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HISTOPATHOLOGICAL SPECTRUM OF GALLBLADDER LESIONS IN CHOLECYSTECTOMY SPECIMENS-A RETROSPECTIVE STUDY IN A MEDICAL COLLEGE HOSPITAL

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ABSTRACT

Background: Gallbladder disease is a common health issue and a major reason for mortality and morbidity globally.It can range from cholelithiasis, cholecystitis to various neoplastic and non-neoplastic conditions.Cholelithiasis can result in diverse histopathological alterations in the mucosa of gallbladder like inflammation (acute, chronic, granulomatous), cholesterolosis, dysplasia and malignancy. Gallbladder carcinoma are often silent clinically in its initial phase and is diagnosed commonly as incidental histological findings following cholecystectomy.Therefore,it should be a regular practice for the surgeons to send all specimens of gallbladder for histopathological examination following surgical resection of gallbladder, to exclude the possibility of gallbladder carcinoma. **Aim:** This study aims to analyze the histopathological alterations in specimens of surgically removed gallbladder. **Materials and Method**: This retrospective, hospital-based study was performed in the department of Pathology of the Medical College for Women and Hospital (MCWH), Dhaka, Bangladesh, over a time period of 1 year beginning from January 2023 to December 2023. Histopathology reports of gall bladder specimens of 251 patients who have undergone resection of gall bladder during the mentioned time frame were included in the study. The specimens received included resected gall bladders of patients diagnosed with acute or chronic cholecystitis secondary to cholelithiasis (gall stone).The information were collected from the records of histopathology reports preserved in the laboratory of MCWH. The analysis of the data was carried out using SPSS version 26.0 software (Armonk, NY: IBM Corp.) .Incomplete information or non-diagnostic samples were excluded from the study. The information was recorded in a predesigned data collection sheet. Statistical analysis was done with frequency and percentage. **Results:** Of the 251 cases,42 and 209 samples were received from male and female patients, respectively. The patients' mean age in this study was 40.92±13.19 years.Out of the various histopathological findings, the most common was chronic cholecystitis, followed by cholelithiasis (25.9%), cholesterolosis (13.5%), and acute cholecystitis (6.8%). A single case of adenocarcinoma was found. Even though premalignant conditions like intestinal metaplasia and reactive atypia was not observed, one case of xanthoglanulomatous cholecystitis (XGC) (a potential premalignant condition) was found. **Conclusion:** Gallbladder diseases often require surgical intervention. Out of these, chronic cholecystitis (a known gallbladder carcinoma risk factor), is one of the most common such disease.It is imperative to perform histopathological examination inorder to detect malignant and premalignant lesions,since these may escape macroscopic detection and progress in to adenocarcinoma.

Keywords: Gallbladder, Resection, Histopathology, Disease, Premalignancy, Malignancy, Early detection, Prevention.

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INTRODUCTION

The disease of the gallbladder is a common problem which is a major reason for mortality and morbidity globally[1]. The gallbladder may become afflicted with inflammatory, neoplastic or congenital diseases[2,3]. Such pathologies result in symptoms and signs that require intervention through surgery (laparoscopic or open cholecystectomy). The pathology of gallbladder that is more common compared to others is that of inflammation which may be chronic, acute, xantho-granulomatous or follicular in nature[4,5]. The most common pathology for gallbladder is cholelithiasis (gallstones) which has 10%-20% incidence rate worldwide[6].Presence of gallstones may illicit chronic cholecystitis which in turn causes irritation of the mucosa of gallbladder, resulting in dysplastic and metaplastic changes. Such changes may eventually place the individuals at a risk of developing gallbladder carcinoma in future [5,7]. Thus inflammatory condition of prolonged duration needs to be treated by means of cholecystectomy.

