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Pathology

HISTOPATHOLOGY OF GALLBLADDER SPECIMENS AFTER CHOLECYSTECTOMY: A RETROSPECTIVE STUDY

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ABSTRACT **Background** Current approach to detect the presence of gallbladder carcinoma involves a routine histopathological examination of all gallbladder specimens, regardless of the clinical characteristics of the patient or macroscopic aspect of the gallbladder. Available pathological reports were interpreted for the following parameters: age, gender, and pathological diagnosis. In addition, the demographic information and clinicopathologic characteristics of the patients with histopathologic findings were assessed in detail, and re-examination of the available specimens was done. **Methods** Inpatient records of the patients who had been operated for elective and emergency cholecystectomies in the hospital associated with Khaja Bandanawaz University – Faculty of medical Sciences; from January 2018 to November 2022, were retrospectively evaluated. **Results** A total of 661 gallbladder specimens submitted for histopathological examination during the study period were included in the study. The results of histopathological examination of these gallbladder specimens showed that chronic cholecystitis was found in 535 (81%), acute cholecystitis in 46 (6.99%), cholesterolosis in 44 (6.5%) patients, Dysplasia was found in 34 (5.14%) patients, and gallbladder carcinoma was detected in 2 (0.30%) patients. **Conclusion** A strategy of selective approach for histopathological examination of gallbladder specimens may be safe in areas with very low incidence of gallbladder carcinoma. Such selective strategy is more cost-effective, reduces the workload of pathologists, and does not appear to compromise patient outcome.

KEYWORDS : Cholecystectomy, Retrospective study, Gallbladder cancer, gallbladder specimen, histopathological examination

Introduction

Cholecystectomy is a trans-abdominal surgical procedure commonly performed worldwide.1 It is a standard practice to direct all gallbladder specimens for routine histopathological examination (HPE) postoperatively, regardless of any grossly visible abnormalities, to exclude unexpected gallbladder cancer (GBC).2 GBC is a rare disease with a dismal prognosis.3 The incidence of GBC varies widely among different geographical regions and ethnic groups. Rates may differ even inside a region or a country. Northern India and Pakistan, East Asia, South America, and Eastern Europe are found to have the highest rates of GBC. Incidental GBC is found in 0.2%-2.9% of all cholecystectomies performed for gallstone disease.4 Patients with incidental GBC diagnosed with stages Tis and T1a can be treated by simple cholecystectomy alone. Patients with stage T1b and beyond should undergo further surgical treatment.2 However; several recent studies have questioned the necessity for routine HPE of all gallbladder specimens. The main debate on selective versus routine histological assessment of gallbladder specimens is based on findings of incidental GBC.[4]

There is an emerging trend to consider selective HPE of cholecystectomy specimens removed for benign gallbladder disease.[5]

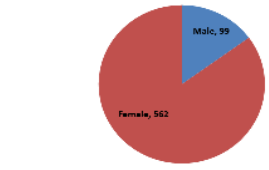
The aim of this study was to retrospectively analyse whether or not it would be safe to adopt a policy of processing only gallbladder specimens with preoperative or intraoperative suspicion for malignancy without compromising patient safety.

Materials and Methods

Inpatient records of the patients who had been operated for elective and emergency cholecystectomies in the hospital associated with Khaja Bandanawaz University – Faculty of medical Sciences; from January 2018 to November 2022, were retrospectively evaluated. The study was performed according to the World Medical Association Declaration of Helsinki. Patient data on age, sex, and histopathological diagnosis were recorded. Incidental GBC is defined as GBC identified only after HPE.1,6 The term incidental GBC was not used when GBC was suspected on preoperative imaging (ultrasound and/or computed tomography), intraoperative, or opening of the gallbladder specimen. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 29.0 software. Data were analysed using the chi-square test.

Results

A total of 661 gallbladder specimens were available for HPE during the study period. Of these 99 were males (14.97%), and 562 were females (85.02%).



Median age of the patients was 40 (14-81) years. Chronic cholecystitis was found in 535 (81%) patients, acute cholecystitis in 46 (6.99%), cholesterolosis in 44 (6.5%), Dysplasia was observed in 34 (5.14%) patients, and GBC was detected in 2 (0.30%) (Table 1)

Table 1. Details of histopathological findings from 661 cholecystectomy specimens

Histopathological diagnosis	Number	Percent
Chronic cholecystitis	535	81.
Acute cholecystitis	46	6.99
Cholesterolosis	44	6.5
Dysplasia	34	5.14
Carcinoma	2	0.30
Total	661	100.0

Both patients with GBC were suspected/diagnosed either preoperatively or intraoperatively. One case was diagnosed by ultrasound and computed tomography, showing abnormalities in the gallbladder wall with suspicion of malignancy. The other had intraoperative finding suggestive of GBC and were confirmed subsequently by HPE as primary GBC. All the malignant specimens were reported as adenocarcinomas from the HPE. One patients was found to have T2 lesions, and the other patient had T3 lesions (Table 2).

Table 2. Details of the patients with a histopathological diagnosis of gallbladder carcinoma

Patient	Age (years)	Sex	Preoperative suspicion	Intraoperative finding	stage (t) and grade
1	47	Male	No	Thick-walled gallbladder, severe inflammation, severe adhesions	T2, WDAC
2	61	Male	Yes by USG and CT	Gallbladder mass, severe inflammation, severe adhesions	T3, PDAC

USG: Ultrasonography; CT: Computed tomography; WDAC: Well differentiated adinocarcinoma; PDAC: Poorly differentiated adinocarcinoma.

