

Histopathological variants of gallbladder after cholecystectomy in Eastern Libya: A report of 3412 specimens

Mohamed Omar Benkhadoura ^{1,*}, Othman Hammad Tajoury ², Khaled Khalil Elgazwi ³, Talal Khalifa Elkhweldi ³, Akrem I. Elshaikhy ³ and Aisling Kraus ⁴

¹ Department of surgery Benghazi Medical Centre, Faculty of medicine, Benghazi university, Libya.

² Department of surgery, Faculty of medicine, Libyan international medical university LIMU, Benghazi, Libya.

³ Department of surgery, Al Jala Hospital, Faculty of medicine, Benghazi university, Libya.

⁴ Department of Obstetrics and Gynecology at eastern health in Melbourne, Australia.

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Abstract

Background: Cholecystectomy is one of the most common surgical operations and is performed routinely for a variant of gallbladder diseases, including chronic and acute cholecystitis and gallbladder cancer (GBC). The gallbladder is one of the most commonly encountered specimens submitted to histopathology department. The aim of this study was to determine the histopathological pattern of gallbladder lesions in cholecystectomy specimens in two university hospitals in the Eastern part of Libya.

Material and methods: From January 2009 to June 2017, all histopathology reports of 3423 consecutive gallbladder specimens after elective and emergency cholecystectomy were retrospectively analyzed in two university hospitals.

Results: Of the 3423 gallbladder specimens sent for histopathological examination during the study period, 486 were male (14.2%) and 2937 were female (85.8%), with a mean age of 42 (14 to 93) years. Chronic cholecystitis was found in 2792 (81.6%), acute cholecystitis in 237 (6.9%) and cholesterosis in 223 (6.5%) patients. GBC was detected in 4 (0.11%) patients. Incidence of chronic cholecystitis was significantly higher in female (n=2425; 82.6%) than in male (n=367; 75.5%) patients ($P < 0.001$). However, acute cholecystitis, empyema of the gallbladder, and gangrenous cholecystitis were more common in males than females (8.6% vs 6.6%; 4.3% vs 0.9%; and 2.5% vs 0.8% respectively).

Conclusion: The histopathological spectrum of gallbladder after cholecystectomy was observed to be quite diverse. The most prevalent diagnosis was chronic cholecystitis followed by acute cholecystitis and cholesterosis of the gallbladder, whereas carcinoma of the gallbladder was rarely observed. Although chronic cholecystitis is more common in females, the incidence of complications such as acute cholecystitis, empyema of gallbladder, and gangrenous cholecystitis were more common in males than females.

Keywords: Gallbladder disease. Gallbladder specimen. Histopathological examination; Cholecystectomy; Gangrenous gallbladder

1. Introduction

Cholecystectomy is a common abdominal operation which is performed routinely for various gallbladder diseases including chronic and acute cholecystitis, polypoid lesions, cholesterosis, fibrosis and Neoplastic conditions that may be detected include gallbladder polyps, gallbladder adenomas, and gallbladder carcinomas [1]. The gallbladder is one

* Corresponding author: Mohamed O Benkhadoura

of the most commonly encountered specimens submitted to histopathology departments. [2] Gallbladder disease is comprised of various histopathological phenomena, including neoplastic and non-neoplastic conditions. A diverse array of diseases affects the gallbladder, and while chronic cholecystitis is the most common, other forms of gallbladder disease often manifest with similar signs and symptoms. [3] These histopathological variants can present with similar clinical symptoms, making accurate diagnosis and appropriate management challenging chronic cholecystitis is often associated with gallstones, which can cause inflammation and fibrosis of the gallbladder wall. Adenomyomatosis is a benign condition that is characterized by the presence of small outpouchings in the gallbladder wall. Cholesterosis is another benign condition that is characterized by the accumulation of cholesterol-filled macrophages in the gallbladder wall. Therefore, understanding the histopathological variants of the gallbladder after cholecystectomy is important for accurate diagnosis and appropriate management of any subsequent disease. In this article, we will review the various histopathological variants of the gallbladder after cholecystectomy. In addition the Gallbladder polyps are growths that protrude from the gallbladder wall and are often discovered incidentally during imaging studies. Most gallbladder polyps are benign, but some may be malignant and require further evaluation. Gallbladder adenomas are rare benign tumors that arise from the glandular tissue of the gallbladder. [4] They are typically small and asymptomatic but may require surgical removal if they are large or causing symptoms.

