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Accuracy of macroscopic examination of gall bladder specimens for malignancy after cholecystectomy

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Abstract

Introduction: Routinely all specimens are sent for HPE due to the possibility of missing incidental gall bladder carcinoma(IGBC) which has a incidence of 0.2-2.9%. Missing IGBC would have a devastating effect on patients. However, many studies have reported thorough macroscopic examination of gallbladder specimen by surgeons would be enough to rule out carcinoma. Those missed carcinomas are at early stage (pT1a) which would not change the management of the patients.

Method: It was a prospective observational study that included all patients undergoing cholecystectomy for benign gallstone disease form July 2019 to June 2020 at Patan Academy of Health Sciences. Data collected were analysed using Fisher's Exact Test.

Result: The negative predictive value and specificity of macroscopic examination by surgeons were 99.6% and 84.1% respectively. Incidence of IGBC was found to be 0.31%.

Conclusion: Detailed mucosal macroscopic examination of gallbladder specimen by a surgeon can exclude primary malignancy of gall bladder. Therefore, selective approach of HPE after cholecystectomy for benign gallbladder disease can be considered a routine practice.

Keywords: Carcinoma; Cholecystectomy; Gallbladder; Gallstones; Incidental Findings

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Introduction

Gall bladder (GB) is one of the commonest surgical specimens sent for histopathology examination (HPE). Routinely all specimens are sent for HPE due to the possibility of missing gall bladder carcinoma.[2] GB carcinoma is the most common cancer of biliary tree and fifth common gastrointestinal (GI) malignancy.[3] The disease has a geographical distribution, being most common in Chile, Japan and North India.[4] In Nepal, the incidence of GB carcinoma is 2.63%.[5] Carcinoma detected only on HPE is known as Incidental gallbladder cancer (IGBC). The incidence of IGBC is 0.2-2.9%.[1,6,7]

Various studies state that missing the diagnosis of IGBC would have a devastating effect on the patient. The increase in lawsuits and surveillance of daily medical practice also make it difficult to change routine practice of sending specimens for HPE to a selective approach. [8-11]

However, several studies state that possibility of missing a neoplasm would be negligible as cases of invasive carcinoma of the gallbladder showed gross macroscopic abnormal appearance either preoperative (ultrasonography) or intraoperative (surgeon).[12,13] Those missed cases are pT1a stage where simple cholecystectomy is adequate. So, HPE finding do not really change the management.[14,15] However, most of these studies are retrospective. Prospective studies to support the value of selective histopathology are limited. At present we send all specimens for HPE after cholecystectomy for benign gall bladder disease at our centre.

Hence, the objective of this study is to analyse the correlation between the macroscopic examination and histopathological reports which aids in supporting the selective approach for HPE of GB specimens.

Method

This study was a prospective observational study conducted at Patan Academy of Health Sciences (PAHS) from July 2019 to June 2020. Ethical approval was taken from Institutional Review Committee (IRC) PAHS. Consent was taken from patients regarding confidentiality and no alteration in treatment process. It was designed with an objective to find out the incidence of IGBC on macroscopic examination, and to correlate the macroscopic and histopathological examination findings gall bladder specimen. All patient undergoing cholecystectomy for gallstone disease in the given period were included. Patients with suspected gall bladder carcinoma, patients who underwent partial cholecystectomy and patients with complicated fistula (mirrizzi, cholecysto-duodenal fistula) were excluded. After cholecystectomy, gall bladder specimens were examined by the operating surgeon or assistant. Gallbladder was cut vertically to reflect the mucosa and detailed examination was done. GB thickness was measured using Vernier calipers. Findings were noted, specimen placed in formalin and sent for HPE. Data were collected through proforma and data entry and analysis were done using Microsoft Excel 2016 and R version 4.1.1

Fischer's exact test was used to analyse the 2/2 table to determine sensitivity, specificity, negative predictive value and positive predictive value of macroscopic examination by surgeons.

Result

A total of 321 patients underwent cholecystectomy for gall stone disease within the study period. The mean age of the patients was 44.33±12.00 years. Fifty-one(15.89%) specimens had abnormal macroscopic findings like diffuse wall thickening, gall bladder mass and calcifications, Table 1. HPE of these specimens showed benign diseases, Table 2. The Specificity and Negative predictive value of macroscopic examination by surgeon was 84.1% and of 99.6% respectively, Table 3. The incidence of IGBC in our study was 1(0.31%). This patient had a TNM stage of pTaN0M0, Table 4.

Table 1. Macroscopic Examination of Gall bladder (N=321)

Macroscopic Findings By Surgeons	N(%)
Normal looking gall bladder	270(84.11)
Abnormal/ Malignant looking gallbladder	51(15.89)
GB mass	2(0.62)
Nodular GB wall	2(0.62)
Necrotic areas	0(0.00)
Porcelain GB with Ulcerations	1(0.31)
Irregular wall thickening	14(4.36)
Empyema gall bladder	6(1.86)
Mucocele of gallbladder	5(1.55)
Inflamed gall bladder	9(2.80)
Contracted gall bladder	4(1.24)
Diffuse wall thickening	7(2.18)
Septate gallbladder	1(0.31)
Total	321(100)

Table 2. Microscopic examination of the gallbladder (N=321)

Microscopic Findings By Pathologist	N(%)
Acute cholecystitis	6(1.86)
Acute on chronic cholecystitis	9(2.80)
Chronic cholecystitis	240(74.7)
Chronic cholecystitis with Cholesterolosis	41(12.77)
Chronic cholecystitis with Adenomyosis	7(2.18)
Chronic cholecystitis with low grade dysplasia	1(0.31)
Chronic cholecystitis with high grade dysplasia	1(0.31)
Mucocele of gall bladder	2(0.62)
Xanthogranulomatous gallbladder	11(3.42)
Others	
Gb adenoma	1(0.31)
Unilocular cyst	1(0.31)
Total	320 (99.69)

