

**ORIGINAL ARTICLE**DOI: <https://doi.org/10.3329/mediscope.v9i1.58519>**Spectrum of Morphologic Changes in Histopathological Specimen of Gallbladder in a Tertiary Care Hospital*****SN Karim¹, MN Nowsher², S Rahman³****Abstract**

Background: Diseases of gallbladder are incidentally found and when symptomatic, present with sign and symptoms of cholecystitis and cholelithiasis. Routine examination of gallbladder both grossly and microscopically shows many interesting findings. **Aim:** The aim of the study was to observe and analyze the diverse morphological and histopathological features of gallbladder specimens following cholecystectomy procedure. **Methods:** This cross-sectional study was carried out at the Department of Pathology, Gazi Medical College, Khulna; from April 2019 to March 2021 and the sample size was 62. After routine tissue processing and H/E staining all the slides were thoroughly examined under light microscope stains to confirm the diagnosis as well as to evaluate histopathologic characteristics. The data was tabulated and statistical analysis was performed. **Results:** Out of 62 cases 30.64% samples belonged to age 26-35 years and the mean age was 44.32 years. 69% patients were female with a female to male ratio 2.26:1. Histologically, majority of the cases (54.83%) were diagnosed as chronic cholecystitis, followed by chronic cholecystitis with cholelithiasis (14.51%). Total 8 (12.91%) patients were found to have carcinoma of gallbladder with 50% of them belonging to grade I. **Conclusion:** Predominance of female gender in gallbladder ailment is clear from this study. Cholecystitis is the most common gallbladder disease. Microscopy varieties of histomorphological changes, including metaplasia and precursor changes are suggestive of high risk for gallbladder malignancy. Therefore, prompt detailed histopathological analysis of the cholecystectomy specimens will help to confirm the benign nature of the disease or to detect any precursors of malignancy.

Introduction

Gallbladder disease is a common health problem and major cause of morbidity and mortality worldwide.¹ It can range from cholelithiasis to various non-neoplastic and neoplastic conditions. Cholelithiasis is the commonest biliary pathology with an incidence of 10-20% of world population.² It can produce diverse histopathological changes in gallbladder mucosa, such as acute inflammation, chronic inflammation, granulomatous inflammation, hyperplasia,

cholesterolosis, dysplasia and carcinoma.³

Many risk factors for gallbladder disease have been identified, such as ethnicity, genetics, age, gender, female sex hormones, oral contraceptive use, obesity, rapid weight loss, diet high in cholesterol, fatty acids and carbohydrates, Diabetes mellitus, sickle cell anemia, spinal cord injury, Wilson's disease and metabolic syndrome.¹

Most of the gallstones are silent (>80%) but can also cause numerous complications. Gallbladder carcinoma is a rare condition and commonly

1. Dr. Syeda Noorjahan Karim, Assistant Professor, Department of Pathology, Gazi Medical College, Khulna.
Email: noorjahanska@gmail.com

2. Dr. Md. Neaz Nowsher, Pathologist, Khulna Medical College & Hospital, Khulna.

3. Dr. Shamim Rahman, Assistant Professor, Department of Pathology, Jahurul Islam Medical College, Bajitpur, Kishoreganj.

diagnosed as incidental histological findings following cholecystectomy for gallstone². So, as a routine standard practice the surgeons should submit all gallbladder, removed surgically, for histopathology. It helps to exclude any gallbladder pathology that can have significant impact on patient management.⁴

Therefore, the aim of the study was to analyze the histopathological changes associated with gallbladder disease.

Methodology

This was a cross sectional observational study carried out at the Department of Pathology, Gazi Medical College, Khulna; from April 2019 to March 2021. The sample size was 62. The study population was all the specimen of surgically resected gallbladder received at Department of Pathology of Gazi Medical College (GMC) during specified time duration. All these specimens were sectioned, stained and studied in Department of Pathology, GMC.

