

UNVEILING HISTOPATHOLOGICAL DIVERSITY IN CHOLECYSTECTOMY SPECIMENS

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Abstract

Background: Cholecystectomy is a common surgical procedure for gallstone-related issues and gallbladder pathologies. Despite its frequency, the histomorphological diversity of gallbladder specimens remains underexplored.

Objectives: This study aimed to investigate the histomorphological patterns in 1036 cholecystectomy specimens and emphasize the utility of routine histopathological examination for precise diagnosis.

Methods: A cross-sectional analysis of 1036 cholecystectomy specimens from 2017 to 2019 was conducted. Traditional histopathological techniques were employed, and pathologists examined slides, classifying cases by age, gender, and diagnosis. Statistical analysis was performed using SPSS.

Results: The study identified various histomorphological patterns, including chronic cholecystitis (40.6%), acute cholecystitis (20.1%), intestinal metaplasia in chronic cholecystitis (4.82%), dysplasia (0.579%), and gallbladder carcinoma (0.772%).

Conclusion: This study demonstrates the significance of routine histopathological examination in diagnosing gallbladder pathologies. The results emphasize the need for meticulous examination of cholecystectomy specimens to ensure accurate diagnosis and appropriate patient management. The findings of this study contribute to the understanding of histomorphological diversity in gallbladder specimens, highlighting the importance of thorough histopathological examination.

INTRODUCTION

The gallbladder frequently removed through surgery, notable 50% increase in the cholecystectomy surgeries over the last ten years¹. In U.S annual surgeries exceed a million, primarily addressing gallstone-related issues, with costs ranging from \$6 to \$8 billion². With over 5-700,000 laparoscopic (only laparoscopic, excluding laparotomies) cholecystectomies yearly, stands as one of the most performed abdominal surgeries³. ERCP aids in identifying gallbladder lesions and gallbladder cancer

predominantly detected in cholecystectomy specimens⁴.

The vital role of histopathological examination serves as a cornerstone in directing patient management, underscoring the importance for pathologists to stay abreast of ever-evolving anatomical and pathological intricacies. In regions such as Asia and the Western world, where gallbladder pathologies are burgeoning due to lifestyle shifts, the meticulous scrutiny and processing of specimens are paramount. Timely

fixation of gallbladders is essential to prevent bile-related autolysis, ensuring the integrity of diagnostic assessments. The preferred approach involves opening the gallbladder from the fundus to the cystic duct and sampling full longitudinal sections. Suspicious findings mandate additional sampling, while 2-4 blocks are generally sufficient for focal epithelial atypia. However, higher risk lesions require more thorough sampling to ensure accurate diagnosis and management⁵.

This study aims to contribute to the ongoing discussion regarding the essential role of routine histopathological evaluation of gall bladder specimen. Through meticulous analysis the prevalence and clinical relevance of histopathological findings and their association with distinct histological patterns across diverse gender and age groups, we aspire to furnish invaluable insights. Our aim is to shed light on the nuanced intricacies surrounding routine histopathology of cholecystectomy specimens, thereby contributing substantive evidence to facilitate a more informed and comprehensive discussion on this matter.

Methodology

This study employed a cross-sectional design, analyzing 1036 cholecystectomy specimens obtained from patients who underwent the procedure at Liaquat National Hospital, Karachi, between 2017 and 2019.

Sampling Method

A consecutive sampling method was used to select cases from the archive of our institution's pathology department.

Subject Selection

The study included all cholecystectomy specimens received between 2017 and 2019. Cases were stratified based on gender and age.

Histopathological Examination

Experienced histopathologists examined the slides using light microscopy (Nikon, Japan) and recorded the histopathological diagnoses. The examination procedure involved routine processing, embedding, and staining with hematoxylin and eosin (H&E).

Statistical Analysis

Statistical analysis was performed using SPSS (version 26.0, IBM, Armonk, NY, USA). Descriptive statistics were used to summarize demographic data. Frequency analysis was used to determine the distribution of histomorphological types. Chi-squared test was used to compare categorical variables. Exact p-values and 95% confidence interval (CI) limits were calculated for all statistical tests.

Data Presentation

All percentages are presented with actual numbers. Continuous variables are presented as mean $\pm$ standard deviation.

RESULTS:

During our examination of 1,036 gallbladder specimens from 2017 to 2019, a significant gender disparity was observed. Among these specimens, majority were from female patients (see Table 1)

Table 1: Gender distribution

Gender	Frequency	Percent
Male	279	26.9
Female	757	73.1
Total	1036	100.0

Majority of cases were in the middle-aged adult category (35-54 years), followed by the adult age category (55-64 years), as illustrated in Figure 1.

