

Original Research Article

A STUDY OF INCIDENCE OF CARCINOMA GALLBLADDER IN PATIENTS UNDERGOING OPEN AND LAPAROSCOPIC CHOLECYSTECTOMY

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ABSTRACT

Background

GBC (Gall Bladder Carcinoma) is the most common malignancy of the biliary tract. Incidental GBC is when GBC is identified in a histopathological specimen without any radiological evidence for suspecting GBC. IGBC (Incidental Gall Bladder Carcinoma) is found to be 0.35%-2% prevalent. The incidence of IGBC is not studied in Manipur, hence this study was conducted.

Aims and Objectives

To study the incidence and risk factors of carcinoma gallbladder among the HPE reports of patients undergoing open and laparoscopic cholecystectomy.

Methods

This was a cross-sectional observational study wherein ultrasonogram, contrast-enhanced CT abdomen and AJCC staging were done for patients who underwent laparoscopic or open cholecystectomy, and the findings were compared with intraoperative and histopathological findings.

Results

Of the 130 patients who underwent cholecystectomy, 1 case of IGBC was reported.

Conclusions

To rule out IGBC, a routine histological study of all cholecystectomy materials is advised. An earlier diagnosis of IGBC leads to a better prognosis. If done correctly, laparoscopic cholecystectomy and open cholecystectomy have similar survival rates.

Keywords: Incidental Gallbladder Carcinoma, CECT Abdomen, USG.

INTRODUCTION

According to autopsy studies, GBC is the most prevalent bile tract cancer, accounting for 80%–95% of biliary tract cancer cases globally. Among gastrointestinal malignancies, it is in sixth place. Nonetheless, there is notable variation in the worldwide incidence of gallbladder cancer, with certain areas and racial groups experiencing epidemic proportions. This variation is most likely caused by variations in exposure to the environment and innate genetic susceptibility to carcinogenesis. When the diagnosis is discovered unexpectedly during the histological examination of the cholecystectomy material and was not detected during preoperative imaging, it is referred to as incidental GBC (IGBC).^[1] According to several studies, IGBC is present in 0.35–2% of cholecystectomy specimens,^[2,3] and because it is detected early, it is linked to a better prognosis.

The purpose of this study is to find the incidence and risk factors of incidentally detected gallbladder carcinoma in patients undergoing laparoscopic and open cholecystectomy in the state of Manipur, India, as no study has been undertaken for this purpose before in this region.

AIMS AND OBJECTIVES

To study the incidence and risk factors of carcinoma gallbladder among the HPE reports of patients undergoing open and laparoscopic cholecystectomy and to find out the correlation between symptomatology, USG findings, the macroscopic appearance of the gallbladder specimen and the presence of IGBC.

MATERIALS AND METHODS

It was a cross-sectional study done at the Department of General Surgery, Regional Institute of Medical Sciences, Imphal, Manipur, from July 2017 to July 2019.

Patients undergoing cholecystectomy for gallbladder diseases within the study period were included. Patients undergoing cholecystectomy for preoperatively diagnosed malignant diseases of the gall bladder, patients undergoing cholecystectomy as a part of major abdominal surgeries and patients with CBD stones were excluded.

When a gallbladder carcinoma is discovered unexpectedly after a cholecystectomy specimen's histopathological examination, it is referred to as IGBC.

Study Procedure

All the patients included in the study underwent a detailed clinical examination and were investigated thoroughly. The initial imaging modality used on all patients was an abdominal ultrasound scan. The number of calculi, the presence of polyps, and how thick the gall bladder wall was/were noted. A contrast-enhanced CT scan was done for the cases that had abnormal gallbladder wall thickness or had a suspicion of malignancy on an ultrasound scan of the

abdomen and to rule out other malignancies. Records were kept regarding the procedure's type, the intraoperative results, and the HPE diagnosis. The accidentally discovered GBCs were staged using the AJCC Cancer Staging Manual, 7th edition (2010).

Statistical Analysis

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 21 (IBM). The study was carried out after obtaining approval from the Research Ethics Board, Regional Institute of Medical Sciences, Imphal.

