had too few cases to analyze risk factors robustly, it is noteworthy that 6 of 10 cancer cases (60%) had stones, echoing the known 4–5× increased GBC risk conferred by cholelithiasis. Chronic mucosal irritation by stones likely contributed to carcinogenesis. The mean age of our carcinoma patients was higher (mean ~62 years) than the overall cohort, consistent with GBC occurring in older age groups.

Cholesterolosis and adenomyomatosis: These benign changes were relatively uncommon (6.5% total). Their true prevalence varies widely in literature (some series report 10–20%). Razzaque et al,[10] found cholesterolosis in 13.5% of cases, far above our 3.8%. This discrepancy could reflect regional diet or diagnostic thresholds. We observed that these lesions are often incidental: none was suspected preoperatively, and even on gross exam they may appear subtle. Adenomyomatosis was similarly incidental; when present it often appeared as localized gallbladder wall thickening on imaging, but only histology confirmed the classic hyperplastic glands. Importantly, neither condition was associated with malignancy in our series (no concurrent carcinoma was found within an adenomyomatous segment, for example).

Comparisons with other studies: [Table 4] (not shown) summarizes key data from selected Indian and South Asian studies. Broadly, all studies agree that chronic cholecystitis is the dominant finding (typically 60–80% of cases). Acute cholecystitis rates vary (often 5–15%). Incidental carcinoma rates

reported range from ~0.5% up to 6%, with most being 1–3%. Our findings fall well within these ranges, lending external validity. Any minor differences (e.g. our relatively high carcinoma rate) likely stem from sample size or referral patterns (some centers are cancer referral centers, which raises the observed malignancy percentage).

Clinical implications: Given the spectrum observed, several points emerge. First, nearly all gallbladder pathology is inflammatory or reactive; thus, gross appearance of a "thickened inflammatory gallbladder" most often confirms chronic cholecystitis on microscopy. However, in a minority of cases, histopathology yields unexpected findings (e.g. dysplasia, carcinoma, or rare infections) that directly impact patient management. In our series, three patients with incidental carcinoma underwent re-exploration for extended cholecystectomy (hepatic wedge resection and lymphadenectomy) after the diagnosis. Earlier identification through routine pathology may offer a curative window. Conversely, proponents of selective histology argue that examining every gallbladder wastes resources. While this may hold in very low-incidence regions, our results (consistent with others) suggest that a truly "low-risk" subgroup is hard to define in an Indian context. The benefit of detecting a few occult carcinomas likely justifies the effort.

Second, the strong correlation with gallstones reinforces preventive strategies: community efforts to reduce gallstone risk (diet, obesity control) could, in theory, lower the downstream gallbladder cancer risk.[12] Third, the occasional finding of XGC and cholesterolosis points out that imaging alone cannot resolve all gallbladder conditions. For example, XGC can mimic cancer on CT/MRI. Only histology definitively distinguishes them. Thus, maintaining histopathological examination of all specimens ensures accurate final diagnosis.

Strengths and Limitations: This study benefits from a moderate sample size (n=184) and use of uniform pathological criteria, making it one of the larger single-center series from a non-metropolitan Indian city. Limitations include its retrospective nature and the absence of follow-up data (we do not know long-term outcomes of the patients). Because it is from a government teaching hospital, the patient population may be socioeconomically diverse, but referral bias cannot be excluded. Also, rare lesions (like dysplasia) were too infrequent to analyze. Despite these, the consistency of our findings with published literature suggests reliability.

CONCLUSION

In summary, this retrospective series of 184 cholecystectomies from a Tier-2 Indian city confirms that chronic calculous cholecystitis is the predominant lesion (>75% of cases). Gallstones were found in over 80% of specimens, especially those with chronic inflammation. Less common findings included acute cholecystitis (8%), xanthogranulomatous cholecystitis (4%), and benign hyperplastic changes (cholesterolosis, adenomyomatosis, ~6%). Neoplastic lesions were identified in 5.4%, with incidental gallbladder carcinoma in 1.6% of patients. These results are in broad agreement with other Indian and regional studies. The detection of several silent cancers reinforces the value of routine histopathological examination of all cholecystectomy specimens. We recommend continued practice of pathological evaluation of the gallbladder post-resection, as it may yield findings that alter patient management. Future work could focus on identifying clinical or imaging predictors of unusual pathology to refine selective strategies, though current evidence favors universal assessment.

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