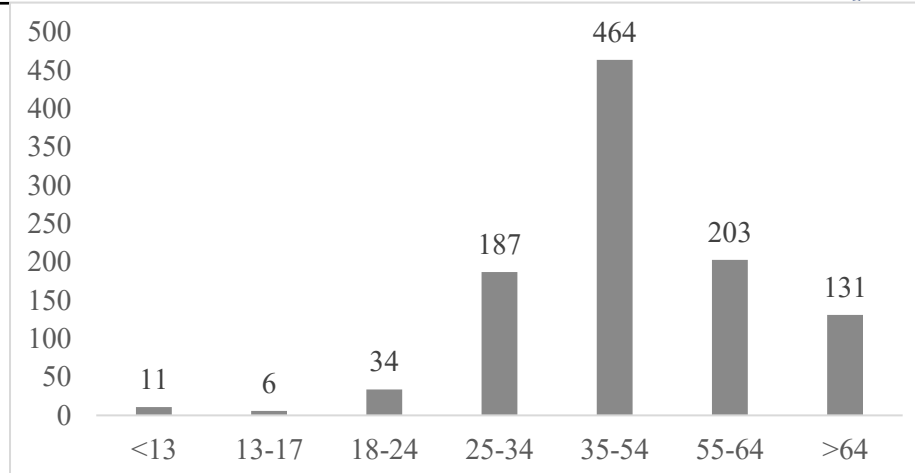


Figure1: Frequency of gallbladder lesions in different age groups

Upon microscopic examination of the 1,036 gallbladder specimens, we identified several histomorphological variants, the most common being chronic cholecystitis, followed by acute on chronic, as shown in figure 2, cases with incidence rate <10 were grouped into others which can be seen in table 2.

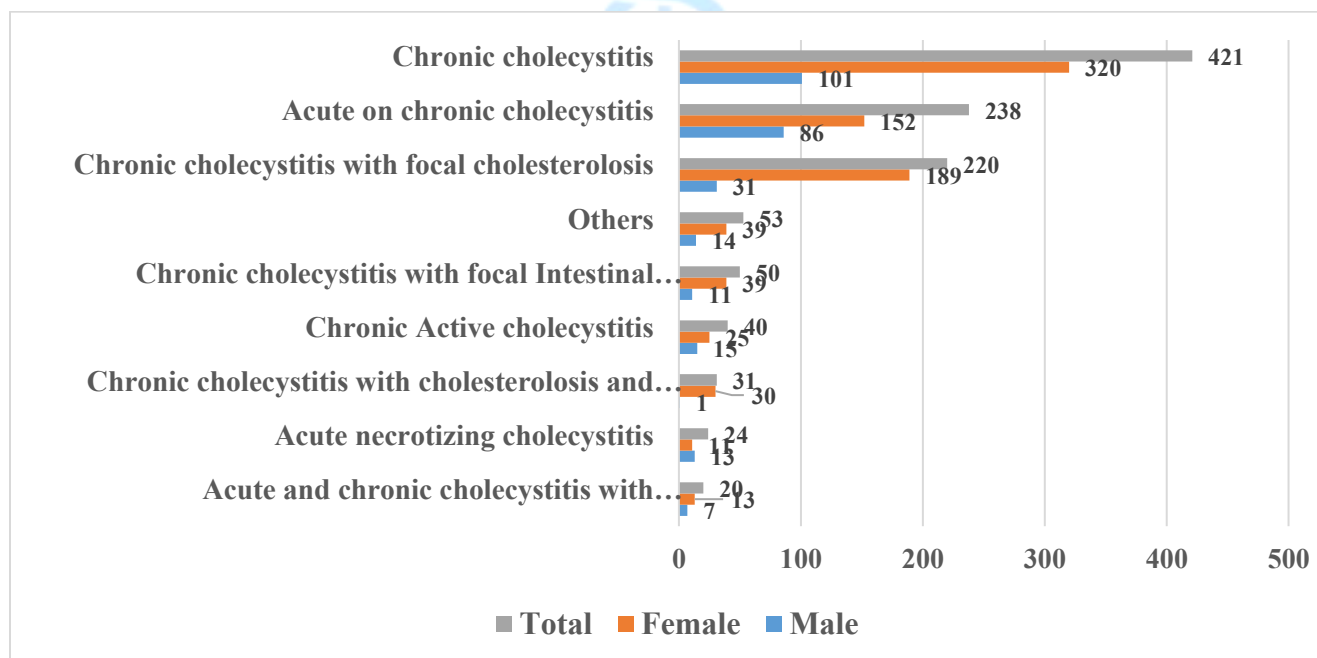


Figure 2: Frequency of histomorphological variants in cholecystectomy specimen

Table 2: Cases classified as others:

Histomorphological Types	Male	Female
Acute on chronic cholecystitis with focal intestinal metaplasia and low grade dysplasia with focal cholesterolosis	0	1
Chronic cholecystitis with cholesterolosis and low grade dysplasia	0	1
Acute hemorrhagic cholecystitis.	1	0
Extensively Autolysed tissue.	0	1
Acute cholecystitis with perforation	1	0
Acute cholecystitis	0	1
Chronic active cholecystitis with focal intestinal metaplasia	0	1
Moderate to poorly differentiated infiltrating adenocarcinoma	0	1
Follicular cholecystitis	0	2
Chronic active cholecystitis and focal cholesterolosis with intestinal metaplasia	1	2
Chronic active cholecystitis and focal cholesterolosis	1	4
Acute on chronic xanthogranulomatous cholecystitis	4	2
Chronic cholecystitis with focal intestinal metaplasia and low grade dysplasia	2	4
Moderate differentiated infiltrating adenocarcinoma	0	7
Acute on chronic cholecystitis with focal intestinal metaplasia	1	7
Xanthogranulomatous cholecystitis	3	5

Amongst our study population, the incidence of gallbladder cancer was relatively low, with 8 reported cases of adenocarcinoma. Among these cases, 7 were classified as moderately differentiated, while 1 case was moderate to poorly differentiated. The distribution across age groups revealed that 4 patients were in the elderly age group (65 years or older), followed by 2 cases in adults (55-64 years) and 1 case in middle adults (35-54 years). In terms of tumor extent, 7 out of the 8 gallbladder cancer cases were staged. Among these, 6 cases were classified as T2, indicating involvement of surrounding adipose tissue. Additionally, 1 case was limited to the muscularis propria (T1 stage). The extent of adenocarcinoma in the remaining case was diagnosed on a trucut biopsy, precluding detailed commentary.

DISCUSSION:

Our analysis revealed that the highest number of instances occurred within the middle adult age bracket (35-54 years), indicating a significant prevalence of gallbladder disorders in this demographic. Interestingly, we observed that the number of cholecystectomy cases in the children's age group (1-12 years) surpassed that in the

adolescent age group, indicating a potential shift in disease burden across different age categories. Our findings are consistent with international research conducted in various regions, including China⁶ and Jammu⁷, as evidenced by similar trends in age distribution and disease prevalence.

Our study found a significant predominance of gallbladder disorders in women, with 757 cases compared to 279 in men, indicating a male-to-female ratio of less than 1:3. This trend is consistent with findings from other studies, such as those conducted in northeast India⁸ and by Virginian doctors, where 66% of cases were female and 34% male⁹ as well as in Africa (Tunis) reported a more balanced gender distribution with a sex ratio of 1:2.78¹⁰.

Regarding histological types, our study highlighted **chronic cholecystitis** as the predominant type, accounting for 40.6% of cases, followed by acute-on-chronic cholecystitis at 20.1%. Similar findings were reported in studies from Jammu and by Limaïem F et al., with chronic cholecystitis rates of 50% and 67%, respectively¹¹. Benkhadoura M et al. observed a slightly higher prevalence of chronic cholecystitis at 70.47%¹². The study by Benkhadoura M et al. reported a slightly higher incidence of chronic cholecystitis at 70.47%, while study from africa

mentioned a higher rate of 88.8%. Interestingly, a substantial number of cases (18.2%, totaling 189) in our study exhibited solely cholesterolosis alongside chronic cholecystitis. In contrast, a different study identified cholesterolosis in 62 cases (11%), all associated with chronic cholecystitis¹³. However, our findings indicate that the majority of cases of **cholesterolosis** are associated with chronic cholecystitis, followed by chronic cholecystitis with focal intestinal metaplasia and with acute and chronic cholecystitis (31 and 21 cases, respectively). We noted cholesterolosis with low-grade dysplasia in just 2% of cases.

Analyzing **acute inflammation of the gallbladder**, we identified it in 1% of cases, some studies reported slightly higher prevalence rates, such as 4%¹⁴ and 7.1% in African study.