All the specimens were fixed in 10% formalin and kept for overnight fixation. Next day, the tissues were examined during grossing and were embedded accordingly. Tissue processing was performed manually following standard protocol for paraffin embedding. The paraffin blocks were sectioned with a rotary manual microtome at 5 micrometer thickness. From each paraffin block tissue sections were taken on glass slides. After deparaffinization with xylene the slides were rehydrated with decreasing graded alcohol. Then slides were stained with routine Haematoxylin and Eosin (H&E) stain. Slides of all cases were examined thoroughly to confirm the diagnosis and to evaluate histopathologic characteristics. In case of carcinoma of gallbladder, evaluation of type of tumor, histologic grade of tumor, presence of lymphovascular invasion, perineural invasion and presence of necrosis were observed. Tumors were graded as well, moderate and poorly differentiated carcinoma. Pathologic staging was done according to TNM staging system.

Results

This cross-sectional study was aimed to assess different morphologic changes in gallbladder in

different disease. In this study age of the patients varied from 26-80 years. Out of 62 cases 30.64% samples belonged to age 26-35 years and mean age was 44.32 years (Table 01). Total 69% patients were female with a female to male ratio 2.26:1 (Figure 01). Histologically, 5(8.06%) patients were diagnosed as Acute Cholecystitis, 34 (54.83%) patients as Chronic cholecystitis, 9 (14.51%) patients as Chronic cholecystitis with Cholelithiasis, 2 (3.22%) patients as Follicular Cholecystitis, 2 (3.22%) patients as Xanthogranulomatous Cholecystitis, 2 (3.22%) patients as Empyema and 8 patients as (12.91%) Carcinoma (Figure 02). Among 8 carcinoma patients, 5 patients were diagnosed as adenocarcinoma, NOS; 1 patient as papillary adenocarcinoma, 1 patient as adenosquamous carcinoma, 1 patient as undifferentiated carcinoma (Table 02). In the present study, among 8 carcinoma patients, 50% belongs to grade I, 37.5% belongs to grade II and 12.5% belongs to grade III (Table 03).

Figures:

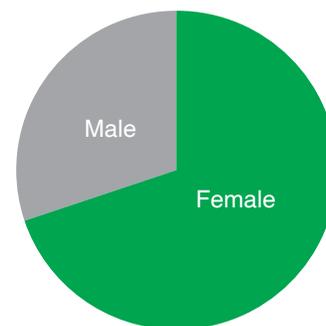


Figure 01: Pie chart showing distribution of patients according to sex, n=62

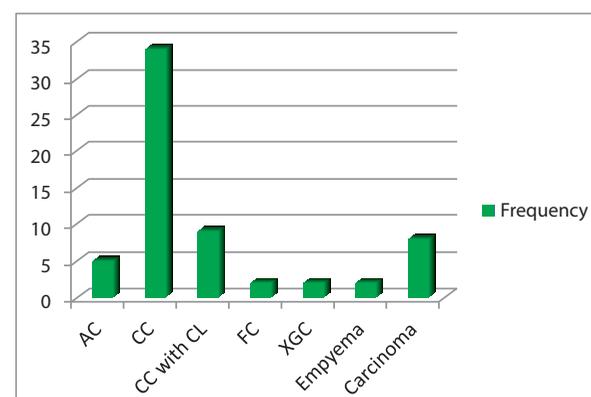


Figure 02: Distribution of patients according to histologic diagnosis, n=62

Tables:**Table 01: Distribution of patients according to age, n=62**

Age Range	Frequency (%)
26-35	19 (30.64%)
36-45	13 (20.96%)
46-55	17 (27.41%)
56-65	11 (17.74%)
66-75	1 (1.61%)
76-85	1 (1.61%)
Total	62 (100%)

Table 02: Distribution of carcinoma patients according to histologic type of carcinoma, n=8

Types of carcinoma	Frequency (%)
Adenocarcinoma, NOS	5 (62.5%)
Papillary Adenocarcinoma	1 (12.5%)
Adenosquamous carcinoma	1 (12.5%)
Undifferentiated carcinoma	1 (12.5%)
Total	8 (100%)

Table 03: Distribution of carcinoma patients according to grade of carcinoma, n=8

Grade	Frequency (%)
Well differentiated (G1)	4 (50%)
Moderately differentiated (G2)	3 (37.5%)
Undifferentiated (G3)	1 (12.5%)
Total	8 (100%)

