



Original Article

Barriers Leading to Delayed Presentation of Patients with Gallbladder Cancer

Islam MS¹, Eastiak MF^{2*}, Jahan N³, Hasan ASA⁴, Alam RJ⁵, Hossain MJ⁶

Abstract

Introduction: Gallbladder cancer carries a poor prognosis because early disease is often asymptomatic and many patients are identified only after the tumour has progressed to an advanced, frequently unresectable stage. This study explored factors contributing to delayed recognition of gallbladder cancer, with attention to radiological findings and histopathological features observed in resected gallbladder specimens. The objective of this study is to examine patient-related and diagnostic contributors to delayed detection of gallbladder cancer, particularly socioeconomic barriers and limitations of commonly used investigations.

Methods: A prospective observational study was performed between January 2021 and December 2022 among 42 patients with gallbladder cancer identified on imaging. For patients who underwent surgery, histopathological examination of resected specimens was used to verify malignancy. Information was gathered using a structured questionnaire and analyzed accordingly.

Results: Among the 42 patients, 30 (71.43%) were women. A large proportion lived in rural settings (33, 78.57%), had education below the SSC level (29, 69.05%), and came from low-income households (28, 66.67%). The leading presenting features were abdominal pain (30, 71.43%), jaundice (13, 30.95%), weight loss (9, 21.43%), and abdominal mass (5, 11.90%). On CECT of the abdomen, the most frequent findings included a gallbladder mass (20, 47.62%), hepatic invasion (9, 21.43%), gallstones (6, 14.29%), choledochal cyst (3, 7.14%), enlarged porta hepatis lymph nodes (3, 7.14%), and ascites (1, 2.38%). CA 19-9 was elevated in 24 patients (57.14%). Histopathology demonstrated associations between gallbladder malignancy and gallstones in 6 patients (14.29%), choledochal cyst in 3 (7.14%), and gallbladder polyp in 11 (26.19%).

Conclusion: Delayed identification of gallbladder cancer is likely shaped by a combination of patient and diagnostic factors. Low socioeconomic status, residence in rural areas, and limited educational attainment were prominent barriers, while poor awareness of early symptoms and the limited diagnostic yield of commonly used imaging and tumour markers further contributed to delay. Interventions targeting these modifiable factors may facilitate earlier diagnosis and more timely treatment.

Key words: Delayed presentation, benign gall bladder disease, gallbladder cancer (GBC).

1. Md. Saiful Islam, Associate Professor, Department of General Surgery, Bangladesh Medical University, Dhaka, Bangladesh.
2. Mohammad Faroque Eastiak, Associate Professor, Department of General Surgery, Bangladesh Medical University, Shahbagh, Dhaka.
3. Nelema Jahan, Professor, Department of Surgery, Sir Salimullah Medical College, Dhaka, Bangladesh.
4. Ahmed Sami Al Hasan, Associate Professor, Department of Surgery, Dhaka Medical College Hospital, Dhaka, Bangladesh.
5. Rana Jahangir Alam, Assistant Professor, Department of General Surgery, Bangladesh Medical University, Dhaka, Bangladesh.
6. Md. Jahangir Hossain, Associate Professor, Department of Surgical Oncology, Bangladesh Medical University, Dhaka, Bangladesh.

***Correspondence:** Dr. Mohammad Faroque Eastiak, Associate Professor, Department of General Surgery, Bangladesh Medical University, Dhaka, Bangladesh. Email: eastiak55@bsmmu.edu.bd
Phone no. +8801711822574.

Introduction

Gallbladder cancer (GBC) is an aggressive epithelial malignancy and one of the most fatal neoplasms of the biliary tract^{1,2}. Although it is relatively uncommon among gastrointestinal cancers, it carries major clinical significance because of its rapid progression, early local invasion, and poor survival once symptomatic disease has developed^{3,4}. Prognosis is closely related to stage at diagnosis. Patients identified at an early stage may benefit from curative resection, whereas most patients present with advanced disease that is no longer amenable to simple surgical treatment^{4,5}. Consequently, overall survival remains poor, and delayed presentation continues to be a major barrier to effective management.