Early gallbladder malignant lesions are often missed when cholecystectomy is carried out having been diagnosed for benign diseases on the basis of clinical, computerized tomography and ultrasonography[8,9]. The resected gallbladder specimen should be evaluated by histopathology to ensure that the patient has not developed any premalignant or malignant lesions[10,11]. Gallbladder carcinoma although rare, once develops, is silent clinically and is linked to cholelithiasis of longstanding nature[12]. Gallbladder carcinoma incidence due to chronic cholecystitis with gallbladder stone range between 0.3% to 12%[13,14]. Thorough histopathological examination is warranted of resected specimens of gallbladder from patients who were suffering from chronic cholecystitis of prolonged duration, out of suspicion of malignancy[10,12]. Gallbladder histopathology is imperative to avoid complications that may lead to demise like incase of gallbladder carcinoma[7,15,16]. Mortality rate in case of gallbladder carcinoma is one of the highest among mortality rates for all cancers[8]. If gallbladder carcinoma is diagnosed in stage I of the disease the prognosis expected is good for the patients and this may be possible through histopathological examination of resected gallbladder[8,13]

In developing countries, carrying out histopathological studies of specimen of gallbladder at peripheral hospitals is often difficult due to lack of sufficient resources and the massive number of patients[17]. Specimens displaying remarkable abnormalities macroscopically are usually sent for evaluation by histopathology[18]. However, globally all specimens of gallbladder obtained through surgery are sent for performing histopathological study for discerning the presence of any lesions of malignant or pre-malignant nature[18]. Pre-malignant lesions are often unremarkable macroscopically and may only be found through histopathology[19]. This study aims at elucidating the histopathological ailments spectrum that gallbladder is commonly affected by that requires surgical procedure. Such study may help stress the need for histopathological examination of gallbladder following its resection regardless of the presence or absence of gross macroscopic abnormalities.

MATERIALS AND METHOD

This retrospective, hospital-based study was performed in the department of Pathology of the MCWH, Dhaka, Bangladesh, over a time period of 1 year beginning from January 2023 to December 2023. The ethical clearance was obtained from the Institutional Review Board of MCWH memo no. MCWH/Ethical committee/2025/20(8). Histopathology reports of gall bladder specimens of 251 patients who have undergone resection of gall bladder during

the mentioned time frame were included in the study.The specimens received included resected gall bladders of patients diagnosed with acute or chronic cholecystitis secondary to cholelithiasis (gall stone).Inadequate tissue samples, incomplete patient information and reports that did not reach a definitive diagnosis and patients with confirmed evidence of gall bladder carcinoma or gross gall bladder abnormalities that suggest infiltrative or localized malignancy at the time of surgery were excluded from the study. The sampling technique used here was that of convenient sampling. The data was gathered in a standardized data form which included patient's age, type of specimen, clinical diagnosis and the histopathological diagnosis. These information were collected from the records of reports preserved in the histopathology laboratory of MCWH. The analysis of the data was carried out using SPSS version 26.0software (Armonk, NY: IBM Corp.).

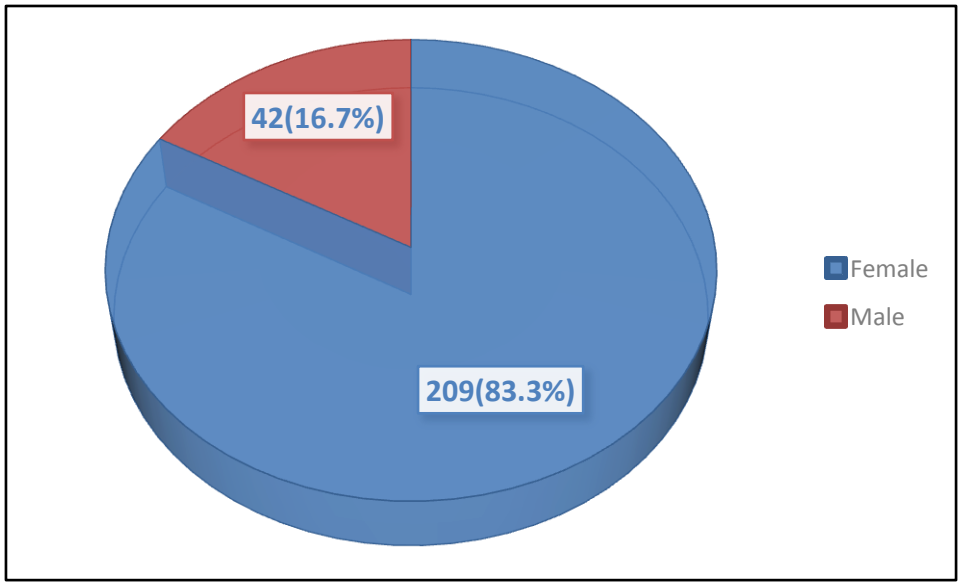
RESULTS

The present study involved 251 cases, 42 and 209 samples were received from male and female patients, respectively.The patients' mean age in this study was 40.92±13.19 years. Most of those who had undergone cholecystectomy belonged to the fourth decade of life (29.1%). Table 1 depicts the breakdown of the patients into different age groups. The breakdown of the patients in relation to gender is illustrated in Figure 1.