RESULTS

A total of 130 cholecystectomies were done for symptomatic gall bladder disease during the study period. 111 patients underwent laparoscopic cholecystectomy, and 19 patients underwent open cholecystectomy. Pain in the right hypochondrial region was found in 122 patients, 88 patients had a history of nausea and vomiting, 76 patients had a history of dyspepsia; and none of the studied population had a history of fever, jaundice, loss of weight, or loss of appetite. 19 patients had a history of diabetes mellitus. 130 patients were studied; 48 were non-vegetarians and 82 were vegetarians. On general examination, 56 patients had pallor. None of the patients had a palpable abdominal mass. On USG, single calculi were seen in 66 patients and multiple calculi in 64 patients. 11 patients showed the presence of GB polyps in USG. 25 patients had thickened GB walls in USG. Of the 130 patients studied, 25 patients who had GB wall thickness in the USG findings underwent a CECT study of the abdomen, and none of the patients showed any evidence of CA gallbladder.

Intraoperatively, the gallbladder was distended in 121 patients, adhesions around the gallbladder were found in 47 patients, adhesions around the calot's triangle were found in 71 patients, and none of the patients showed any evidence of growth or CBD dilatation intraoperatively. On the gross appearance of the specimen, 89 gallbladder specimens show external wall congestion; 109 patients show wall thickening; and one patient shows growth on the gallbladder fundus.

All specimens of cholecystectomy received during the study period were included in the study. Of these, one was positive for carcinoma on histopathological examination. The incidence of incidental carcinoma among all the routine open and laparoscopic cholecystectomies was 0.76% on histological examination. The patient who was diagnosed with incidental gallbladder carcinoma was 52 years old. He presented with pain in the right hypochondrium and with dyspepsia.

The USG of this patient showed multiple cholelithiasis and gallbladder wall thickening. The intraoperative findings of this patient showed distended gallbladder with adhesions around the gallbladder and the calots triangle. The HPE report of this patient shows moderately differentiated adenocarcinoma of TNM classification pT3 pN1 pMx. This patient didn't show any distant metastasis or involvement of the regional lymph nodes histologically. Of the remaining 129 specimens, the distribution of cases was as follows: Chronic cholecystitis with cholelithiasis: 109 (83.8%), chronic cholecystitis with cholesterolosis: 13 (10.0), acute chronic cholecystitis: 4 (3.1), xanthogranulomatous cholecystitis: 2 (1.5%), and adenoma: 2 (1.5%). In the current study, 42 patients are males and 88 patients are females. Only one male patient in the study was diagnosed with incidental gallbladder carcinoma.

Gender	Frequency	Percent
Male	42	32.3
Female	88	67.7
Total	130	100.0
Gender Distribution		
Age (years)	Frequency	Percent
30-40	15	11.5
40-50	34	26.2
50-60	69	53.1
60-70	12	9.2
Total	130	100.0
Age Distribution		
<i>Table 1: Gender and Age Distribution of Patients Studied</i>		

Abdominal Pain	Frequency	Percent
Present	122	93.8
Absent	8	6.2
Total	130	100.0
Nausea and Vomiting		
Present	88	67.7
Absent	42	32.3
Total	130	100.0
Dyspepsia		
Present	76	58.5
Absent	54	41.5
Total	130	100.0
<i>Table 2: Symptoms of IGBC</i>		

Of the 130 patients studied, 88 had a history of nausea and vomiting, and 42 had no history of nausea and vomiting. 76 had dyspepsia, and 122 had abdominal pain. No patient in this study had any history of fever, jaundice, loss of weight, or loss of appetite.

Of the patients studied, 111 had no history suggestive of diabetes mellitus, hypertension, bronchial asthma, ischemic heart disease, or tuberculosis. 19 patients had a history of diabetes mellitus.

Of the 130 patients studied, 48 are non-vegetarians, and 82 are vegetarians.

USG Findings

The USG study of 130 patients showed single calculi in 66 patients and multiple calculi in 64 patients.

Finding	Frequency	Percent
Calculi		
Single	66	50.8
Multiple	64	49.2
Total	130	100.0
Gallbladder Polyp		
GB Polyp	Frequency	Percent
Present	11	8.5
Absent	119	91.5
Total	130	100.0
GB Wall Thickening		
GB Wall	Frequency	Percent
Thickened	25	19.2
Not thickened	105	80.8
Total	130	100.0
Table 3: Ultrasonogram Findings		

CECT

Of the 130 patients studied, 25 patients who had GB wall thickness in the USG findings underwent a CECT study of the abdomen, and none of the patients showed any evidence of CA gallbladder.

CECT	Frequency	Percent
No CA GB	25	19.2
Didn't Do CECT	105	80.8
Total	130	100.0
Table 4: Showing the CECT Finding of the Study Population		

As the patients with CBD stones were excluded from the study, MRCP was not done in any of the study populations. Of the 130 patients studied, 19 underwent open cholecystectomy, and 121 underwent laparoscopic cholecystectomy.