The occurrence of GBC shows marked geographic variation, with higher incidence reported in parts of South Asia, East Asia, and Latin America. Women are affected more frequently than men, and several chronic gallbladder conditions have been associated with malignant transformation, including gallstones, chronic cholecystitis, gallbladder polyps, porcelain gallbladder, anomalous pancreaticobiliary junction, and choledochal cysts. Chronic mucosal irritation and inflammation are believed to contribute to dysplasia and carcinogenesis. In low- and middle-income settings, these predisposing conditions may remain undetected or untreated for prolonged periods, thereby increasing the risk that malignancy will be recognized only after progression to an advanced stage.^{3,5}

Early diagnosis of GBC is particularly difficult because initial manifestations are often absent or nonspecific. Patients may present with vague upper abdominal discomfort, dyspepsia, nausea, anorexia, or intermittent pain that resembles benign biliary disease. More specific symptoms, such as persistent right upper abdominal pain, jaundice, weight loss, or a palpable abdominal mass, usually occur only after local extension or metastatic spread has developed. For this reason, many cases are discovered incidentally during or after cholecystectomy performed for presumed benign gallbladder pathology, while others are diagnosed only when advanced symptoms prompt further investigation.^{6,7}

Diagnostic delay may arise at both the patient and healthcare-system levels. Patient-related delay may result from poor awareness of symptoms, financial hardship, transport barriers, limited health literacy, or delayed consultation. System-related delay may occur because of misinterpretation of symptoms, limited access to imaging, delayed referral, or the absence of structured pathways for suspected malignancy⁶⁻¹⁰. These factors are especially important in GBC, where the interval for potentially curative treatment is narrow. In addition, the diagnostic performance of commonly used tools remains imperfect. Abdominal ultrasonography is useful as an initial investigation but may not reliably distinguish inflammatory from malignant gallbladder disease or accurately define stage. Cross-sectional imaging can improve lesion characterization and assessment of local invasion, but access may be limited. Tumour markers such as CA 19-9 and CEA may support suspicion, yet neither is sufficiently sensitive or specific to establish the diagnosis independently.

In Bangladesh, delayed presentation may be further influenced by disparities in residence, education, and socioeconomic status. Individuals from rural areas often face difficulties in accessing specialist consultation and advanced diagnostic facilities, while limited literacy may reduce awareness of the significance of persistent abdominal symptoms. Moreover, the high prevalence of benign gallbladder disease may obscure early malignant change and contribute to repeated symptomatic treatment before definitive evaluation is undertaken. Against this background, the present study was designed to examine the barriers leading to delayed presentation of patients with gallbladder cancer, with particular emphasis on patient-related factors and diagnostic limitations in a tertiary care setting. A clearer understanding of these barriers may help support earlier clinical suspicion, more timely referral, and improved opportunities for intervention.

Materials and methods

This was a prospective study conducted over 42 patients of carcinoma of gallbladder evaluated perioperatively from January 2021 to December 2022, in the general surgery department of BSMMU. Both sexes aged above 20 years and diagnosed by imaging, per operative findings, and histopathological report of the specimen were included in this study. Patients diagnosed with previously treated for gallbladder malignancy and patients unfit for general anaesthesia, acute abdomen were excluded from this study. There was no ethical issue, informed consents from the patients were taken. Diagnosis of carcinoma of gallbladder was established by taking thorough clinical, socio-economic, family history along with imaging (USG of abdomen, CECT of abdomen, MRCP), CA 19-9, CEA level and Liver function tests. After taking consent for the operative procedure the patient was further investigated for general fitness for the operation. During operation, Reverse-L incision was made for pre-operatively diagnosed cases for carcinoma of the gallbladder, laparoscopy for gall stones, gallbladder polyp and Kocher's incision for choledochal cyst. After operation, resected specimen was sent for histopathology and evaluation of report for diagnosis of carcinoma of the gallbladder. All the data were collected and analyzed, then the results were established in a tabulated form.