Table 1: Distribution of study subjects according to age (N=251)

Age (Years)	Frequency	Percentage
11 - 20	7	2.8
21-30	60	23.9
31-40	73	29.1
41-50	50	19.9
51-60	44	17.5
61-70	14	5.6
71-80	2	0.8
>80	1	0.4
Mean±SD	40.92±13.19	

Data were expressed as frequency and percentage, N=Total number of subjects



Data were expressed as frequency and percentage

Figure 1: Distribution of study subjects according to gender (N=251)

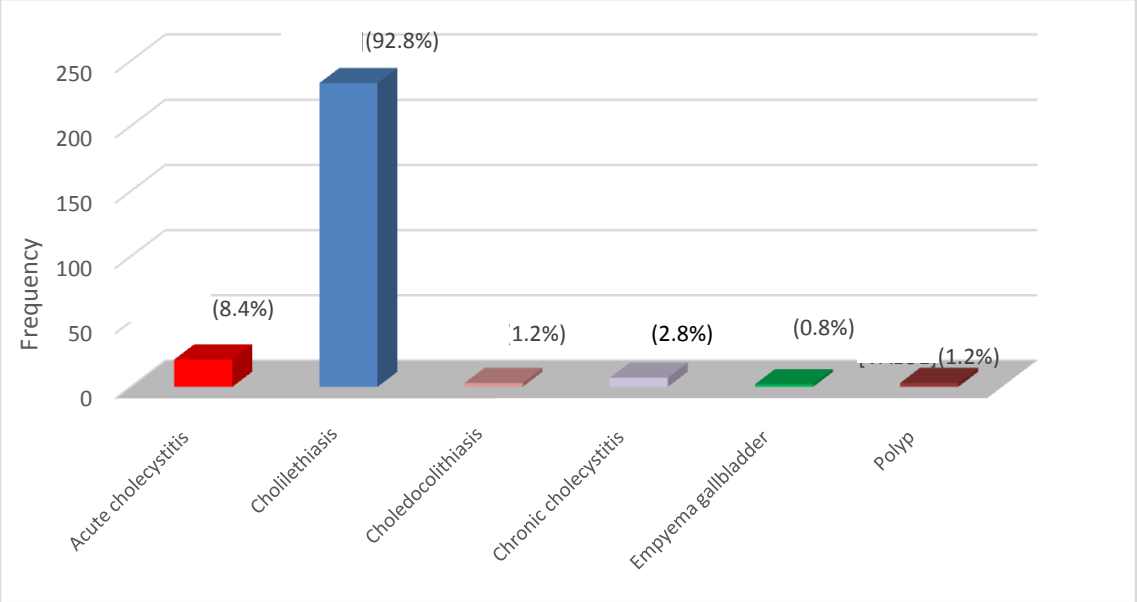
Chronic cholecystitis was observed in 89.2 % of the total patients. This demonstrates that chronic cholecystitis to be the most common histopathological findings of this study. Also common in our study were cholelithiasis (25.9%), acute cholecystitis (6.8%) and cholesterolosis (13.5%). This study, however, observed only a single case of adenocarcinoma of the gallbladder. Table 2 shows the spectrum of different histopathological features in respect to gender.

Table 2: The diverse spectrum of the histopathological outcomes observed in the study population with respect to gender (N=251)

Histopathology	Male (n=42)	Female (n=209)	Total (N=251)
Acute cholecystitis	5	12	17 (6.8%)
Acute-on-chronic cholecystitis	1	6	7 (2.8%)
Adenocarcinoma	1	0	1 (0.4%)
Cholesterolosis	3	31	34 (13.5%)
Chronic cholecystitis	34	190	224 (89.2%)
Cholilelithiasis	8	57	65 (25.9%)
Empyema gallbladder	1	0	1 (0.4%)
Follicular cholecystitis	0	1	1 (0.4%)
Intestinal metaplasia	0	0	0 (0%)
Lymphocytic cholecystitis	0	0	0 (0%)
Polyp	1	3	4 (1.6%)
Reactive atypia	0	0	0 (0%)
Xanthogranulomatous cholecystitis (XGC)	0	1	1 (0.4%)

Data were expressed as frequency and percentage, Multiple responses present;
N=Total number of subjects

Figure 2 demonstrates the various clinical diagnosis of the patients that led to the decision of performing surgical procedure.Most of the patients were diagnosed for cholelithiasis (92.8%) and second most common was acute cholecystitis and next common was chronic cholecystitis. Other clinical diagnosis included choledocolithiasis, polyp and empyema of gall bladder. Table 3 shows the different comorbidities suffered by patients and the most common comorbidities were diabetes mellitus and hypertension.