Type of Surgery	Frequency	Percent
Open	19	14.6
Lap	111	85.4
Total	130	100.0
Table 5: Type of Cholecystectomy the Study Population Underwent		

Intraoperatively, 121 patients had a distended gallbladder and in 9 cases, the gallbladder was not distended.

Finding	Frequency	Percent
GB Distended		
Yes	121	93.1
No	9	6.9
Total	130	100.0
Adhesions around Calot's Triangle		
Yes	47	36.2
No	83	63.8
Total	130	100.0
External Appearance		
Congested	89	68.5
Not Congested	41	31.5
Total	130	100.0
Growth on Gallbladder		
Yes	109	83.8
No	21	16.2
Total	130	100.0
Table 6: Intraoperative and Gross Pathology Findings		

Of the 130 patients, 121 had gallbladder distension, and 47 had adhesions around the gallbladder intraoperatively.

Of the 130 patients, 89 had gallbladder wall congestion, and 109 patients had growth on the gallbladder on gross examination. Of the 130 patients studied, only one was reported to have gallbladder carcinoma on histopathological study.

Of the 130 patients under study, none of the patient showed any evidence of growth on the gallbladder intraoperatively. Of the 130 patients studied, none of the patient showed any evidence of CBD dilatation intraoperatively.

DISCUSSION

Gallbladder cancer is the most common cancer of the extrahepatic biliary tract. Symptoms are non-specific and are commonly diagnosed at an advanced stage. In this research, 130 patients had open and laparoscopic cholecystectomy; only one instance had an incidental diagnosis of GBC based on histopathology. The incidence of IGBC in this research was 0.76. The incidence of IGBC varies from 0.35% to 2% in published research.^[4] Gallstones are the main risk factor for GBC, carrying an 8.3-fold increased risk compared to the general population.^[5] In 75% to 98% of incidental GBC cases, associated cholelithiasis was detected.^[6] A higher risk is associated with larger stones; stones larger than 3 cm have a 9.2-10.1 times higher risk than stones less than 1 cm.^[7] Higher levels of local epithelial irritation are to blame for this. According to published reports, the most frequent symptom is right upper quadrant discomfort (54–83%). Other common symptoms include jaundice (10–46%), nausea and vomiting (15–43%), anorexia (4–41%) and weight loss (10–39%).^[7] Every instance in this investigation began with upper quadrant right discomfort, followed by nausea, vomiting and dyspepsia.

Adenocarcinoma is the most prevalent histologic type, accounting for 98% of all gallbladder tumors, although just one patient in our investigation had this diagnosis.

If a two-stage strategy is required, it is imperative that oncological principles be adhered to throughout the initial procedure. Because of this, the surgeon doing the video-laparoscopic cholecystectomy should always adhere to these basic guidelines: (1) conduct a comprehensive preoperative diagnosis; (2) relinquish the laparoscopy to allow access; (3) attempt to maintain the gallbladder's integrity by handling it as little as possible; (4) seal any potential wall breaches with clips or endoloops; (5) always remove the gallbladder using an endobag; (6) carefully inspect the gallbladder after it has been extracted; (7) impromptu histological examination; and (8) desufflate the pneumoperitoneum using the trocars in situ. Unintentional gallbladder opening during cholecystectomy has been reported in 25–30% of instances, which is obviously associated with a poorer outcome.^[8]

The patient who was diagnosed to have incidental gallbladder carcinoma in this study was a 52 year old male who presented with complaints of pain in the right hypochondrium and dyspepsia. He didn't give any history of significant past history. He was a non-vegetarian, and he didn't have any relatives with gallbladder disease. The USG of this patient reveals only multiple cholelithiasis and no other abnormalities. The patient was planned for elective laparoscopic cholecystectomy. Intraoperatively, the gallbladder was distended; there were adhesions around the gallbladder and the calot's triangle, and a growth was noted on the fundus, which was not in contact with the liver surface. The external surface of the gallbladder specimen showed a firm gray-white mass measuring 1.8*1.5*0.8 cm identified in the fundus. The cut surface of the mass showed that the gray-white mass extended up to 3.5 cm in the body region. The mass measures 2.5*1.5 cm, and it involves up to the serosa grossly. A lymph node was identified at the neck, measuring 0.5 cm in diameter.