Result

A total of 42 patients with gallbladder cancer were included in the study. The results are presented below

to demonstrate the demographic profile, presenting symptoms, imaging characteristics, tumour marker patterns, and histopathological associations observed among the study participants. (Table I)

Table I: Demography of patient (n=42)

Age (years)		No. of cases	Percentage (%)
20-30		2	4.76
31-40		07	16.67
41-50		13	30.95
51-60		11	26.19
61-70		09	21.43
Sex	Female	30	71.43
	Male	12	28.57
Social Status			
Residence	Rural	33	78.57
	Urban	09	21.43
Education	< SSC	29	69.05
	>SSC	13	30.95
Economy	Low	28	66.67
	Middle	14	33.33
	High	0	0

Most patients were middle-aged or older, with the highest proportion belonging to the 41–50 years age group (30.95%), followed by the 51–60 years group (26.19%) and the 61–70 years group (21.43%). Female patients predominated, accounting for 71.43% of the study population. A substantial majority of the patients resided in rural areas (78.57%), had educational attainment below the SSC level (69.05%), and belonged to low-income households (66.67%). These

findings indicate that gallbladder cancer in this series was more frequently encountered among women from socioeconomically disadvantaged and rural backgrounds.

The clinical presentation of the patients was predominantly nonspecific. Abdominal pain was the most frequent presenting complaint, while jaundice, weight loss, and abdominal mass were observed in smaller proportions. The distribution of presenting symptoms is shown in Table II.

Table II: Common symptoms of patients (n=42)

Symptoms	No. of cases	Percentage (%)
Abdominal pain	30	71.43
H/O jaundice	13	30.95
Abdominal mass	05	11.90
Weight loss	09	21.43

Abdominal pain was present in 30 patients (71.43%), making it the leading symptom at presentation. A history of jaundice was reported by 13 patients (30.95%), whereas weight loss occurred in 9 patients (21.43%). Abdominal mass was documented in 5 patients (11.90%). Overall, the symptom profile suggests that many patients presented after the onset of features compatible with advanced or clinically significant disease rather than during an early asymptomatic stage.

Radiological evaluation using MRCP, ultrasonography, and contrast-enhanced computed tomography (CECT) demonstrated a range of findings associated with gallbladder malignancy and related hepatobiliary abnormalities. These imaging findings are detailed in Table III.

Table III : Imaging findings (n=42)

Name of imaging	Findings	No. of cases	Percentage (%)
MRCP	Intrahepatic and extrahepatic biliary dilatation	10	23.81
	Choledochal cyst	3	7.14
USG of abdomen	Gall stones	6	14.29
	Gall bladder polyp	11	26.19
	Gall bladder wall thickening	11	26.19
	gall bladder mass	11	26.19
	Hepatic invasion	03	7.14
CECT of abdomen	Ascites	1	2.38
	Gall stones	6	14.29
	Choledochal cyst	3	7.14
	Gall bladder mass	20	47.62
	Hepatic invasion	09	21.43
	Porta hepatic lymph nodes(enlarged)	03	7.14

On MRCP, intrahepatic and extrahepatic biliary dilatation was noted in 10 patients (23.81%), while choledochal cyst was identified in 3 patients (7.14%). Ultrasonography of the abdomen showed gallbladder polyp, gallbladder wall thickening, and gallbladder mass in 11 patients each (26.19%), whereas gallstones were seen in 6 patients (14.29%) and hepatic invasion in 3 patients (7.14%). On CECT of the abdomen, a gallbladder mass was the most frequent finding, present in 20 patients (47.62%), followed by hepatic invasion in 9 patients (21.43%), gallstones in 6 patients (14.29%), choledochal cyst in 3 patients (7.14%), enlarged porta hepatis lymph nodes in 3 patients (7.14%), and ascites in 1 patient (2.38%). These findings indicate that cross-sectional imaging frequently detected mass lesions and evidence of local extension, suggesting that many patients were evaluated after the disease had already progressed beyond an early stage.