Data were expressed as frequency and percentage, Multiple responses present

Figure 2: Distribution of study subjects according to clinical diagnosis (N=251)

Table 3: Distribution of study subjects according to comorbidities (N=251)

Comorbidities	Frequency	Percentage
Diabetes	17	6.8
Hypertension	25	10.0
Ischemic Heart Disease	1	0.4
Pancreatitis	3	1.2
Gastritis	2	0.8
Hypothyroidism	3	1.2
Hypocalcemia	1	0.4
Umbilical hernia	2	0.8
Nephrolithiasis	1	0.4

Data were expressed as frequency and percentage, Multiple responses present;
N=Total number of subjects

DISCUSSION

One of the surgical procedures that is performed widely is cholecystectomy and is done to manage various gall bladder pathologies which includes cholecystitis, cholelithiasis, polyps of gall bladder and carcinoma of gall bladder. One of the most prevalent pathologies of gall bladder is cholelithiasis with 10% to 15% global prevalence[20].Even though the condition is benign itself, gall stone has been linked to a raised risk of gall bladder and hepatobiliary carcinoma [21].Gall bladder carcinoma prevalence among the general population is small, however, of all the biliary tract carcinomas gall bladder carcinomas are more common with

prevalence rate of 80% [22]. This carcinoma exhibits a poor prognosis with a survival rate of 5 years due to the late presentation of the disease[23].

In this study there was a predominance of females within the study population. It was similar to the study that reported a male to female ratio of 1:2.4 in India [24,25]. The gender of female is one of the risk factors for the development of gall stones [19]. Most of the subjects in this study had the presentation of cholelithiasis and this can eventually lead to several pathologies, like acute cholecystitis ,chronic cholecystitis, cholesterolosis, and follicular cholecystitis .Figure 3A and 3 B demonstrates the histopathology of acute and acute on chronic cholecystitis as has been observed in this study. The chronic cholecystitis prevalence in our research was observed to be 89.2% .Figure 4 A shows the microscopic view of a chronic cholecystitis specimen and Figure 4 B illustrates the histopathology of cholesterolosis under the microscope as observed in this study. A study done by Sanwan et al. noted similar outcome with a prevalence rate of 79.8% [26]. Gall bladder wall thickening with associated calcification is a characteristics of chronic cholecystitis which can eventually result in a pathology known as porcelain gall bladder [19].Presence of this condition is a well known factor for risk of developing gall bladder carcinoma[12].

Cholesterol esters and triglycerides tend to accumulate in a polypoid or diffuse manner within the macrophages present in the gall bladder wall when there is mucosal villous hypertrophy and is know as cholesterolosis (Figure 4B). In this study, cholesterolosis was noted in 13.5% of specimens. Mondol et al. observed 2.9% of the patients suffered from this pathology and Sangwan et al. noted 9.43% prevalence[7,26].

When there is acute cholecystitis ramification, empyema occurs and is found in one of the cases in our study[27]. The gall bladder wall is surrounded by marked edema, fibrous exudate and inflammation in empyema. Pathologically it is presented with distended, pus filled gall [27]. Figure 5 A exhibits the microscopic view of cholesterol polyp and 5 B demonstrates empyema of gall bladder from our study. In this study 1 of the cases had empyema of gall bladder that is similar to 0.71% prevalence rate reported by another research [10] .Follicular cholecystitis is a rare condition observed in 0.1%-1% of patients with chronic cholecystitis [28].In this condition the gall bladder consists of lymphoid follicles exclusively and in order to be follicular cholecystitis, there must be presence of three or more lymphoid tissue / cm of gall bladder tissue [29,30].Follicular cholecystitis showing lymphocytic infiltration with formation of lymphoid follicle in the lamina propria can be observed in Figure 6A.