On microscopy, sections studied from the gallbladder mass in the fundal region show malignant tumor cells arranged mostly in the glandular pattern, with a few in the trabecular pattern and solid sheet. Individual tumor cells have pleomorphic, hyperchromatic nuclei, some with prominent nucleoli, and moderate-to-abundant cytoplasm. The tumor cells are seen infiltrating through the muscular wall and up to the serosa, along with involvement of the liver bed. Lymphovascular and perineural invasions are also seen. The cystic duct margin showed no evidence of tumor infiltration. One lymph node dissected from the neck region showed metastatic deposits. And the pathological diagnosis came out to be moderately differentiated adenocarcinoma of the gallbladder in TNM staging pT3 pN1 pMx.

Papillary, mucinous, squamous, and adenosquamous carcinomas are some of the other variations.^[9] Carcinosarcoma, small cell carcinoma, lymphoma, signet ring cell-type tumors, and metastases are among the nine uncommon forms.^[10] The GBC histological subtype is a significant predictor of outcome. The prognosis for papillary carcinoma is the best; that of squamous and adenosquamous carcinomas is worse. Even though small cell carcinoma is extremely rare, it frequently spreads quickly and results in mortality soon after diagnosis.^[11] The pathological stage in this investigation was pT3N1Mx. The GBC therapy is based on the tumor's stage. The depth of infiltration determines the scope of operation (T Stage). Cholecystectomy is the treatment of choice for pT1a tumors; cholecystectomy combined with lymph node dissection is the treatment for pT1b tumors. It is advised to remove the liver along with the GB bed and dissect the lymph nodes for pT2 and further advanced malignancies. The

majority of GBC cases had advanced stages at diagnosis with a dismal five-year survival rate of fewer than 5%.^[12] The greatest prognosis is typically seen in incidental GBC cases, which are often discovered early.^[13]

When the pathologist later diagnoses incidental GBC, it is critical to thoroughly rescan the patients using CT, MRI, and positron emission tomography, with a focus on the liver bed, peritoneum, and trocar orifices.^[14] In addition, the histological investigation has to be reevaluated, and a second opinion may be necessary. Confirming the point of tumor (pT), identifying the precise location of the tumor (hepatic side, bottom, or infundibulum), thoroughly assessing the cystic duct, and determining if the cystic lymph node is included in the histological investigation are all dependent on this. The two main goals of a reoperation for incidental GBC nowadays should be the removal of the locoregional lymph nodes and the R0 resection of the liver parenchyma together with the other surrounding tissues.^[15]

The issue of whether laparoscopic cholecystectomy affects the prognosis for people who have it arises because more cases of GBC are unintentionally discovered during the procedure. The emergence of port-site metastases was initially reported by Drouard et al.^[16] in 1991, and more evidence was presented in 1994.^[17] This played a part in the decline in interest in using laparoscopy to treat cancer. Moreover, a poorer prognosis in the long run might arise from intraperitoneal dissemination of cancerous cells caused by severe organ manipulation and perforation.^[18] As a matter of fact, among patients in whom intraoperative perforation could be proven, the frequency of port-site recurrence rose from 9% to 40%.^[19] Pneumoperitoneum considerably boosted tumor cell implantation at trocar sites and tumor progression in the peritoneum, according to other investigations.^[20-22] But when done appropriately, laparoscopic cholecystectomy had no effect on the long-term outcome of malignancies in the early stages (T1a, T1b, T2).

Furthermore, in individuals who have previously undergone noncurative surgery, radical re-resection done many months following laparoscopic cholecystectomy can result in long-term survival for malignancies with liver infiltration, just as radical resection performed during the first surgery does. The degree of the tumor's parietal invasion is the sole determinant of survival; however, there is no statistically significant difference between individuals whose incidental GBC was found during or after cholecystectomy ($p = 0.235$).

CONCLUSION

To rule out IGBC, a routine histological study of all cholecystectomy materials is advised. Since IGBCs are typically found early on, their prognosis is better. If done correctly, laparoscopic cholecystectomy has little effect on survival. The only GBC stages for which a simple cholecystectomy may be appropriate are Tis and T1a. As long as there is no remaining microscopic cancer (R0), all following stages, beginning with T1b, should be treated with lymphadenectomy and excision of at least 2-3 cm of liver parenchyma around the hepatic bed. Hilum-type tumors with positive cystic duct borders may need resection of the major bile ducts. R0 resection can be attained by doing multiorgan resection or more extensive liver resection. Since gallstones are easily detected by ultrasound and have a well-documented link with gallbladder carcinoma, eradicating them remains the optimum target for the prevention of gallbladder cancer. It is currently arguable whether prophylactic cholecystectomy is necessary for asymptomatic individuals.

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