Discussion

Worldwide gallbladder disease is a common health problem.⁵ The histopathological entities encountered in gallbladder ranges from cholelithiasis on one end of spectrum and carcinoma on another.⁶ Gallbladder cancer is the most common and aggressive malignant tumor of the biliary tract. It has shortest median survival from the time of diagnosis^{7,8}. So early diagnosis is essential for better prognosis. It is commonly diagnosed by the pathologist as an incidental histologic finding after a routine cholecystectomy for benign disease.⁹ So, as a routine, every specimen should be submitted for histopathology. There are various risk factors for gallbladder diseases. Among them sex is an important risk

factor. In the present study, it was observed that majority (69%) of the patients were female with a female to male ratio 2.26:1. Similarly, some authors found most of the patients were female with a female to male ratio 1.5: 1.1 Another group of authors also observed female predominance with a female to male ratio 3.5: 1.¹⁰ Similar female predominance was observed in some other studies^{3,4,11,12}.

In this study, age of the patients varied from 26-80 years. Majority of the patients (30.64%) were between the age group of 26-35 years and mean age was 44.32 years. Our results were comparable with some other studies where the mean age was 44.0, 44.1, 41.30 and 45.77.^{4,10,11,13}

In this study, out of 62 patients, histologically, 5(8.06%) patients were diagnosed as Acute Cholecystitis, 34 (54.83%) patients as Chronic cholecystitis, 9 (14.51%) patients as Chronic cholecystitis with Cholelithiasis, 2 (3.22%) patients as Follicular Cholecystitis, 2 (3.22%) patients as Xanthogranulomatous Cholecystitis, 2 (3.22%) patients as Empyema and 8 patients as (12.91%) Carcinoma.

Our study revealed, among 8 carcinoma patients, 5 diagnosed as adenocarcinoma, NOS; 1 patient as Papillary Adenocarcinoma, 1 patient as Adenosquamous carcinoma, 1 patient as Undifferentiated carcinoma.

Another study is quite similar to ours. In that study, 164 (82%) cases were diagnosed as chronic cholecystitis, 21 (10.5%) cases were diagnosed as acute on chronic cholecystitis, 6 (3.5%) cases were diagnosed as acute cholecystitis, 5 (2.5%) cases as cholesterolosis, 2 (1%) cases as Xanthogranulomatous Cholecystitis, 1 (0.5%) case as empyema and another 1 (0.5%) case as carcinoma². Some other authors found more or less same results^{14,15,16}.

A group of authors found that, among 442 cases, 348 (78.7%) cases were diagnosed as chronic cholecystitis, 72 (16.3%) cases were diagnosed as acute on chronic cholecystitis, 11 (2.5%) cases were diagnosed as acute cholecystitis, 145 (32.8%) cases as cholesterolosis, 5 (1.1%) cases as Xanthogranulomatous Cholecystitis, 5 (1.1%)

case as empyema, 2 (0.5%) case as follicular cholecystitis and 1 (0.2%) case as carcinoma.¹³ Another study showed that, among 500 cases, 355 cases were diagnosed as chronic cholecystitis, 13 cases were diagnosed as acute on chronic cholecystitis, 3 cases were diagnosed as follicular cholecystitis, 1 case as cholesterolosis, 4 cases as empyema and 7 cases as carcinoma¹⁰.

In the present study, among 8 carcinoma patients, 4 (50%) belongs to grade I, 3 (37.5%) belongs to grade II and 1 (12.5%) belongs to grade III. Another study showed that among 11 carcinoma patients, 4 belong to grade I, 5 belongs to grade II and 2 belongs to carcinoma in situ.⁴

Limitations

This study had few limitations. Firstly, limited study period and small sample size. Secondly, the study was conducted using data from a single hospital and it may not be representative of the entire region or country. Thirdly, TNM staging was not possible in every carcinoma cases.

Conclusion

From this study it was found that almost all of the gallbladder lesions are inflammatory in origin, of which the most common disease being chronic cholecystitis and malignancy of the gallbladder in this population is a rare occurrence. In addition to the direct conclusions from the study, it must be noted that prompt detailed histopathological analysis of the cholecystectomy specimens will help to confirm the benign nature of the disease or to detect any precursors of malignancy. This will be decisive in the management and prognosis of the patient. Therefore, care must be taken to ensure adequate and immediate fixation of specimen by the surgeon accompanied by meticulous macroscopic and microscopic evaluation by the pathologist.

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