A chronic, focal, or diffuse fibroinflammatory process that occurs due to foamy histiocytes accumulation is known as XGC (Figure 6B). This condition was noted in a single case. The intraoperative and preoperative findings of XGC is similar to that of gall bladder carcinoma [31].In XGC there is involvement of liver , infiltration of pericholecystic region and lymphadenopathy. This may delay the diagnosis of the condition and thus require an extraneous radical surgery instead of standard cholecystectomy[32]. The association of XGC and gall bladder carcinoma is well known[26,29]. Even though there were no cases of reactive atypia and intestinal metaplasia in our study, they can result in malignancy, since these two are premalignant conditions[19]. The older age group were found to suffer from these conditions in this study suggesting that older age at presentation raises the risk of malignancy[7,22]. These lesions would contribute to pathogenesis of gall bladder cancer if not detected early. Thus it is imperative that there is thorough histopathological evaluation of specimen of gall bladder, regardless of the

intraoperative macroscopic appearance. This would help in early diagnosis of high-risk patients, reducing the chance of progression to advanced disease. Adenocarcinoma of gall bladder was found in one of the cases in this study. Figure 7 shows moderately differentiated adenocarcinoma of gallbladder. Infiltrative irregular glands lined by anaplastic epithelial cells are invading the lamina propria and the muscularis propria. Most of the glands are dilated and filled with necrotic debris. Other research works have reported 0.5% to 1.05% prevalence rate [6,12].

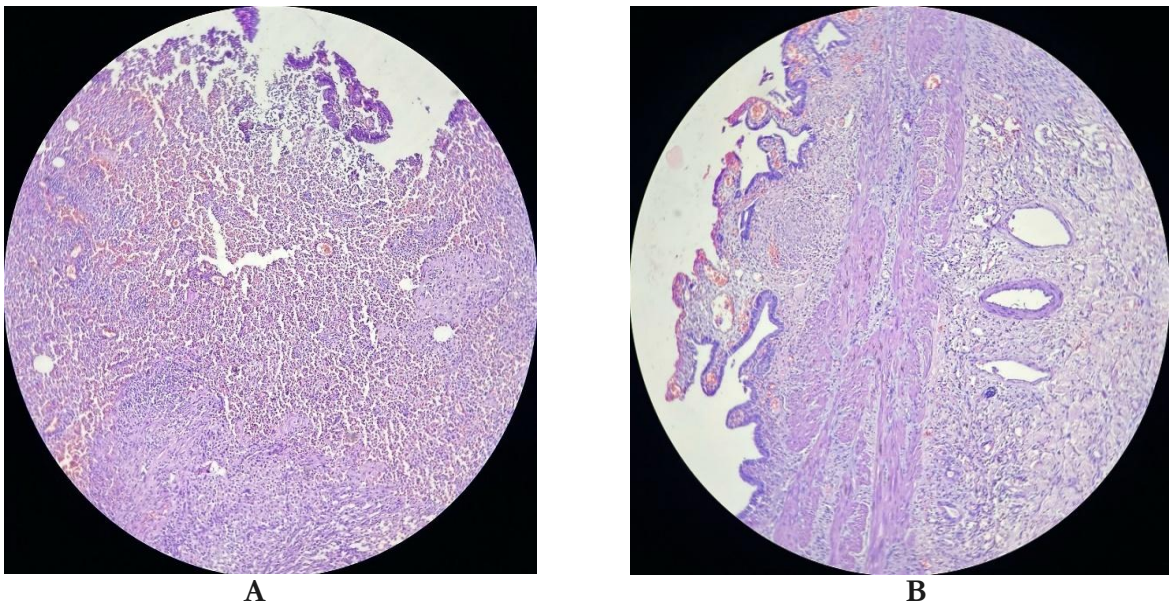
The diagnosis of gall bladder carcinoma occurs at late stage and is linked to poor prognosis despite the advancement of modern diagnostic techniques[6]. Prompt detection remains difficult as gall bladder carcinoma remains silent clinically in its initial stages. Careful histopathological examination, specific diagnostic markers and ameliorated imaging techniques can lead to early diagnosis and thus improve disease outcome.