Table 3. Accuracy of macroscopic examination compared with microscopic examination (N=321)

Macroscopic \ Microscopic	Malignant	Non malignant	Total
Malignant	0	51	51
Non malignant	1	269	270
Total	1	320	321

Sensitivity(%)	**0.00**	**PPV(%)**	**0.00**
Specificity(%)	**84.06**	**NPPV(%)**	**99.63**

Table 4. Characteristics of patient diagnosed as carcinoma gall bladder

Age/Sex	History	Ultrasonography	Intraoperative Findings	Adenocarcinoma pT1aN0M0
36yrs/Female	Recurrent biliary colic	Multiple GB stones largest measuring 8mm	Normal	Adenocarcinoma pT1aN0M0

Discussion

Gallstone disease is a common surgical problem and annually a large number of patients undergo cholecystectomy. Although there are several studies which focus on thorough macroscopic evaluation of gall bladder specimens, they emphasize on sending all gallbladder specimens for HPE following cholecystectomy for gallstone disease due to the possibility of missing the true IGBC.

Recently, various reports have questioned the role of routine HPE due to low incidence of IGBC in their study. The incidence of IGBC is similar to a study by Darmas who reported IGBC in only 4 of 1452(0.3%) patients for whom cholecystectomy specimens were examined over a period of 5 years.[16] Gurung KB in his study done in Nepal had an incidence of IGBC (0.9%, 1 out of 313). Among these specimens harbouring malignancy only 1(0.3%) had true IGBC.[17] Gulwani (0.76%) and Shrestha R (1.4%) have found the results closer to our study.[18,19] However Siddiqui in their study in Pakistan reported incidence of IGBC to be 2.8%.[6] The low incidence of IGBC in our study could be low incidence of gall bladder carcinoma in Nepal.

In our study, the specimens which were abnormal looking macroscopically were diagnosed as xanthogranulomatous cholecystitis and acute on chronic cholecystitis. Two cases had suspicious mass on macroscopic examination which were reported as gall bladder adenoma and unilocular gall bladder cyst respectively. One(0.31%) case which had porcelain gall bladder with ulcer on macroscopy had high grade dysplasia on HPE. Bazoua studied 2890 cases and reported 38.02% cases to have abnormal macroscopy in the form of thickened GB wall, 5(0.45%) cases with thickened gall bladder wall had gall bladder malignancy. Other cases had HPE findings similar to our study.[12] Rathanaswamy reported their experience with 1312 cholecystectomy cases over a 10-year period. Of these, 610(46.5%) cholecystectomy specimens

showed macroscopic abnormalities in the form of thickening, mucosal ulcerations or polypoidal lesions.[20] In our study macroscopically abnormal gall bladder didn't harbour malignancy because gross macroscopic abnormalities like fistulas, mirrizzi syndrome, partial cholecystectomy found in the intraoperative period were excluded. These cases were excluded due to anticipation of incomplete macroscopic evaluation including measurement of wall thickness. Gall bladder polyps which are considered to be premalignant were also excluded preoperatively because this inclusion didn't fall in the boundary of the specific objective. Those specimens which were excluded might have harboured primary gall bladder malignancy.

In our study, 270(84.1%) had normal macroscopic findings on examination by surgeon. One case harboured malignancy while other cases were confirmed as benign pathology by microscopy. The most common histopathology was chronic cholecystitis. These findings correlated with each other. The findings of strawberry gallbladder in macroscopic examination also correlated with the HPE of Cholesterolosis. These findings are similar to Bazoua et al. The specificity and negative predictive value of macroscopic examination in our study is 84.1% and 99.6% respectively. This is similar to a study done by González et al who have reported a specificity of 100% and negative predictive value of 99.6%.[21]

The value of histopathological examination depends mainly on the therapeutic options arising from the diagnosis. The majority of true incidental carcinomas are expected to be at the early stage of the disease. Simple Cholecystectomy would suffice the treatment in early cases. In our study, the patient diagnosed with primary GB carcinoma had TNM stage T1a disease. KB Gurung et al also had reported 1(0.32%) case of true IGBC which had Stage T1a disease. Poudel R et al in their study identified 7(1.6%) primary malignancy. They reported 0.71% cases of IGBC with stage T1a, 0.47% of stage T1b and 0.23% cases of T2 disease.[22] Ghimire et al reported 2(20%) cases of IGBC at stage T2.[23] The results in our study might be due to thorough preoperative evaluation of patients with benign disease.

Since our patient with IGBC had a pathological stage of T1aN0M0, she did not need further treatment after cholecystectomy. Therefore, despite not being detected on preoperative evaluation and macroscopic examination, it did not alter the patient management and had no adverse effects on the patient.

Low number of gall bladder specimens studied and a short study period are the important limitations. Also, our study could not correlate the macroscopic abnormalities with GB carcinoma due to no case of suspected GB carcinoma diagnosed as GB malignancy. Hence, we cannot comment on the exact sensitivity and PPV and their inferences.

Conclusion

Macroscopic examination of gall bladder specimens most often correlate with the microscopic findings. Selective approach would therefore be a justifiable option for patients with a grossly normal looking gallbladder specimen.

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Conflict of Interest

None

Author's contribution

Concept, design, planning: SS; Literature review: SS; Data analysis: SS; Draft manuscript: SS; Revision of draft: SS,SaS,SuS,SBM,SP,SS; Final manuscript: SS; Accountability of the work: SaS,SajS,SuS,SBM,SP,SS

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