Gallbladder carcinomas are rare but aggressive malignant tumors that can invade the gallbladder wall and spread to other organs. They are often diagnosed at an advanced stage when treatment options are limited. Gallbladder cancer is more common in certain populations, such as Native Americans and Hispanics, and is often associated with a history of gallstones. It is important to note that the histopathological findings in the gallbladder after cholecystectomy may vary depending on various factors, such as the underlying cause of the gallbladder disease, the patient's age, sex, and medical history.[5] Therefore, it is essential to interpret histopathological findings in the context of the patient's clinical presentation and other relevant factors.

2. Materials and methods

From January 2009 to June 2017, all histopathology reports of 3423 consecutive gallbladder specimens after elective and emergency cholecystectomy were retrospectively analyzed in two university hospitals.

Patient details such as age, sex, and histopathological diagnosis were recorded.

2.1. Statistical analysis

All statistical analyses were performed by using the Statistical Package for the Social Sciences (SPSS Inc.; Chicago, IL, USA), version 18.0 software program. The data was analyzed using the Chi-square test. A p value <0.05 was considered to indicate statistical significance.

3. Results

Table 1 Age and sex distribution of gallbladder disease

Age group	Male; n(%) n=486	Female; n(%) n=2337	Total; n(%) n=3423
14-20	5 (1.0)	68 (2.3)	73 (2.1)
21-30	59 (12.1)	630 (21.5)	689 (20.1)
31-40	133 (27.4)	947 (32.2)	1080 (31.6)
41-50	120 (24.7)	638 (21.7)	758 (22.1)
51-60	79 (16.3)	411 (14.0)	490 (14.3)
61-70	66 (13.6)	179 (6.1)	245 (7.2)
71-80	18 (3.7)	60 (2.0)	78 (2.3)
81-90	6 (1.2)	3 (0.1)	9 (0.3)
91-93	0 (0)	1 (0.03)	1 (0.03)

Table 2 Details of histopathological findings from 3423 cholecystectomy specimens

Histopathological diagnosis	Male; n(%) n=486	Female; n(%) n=2937	Total; n(%) n=3423
Chronic cholecystitis	367 (75.5)	2425 (82.6)	2792 (81.6)
Acute cholecystitis	42 (8.6)	195 (6.6)	237 (6.9)
Empyema gallbladder	21(4.3)	26 (0.9)	47 (1.4)
Gangrenous gallbladder	12 (2.5)	24 (0.8)	36 (1.1)
Cholesterolosis	24 (4.9)	199 (6.8)	223 (6.5)
Gallbladder polyp	0 (0)	2 (0.1)	2 (0.05)
Gallbladder diverticulum	2 (0.4)	0 (0)	2 (0.05)
Gallbladder adenoma	1(0.2)	1(0.0)	2 (0.05)
Porcelain gallbladder	0 (0)	2 (0.1)	2 (0.05)
Adenomyomatosis	12 (2.5)	55 (1.9)	67 (2.0)
Xanthogranulomatous Cholecystitis	2 (0.4)	2 (0.1)	4 (0.1)
Dysplasia	0 (0)	5 (0.2)	5 (0.1)
Carcinoma	3 (0.6)	1 (0.0)	4 (0.1)

During the study period, 3423 samples of the gallbladder were examined and analyzed for their histopathology. Out of these, 14.2% were male (486) and 85.8% were female (2937), with an average age of 42 (ranging from 14 to 93) years. The age range with the highest occurrence of gallbladder disease in this study was 31-40 years, with 31.6% of the specimens falling in this group, followed closely by the 41-50 age range, which comprised 22.1% of the total specimens. These two age groups together made up 53.7% of all specimens. The distribution of gallbladder disease by age and sex is presented in Table 1. Of all the patients, 81.6% (2792) had chronic cholecystitis, 6.9% (237) had acute cholecystitis, and 6.5% (223) had cholesterolosis, as shown in Table 2. Dysplasia was found in only 0.14% (5) of the patients, while gallbladder cancer (GBC) was detected in 0.11% (4) of the patients. Chronic cholecystitis was found to be significantly higher in females (n=2425; 82.6%) compared to males (n=367; 75.5%) ($P < 0.001$). However, acute cholecystitis, empyema of gallbladder, and gangrenous cholecystitis were more common in males than females, as shown in Table 2.