CONCLUSION

Cholecystectomy is required for majority of gallbladder disease. A vast spectrum of pathologies may be divulged upon histopathological examination of excised gallbladder postoperatively. Out of these, chronic cholecystitis, acute cholecystitis, and cholesterolosis are the most prevalent. Furthermore, remarkable features may be absent macroscopically and premalignant or malignant conditions may escape detection. Thus, it is necessary to perform routine histopathological evaluation of all excised gallbladder specimens to exclude the malignant and premalignant conditions like reactive atypia and metaplasia. The premalignant lesions, if escapes detection, would result in malignant transformation into adenocarcinoma that has poor prognosis.

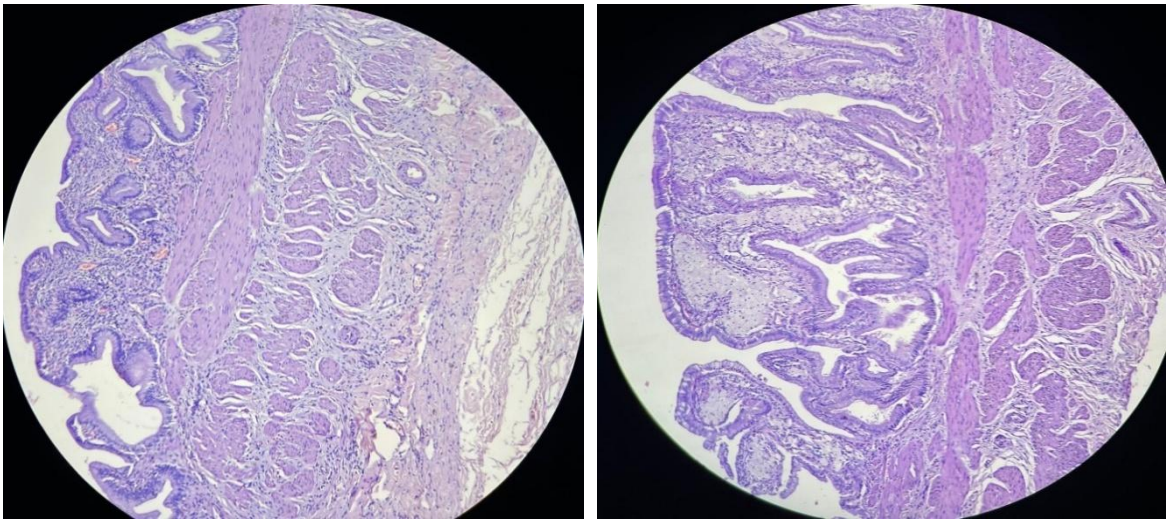
CONFLICT OF INTEREST

There is no conflict of interest.



A B

Figure 3 (A) Acute cholecystitis H&E X 40; (B) Acute-on-chronic cholecystitis H&E X40