Discussion

There has been a debate in the literature regarding routine or selective HPE of gallbladder specimens when cholecystectomy is performed for benign gallbladder diseases. The main debate by those studies that suggest selective HPE is that first, it is unlikely to have incidental GBC in a normal-looking gallbladder specimen.[2] Second, unexpected early GBCs (stages Tis and T1a), which may look normal on gross examination, do not require further treatment as simple cholecystectomy is adequate.[5] Third, routine HPE of all gallbladder specimens overburdens the histopathology department and hospital resources.[6] Studies recommending selective HPE observed that the possibility of missing an early cancer diagnosis is very low, and that almost all incidental GBCs are associated with findings on gross examination of the gallbladder specimen.[5]

Bazoua et al., Emmett et al., and Darmas et al. have reported incidental GBC rates of 0.17% (5/2890), 0.25% (12/4776), and 0.27% (4/1452), respectively.[7] Tayeb et al. have noted incidental GBC in only 3 out of 426 (0.70%) cases.[8] All cases of incidental GBC in these studies had a macroscopically abnormal gallbladder; hence, these studies suggest that it is safe to adopt a selective approach to HPE.

Furthermore, Van Vliet et al. have shown that of the 1375 gallbladder specimens examined macroscopically, not one incidental GBC is found.[9] Of the 185 (13.5%) specimens of all gallbladder specimens that showed macroscopic abnormalities for which they would require further HPE in case of a selective policy, GBC was found in 6 specimens. Similarly, in the study by Mittal et al. of 1305 patients, incidental GBC has been found in 13 patients out of 610 macroscopically abnormal gallbladder specimens.[10] In a macroscopically normal gallbladder specimen, no cases of GBC have been found.

Our study showed that both patients with GBC were diagnosed either preoperatively or intraoperatively, and none of the patients with GBC were diagnosed from the HPE.

There has been a concern about the presence of early GBC in a normal-looking gallbladder specimen. However, simple cholecystectomy is considered adequate in these patients, and no further therapy is required.[11]

Recent studies have recommended patients' age as an additional factor for selecting specimens for HPE of gallbladder specimens.[5] Elshaer et al. have suggested that age should also be used to select gallbladder specimens that should be submitted to HPE as all patients with cancer in their study are above 51 years.[12] This could aid in combination with the intraoperative appearance of the gallbladder to identify those specimens requiring histopathological analysis, especially in an area with a lower incidence of incidental GBCs.

Similarly, Romero-González et al. have considered the age of ≥ 60 years as one of the risk factors for GBC.[13] In their study, the surgeon first identified the risk factors for GBC and then performed a macroscopic analysis of the gallbladder specimen just after surgery. All three histopathologically confirmed GBCs in their study were suspected by the surgeon following macroscopic analysis.

Furthermore, Wrenn et al. have concluded that selective screening based on risk factors (including older patients), intraoperative findings, and on-table examination of the specimen may be a feasible and more cost-effective alternative to universal screening.[14]

On the other hand, studies that recommend routine HPE of gallbladder specimens are based mainly on the identification of high rates of incidental GBCs.[15-20] Siddiqui et al. have identified incidental GBC in 6 specimens out of 220 cholecystectomy specimens, of which 3 patients with advanced stages (T2 and T3) underwent revision surgery.[15] Shrestha et al. have reported 1 stage T2 disease and 3 stage T3 disease out of 9 incidental GBCs in 668 cholecystectomy specimens.[16] Ul Haq et al. have shown 2 patients with stage T2 dis ease out of 5 incidental GBCs in a series of 107 specimens, and Ghimire et al. have found 2 patients with stage T2 disease out of 10 incidental GBCs in a series of 783 specimens.[17] It is noted that almost all of these studies suggesting routine HPE are from geographical areas with a relatively high incidence of GBC. Moreover, most of the studies that recommend submitting all gallbladder specimens for routine HPE regardless of its gross appearance report a definitive gross abnormality in the cases diagnosed with incidental GBC. Kalita et al. have found 18 unsuspected incidental GBC cases in a study of 4115 patients.[19] However, gross examination of these 18 cases showed localized growth in 10 cases and diffuse thickening of the gallbladder wall in 8 cases. In the study by Hamdani et al., 7 cases of incidental GBC have been observed. After reviewing gross findings of these incidental GBCs, 3 cases had a polypoidal mass, 2 cases had wall thickenings, and 2 cases had mucosal irregularity.[20] Similarly, Shreshtha et al. have reported 9 incidental GBCs out of 668 cases of cholecystectomy specimens.[16] However, on gross features of the incidental GBC cases, 5 cases had growth (2 fungating mass and 3 solid gray white mass), 2 cases had an irregular mucosa, 1 case had a contracted gallbladder, and 1 case had a thick fibrosed wall. We recommend that in all patients undergoing cholecystectomy for gallstone disease, the gallbladder specimen should be opened and examined for macroscopic abnormalities before deciding to submit the specimen for HPE. Based on patient characteristics and macroscopic appearance of the gallbladder, it appears safe to adopt a selective approach for those specimens with preoperative or intraoperative suspicion for malignancy, especially in areas with very low incidence of GBC. Pollar DN presents a large multicentric study from Netherland wherein he presents a number of reasons to pause and evaluate the evidence and reasons why routine pathological examination of cholecystectomy specimens is essential for high-quality healthcare, and why this is established medical practice in Neitherland.

Our study has some limitations. First, this is a retrospective study. Second, the patient population is associated with a single region, which may not reflect the demographics of other regions and other medical centers throughout the country. Hence, a prospective, multicenter study is required in order to safely modify the existing guideline.

Conclusions

A policy of selective approach for HPE of gallbladder specimens may be safe in areas with very low incidence of GBC. Such selective approach is more cost-effective, decreases the workload of the histopathology department, and does not appear to compromise patient outcome.

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