We documented 24 cases (2.3%) of **acute necrotizing/gangrenous cholecystitis**, primarily observed in the elderly age group, with a notable slight male predominance (1.18:1). In contrast, additional studies have reported varying incidences of acute gangrenous inflammation. For instance, one study noted 8 cases (1.5%)¹⁵, while a study from Iran indicated a higher prevalence of 19 cases (37.25%)¹⁶, displaying histological evidence of gangrenous cholecystitis with a considerably greater male predilection at approximately 5:1 compared to our findings. Additionally, a study conducted in Turkey documented 26 cases (7.1%) of gangrenous cholecystitis. Our study's findings contrast with others, such as a prevalence of 29.3%¹⁷ and 18.8% of cases with male prominence and a mean age around 64 years, similar to our study. The research from Australia comprised 106 patients (37%) diagnosed with gangrenous cholecystitis, while 184 patients (63%) were included in the study¹⁸, showing male predilection and elderly age, akin to our findings. **Hyalinizing cholecystitis**, display uniform thin layer of hyalinized fibrous tissue, with or without calcification, encountered in about 1% of cholecystectomies. Cancer often detected in cases with minimal or no calcification

Regarding chronic **xanthogranulomatous cholecystitis** (XGC), a pearl point is elevated serum CA19-9 levels have been observed without any identifiable carcinoma in this histomorphological type. We observed 08 cases (0.8%) in our study,

followed by acute on chronic XGC (06 cases). In our investigation, chronic XGC was identified in 08 cases (0.8%), with acute on chronic XGC following closely, noted in 06 cases. Xanthogranulomatous cholecystitis was slightly higher in our study compared to others; for example, Limaïem F et al. reported a 0.30%, while Benkhadoura M et al. documented a frequency of 0.10% for XGC, showing somewhat similar results to ours.

Regarding Cancers, the **gallbladder cancers** are infrequent gastrointestinal cancer, contributing to 1.2% of all cancer incidences. Typically occurring after the age of 60, ranks as the 20th most common tumor and the 17th deadliest cancer. Two-thirds of patients diagnosed with gallbladder cancer are aged over 65 years. There were 08 cases of adenocarcinoma, with 07 cases classified as moderately differentiated and 01 case as moderate to poorly differentiated adenocarcinoma. Among these 6 exhibited a (T2) stage, while only one case was limited to the muscularis propria (T1). The extent of adenocarcinoma in the remaining 1 case is diagnosed on a trucut biopsy, and therefore, a detailed commentary cannot be provided. From a histological perspective, each of the four cases was determined to be well-differentiated adenocarcinoma. Silecchia et al. identified six incidental gallbladder carcinomas in their study¹⁹. Additionally, another study reported 24 cases of incidental gallbladder carcinoma, diagnosed by examining 4317 cholecystectomy specimens over an 8-year period²⁰. We observed a somewhat higher prevalence of cancer compared to Siddiqui et al., where among 220 cholecystectomy specimens, six cases were identified, including three patients with advanced stages (T2 and T3)²¹. Shrestha et al. documented one case of stage T2 disease and three cases of stage T3 disease out of nine incidental gallbladder carcinomas in a series of 668 cholecystectomy specimens²², indicating a higher prevalence compared to our study. Likewise, Haq et al. reported the presence of 2 patients with stage T2 disease among 5 incidental gallbladder carcinomas in a series of 107 specimens²³, while Ghimire et al. identified 2 patients with stage T2 disease out of 10 incidental gallbladder carcinomas in a series of 783 specimens²⁴, both demonstrating a somewhat higher prevalence than observed in our carcinoma cases. However, it's worth noting that the majority of our

cases were also of T2 stage disease (6 out of 7 cases). Cancers such as oral squamous cell carcinoma tend to affect predominantly middle age groups²⁵, while soft tissue sarcomas exhibit variable age group prevalence²⁶, in contrast to carcinoma gallbladder which related to elderly age, as also noted in our study population.

Conclusion:

Cholecystectomy specimens at our institution undergo a standardized histopathological examination. The gallbladder samples are carefully dissected and inspected for any visible irregularities. It is imperative to recognize the significance of identifying gallbladder carcinoma in unsuspected specimens, given that cholecystectomy serves as both the therapeutic approaches for gallbladder cancer and related lesions linked to cholelithiasis. Despite ongoing debates suggesting that the routine histopathological examination process may strain hospital resources and expertise, The main aim of this study is to shed light on nuanced intricacies associated with the routine histopathology of cholecystectomy specimens. By providing substantial evidence, this study aims to contribute to a more informed and comprehensive discussion on the subject.

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Conflict of Interest: The authors declare that they have no conflict of interest

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