A B

Figure 4 (A) Chronic cholecystitits H&E X100; (B) Cholesterolosis H&E X 100

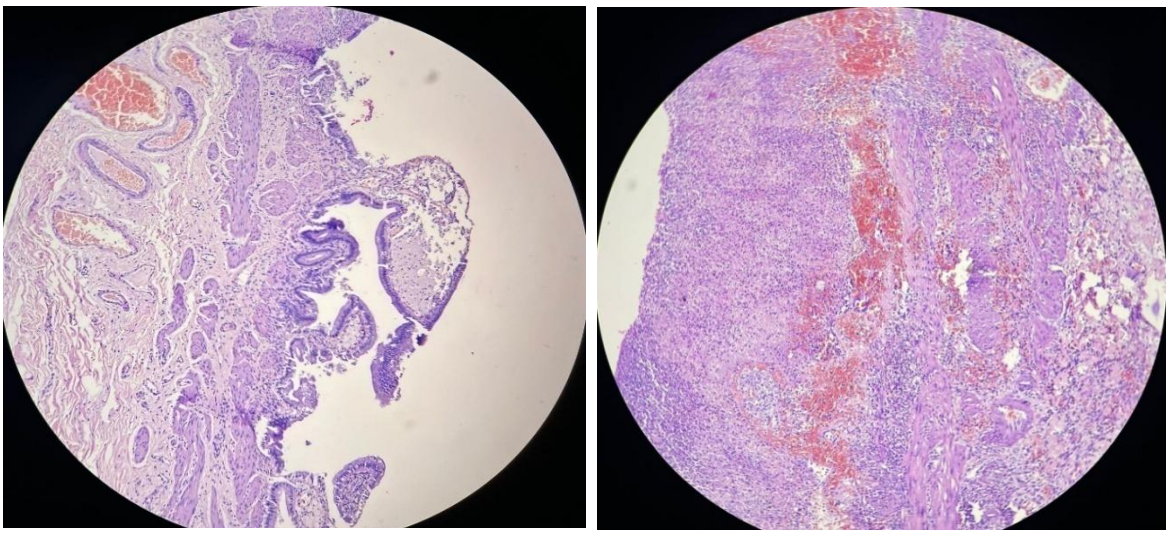


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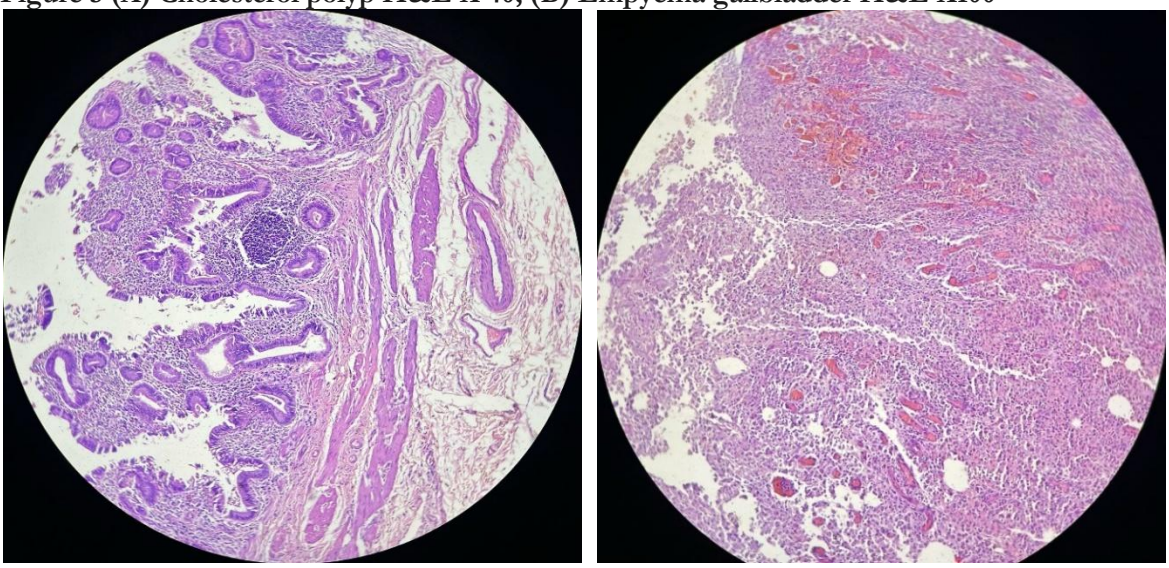
Figure 5 (A) Cholesterol polyp H&E X 40; (B) Empyema gallbladder H&E X100



A B

Figure 6 (A) Follicular cholecystitis H&E X100; (B) Xanthogranulomatous cholecystitis H&E X100

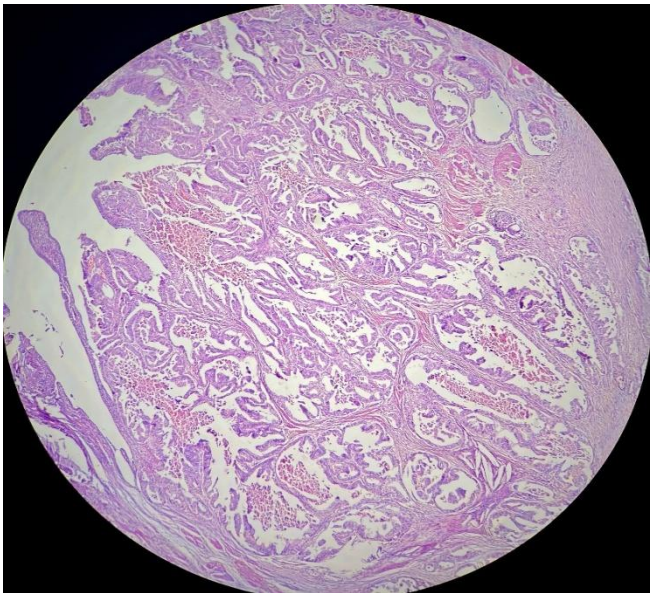


Figure 7: Adenocarcinoma of gallbladder H&EX 100

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