4. Discussion

The histopathological features and incidence of gallbladder lesions varies depending on race, country and institute. [6, 7] It is well known that gallbladder disease affects women more frequently than men, and is seen more frequently in middle aged individuals. [6,7,8,9] In our study, lesions of the gallbladder were more common in females than in males with a mean age of 42 years (Table 1), which is similar to other studies.

Chronic cholecystitis, the most common histopathological finding in our study, constituted 81.6% in this study which is comparable with the study of Chin et al (86%). [9] Meman et al and Sangwan et al reported slightly lower rates of 64.8% and 69.8%, respectively. [10,11] Siddiqui et al reported a higher rate of 92.3%. [12] In our study, chronic cholecystitis is more common in females with a mean age of the patients with of 41.8 years, comparable with the previous studies.

Acute Cholecystitis is characterized by marked congestion, edema, hemorrhage, acute inflammatory infiltrate and fibroblastic proliferation. [13] The rate of acute cholecystitis in histopathological specimens varies from 1.5 to 11.7%. [7,8,9, 11] Acute cholecystitis comprised 6.9% of cases of gallbladder disease in our study, which is consistent with other studies. In contrast to other studies, which showed female preponderance. [11,13] we had male preponderance, consistent with the study of Mazlum et al. [2], The mean age was 42.3 years. This is comparable with Sangwan et al (42.7 years). Kumar et al reported a mean age of 51.9 years. [13]

Distinguishing empyema of the gallbladder from uncomplicated acute cholecystitis often presents a challenge. [12] In numerous reviews, 2% to 11 % of patients undergoing cholecystectomy have been identified as cases of empyema of the gallbladder. [13] Memon et al reported quite a high rate (31.5%) of empyema associated with cholecystitis. [10] In the present study we report 47(1.4%) cases of empyema of gallbladder, consistent with Siddiqui et al (1.3%). [12]

The Mayo Clinic reports that in around 2.5 % of all patients coming for surgical exploration, gangrenous cholecystitis has occurred. [13] Kumar et al reported that the same was true for 2.25% cases, with a slight preponderance in men. [13] Adnan et al found 2% with male predominance. [6] In the present study we found 1.1% gangrenous cholecystitis with male predominance.

Deposition of cholesterol esters in epithelial macrophages and mucosal villous hypertrophy are the characteristic features of cholesterosis. It is usually asymptomatic and diagnosed incidentally following histopathological investigation. [11] Various studies reveal 0-28.6% incidence of cholesterosis of the gallbladder. [14] Our study showed 6.5% incidence of cholesterosis, which is in accordance with the literature. Similarly, the present series revealed a female predominance and a mean age of 39.9 years.

Gallbladder (GB) adenomyomatosis (ADM) is characterized by Rokitansky-Aschoff sinuses, which occur due to hypertrophy of the mucosal epithelium which invaginates into the interstices of a thickened tunica muscularis. In 2017, Golse et al reviewed the literature and found that the prevalence of ADM in cholecystectomy specimens is estimated to be between 1% and 9% with a balanced sex ratio, with the incidence of ADM increasing in patients over the age of 50. [15] ADM is usually asymptomatic. Symptomatic ADM is an indication for cholecystectomy. [15] In the present study the rate is 2% more common in males and the mean age is 42 years.

Xanthogranulomatous cholecystitis (XGC) is often misdiagnosed as carcinoma of gallbladder. [11] Its incidence is reported as 0.7–13.2 % of all inflammatory conditions of the gallbladder. [16, 17] Hale et al assessed 1599 patient records from 29 studies and categorized the findings in terms of geographical region, including the Americas, Europe, India, and Far East. [18] This review found the incidence of XGC to be 1.3–1.9 %, except in India, where the incidence was 8.8 %. Since the incidence in our study is 0.1%, which is low compared with Hale's review, Libya as a North African country is considered an area with very low incidence of XGC. Middle-aged women demonstrate a higher prevalence of XGC. [11, 19] In the presented series, there were two female and two male patients with XGC. Guzmán-Valdivia et al reported male predominance. [20]

Porcelain gallbladder, also known as calcified gallbladder, is an extremely uncommon condition with a reported incidence of 0.06 to 0.8%. It is more common in elderly females. [21] Patients with porcelain gallbladder tend to be asymptomatic and the condition is usually diagnosed as an incidental finding on plain abdominal radiograph, ultrasound, and CT. Porcelain gallbladder is associated with a high risk of malignancy (5-22%); hence, cholecystectomy should not be delayed. [21] In the current study, we found slightly lower incidence of porcelain gallbladder (0.05%) compared to other studies.

A gallbladder diverticulum is a rare phenomenon which is seldom discussed in the literature. A diverticulum can be congenital or acquired. Diverticulum of the gallbladder may exist without causing symptoms, or it may present with an array of signs and symptoms. It is frequently associated with cholelithiasis, and cases of carcinoma have been reported in instances of congenital diverticulum of the gallbladder. [22] In the current study, two (0.05%) male patients had gallbladder diverticulum.

Gallbladder polyps occur with a prevalence of approximately 5%. These lesions are often detected incidentally on ultrasound or CT scans. Gallbladder polyps are divided into a classification system of neoplastic versus non-neoplastic. Although the majority of gallbladder polyps are benign cholesterol polyps, current guidelines recommend cholecystectomy for gallbladder polyps larger than 1 cm in size, due to the higher probability of malignancy associated with them. [23] In our study, only two (0.05%) female cases of gallbladder polyp were identified. The prevalence of this pathology is significantly higher amongst males. [24]

The epithelial phenomena implicated in gallbladder carcinogenesis are dysplasia and adenoma, which each represent a distinct carcinogenetic model. It is suggested that malignant transformation develops through either the adenoma-carcinoma sequence or the dysplasia-carcinoma sequence. [2]

Adenomas, which comprise 10% of gallbladder polyps diagnosed on ultrasound, have been reported in 0.3% to 0.5% of gallbladders removed for either chronic cholecystitis or cholelithiasis. They tend to be asymptomatic. [25] In the present

study 2 (0.05 %) patients had adenomas in their gallbladder specimens and incidence was lower than that of other published studies.

The second carcinogenetic model is the dysplasia-carcinoma sequence. The incidence of dysplasia found in the literature ranges between 0.4 and 33.8%. [2, 26] There are a variety of plausible explanations for the difference, such as varying definitions of precursor lesions, extent of sampling and racial and geographical differences in the incidence of gallbladder carcinoma and its precursors. [2] The incidence of dysplasia seen in our series (0.1%) is lower than that in the literature. It is noted that all the five cases were female.

The histopathological examination revealed adenocarcinoma of the gallbladder in four (0.1%) patients. The incidence of gallbladder cancer in this series was relatively low compared with other studies, which show an incidence ranging from 6.9 to 12%. [6, 12]

5. Conclusion

The histopathological spectrum of gallbladder disease after cholecystectomy was found to be quite diverse. The most common histopathological diagnosis in gallstone disease was chronic cholecystitis followed by acute cholecystitis and cholesterosis. Although chronic cholecystitis is more common in females, the incidence of complications such as acute cholecystitis, empyema of the gallbladder and gangrenous cholecystitis was more common in males than females. Gallbladder cancer is rare in the Eastern part of Libya.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

No conflict of interest was declared by the authors.

Statement of ethical approval

Due to the retrospective design of the study, Ethics Committee Approval was not obtained.

Statement of informed consent

Due to the retrospective design of the study, the informed consent was not obtained.

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