The distribution of tumour marker values is shown in Table IV. Serum CA 19-9 was more frequently elevated than CEA among the study participants.

Table IV: Tumour markers (n=42)

Tumour marker	Normal	Percentage (%)	Raised	Percentage (%)
CA 19-9	18	42.86	24	57.14
CEA	35	83.33	7	16.67

CA 19-9 was within the normal range in 18 patients (42.86%) and elevated in 24 patients (57.14%). In contrast, CEA remained normal in 35 patients (83.33%) and was elevated in only 7 patients (16.67%). These findings suggest that CA 19-9 showed a higher rate of abnormality than CEA in this series, although a substantial proportion of patients still had normal tumour marker values.

Histopathological examination of resected specimens demonstrated several pathological conditions associated with gallbladder malignancy, as summarized in Table V.

Table V : Pathological association with gallbladder malignancy in resected specimen (Histopathology) (n=42)

Common pathology	Malignancy association	Percentage (%)
None	22	52.38
Gall stones	6	14.29
Choledochal cyst	3	7.14
Gall bladder polyp	11	26.19

Histopathology showed no associated common pathology in 22 patients (52.38%). Among the identifiable associated conditions, gallbladder polyp was the most frequent, observed in 11 patients (26.19%), followed by gallstones in 6 patients (14.29%) and choledochal cyst in 3 patients (7.14%). These findings indicate that, in a subset of cases, gallbladder malignancy coexisted with structural gallbladder abnormalities that may be relevant to the disease process or to the opportunity for earlier detection.

Discussion

Gallbladder malignancy is a rare entity, but common in the gastrointestinal tract. Most are diagnosed at advanced stage with dismal prognosis having 5 years survival rate of less than 5.0%.⁹ Detection at the early stage has an excellent prognosis increasing up to 90.0-100.0% 5-year-survival rate. However, early detection is usually not possible due to delayed onset of symptoms or is masked by chronic cholecystitis, and is usually detected during simple cholecystectomy as an incidental finding. Lack of preoperative clinical suspicion, absence of definitive clues on history and physical examination at the early stage, lack of specific findings on radiology and absence of sensitive serological markers are likely contributing factors for the diagnosis of this disease at the advanced stage.^{11,12} Higher incidence of this carcinoma is reported in relation to poor socioeconomic conditions, low level of education and lifestyle factors like smoking, tobacco chewing and alcohol consumption.¹³

In this study, 33(78.57%) patients with carcinoma of the gallbladder reported from rural areas. The reason behind this might be the lack of health care facilities in the rural areas and lack of a proper referral system, which fails to diagnose the disease at an early stage.

In carcinoma of the gallbladder, a major proportion of patients' educational level 29(69.05%) were below SSC. Most of the patients were from low-income families 28(66.67%). As gallbladder carcinoma does not become symptomatic in the early stages and the poor illiterate people of our country ignore mild health problems, presents late to appropriate health care provider and at that time their disease becomes advanced. Persistent insult to gallbladder mucosa is the reason upheld for the association of gallstone disease 6(14.29%) with carcinoma of the gallbladder. Presence of gallstone, duration of gallstone disease, number of gallstones, and size of gallstones are various factors which are directly associated with chronic insult to gallbladder mucosa. Gallbladder polyp of ≥ 10 mm is considered a risk factor for malignant transformation.^{12,13} In this study we found that gallstones 6(14.29%), gallbladder polyp 11(26.19%), choledochal cyst 3(7.14%) were associated with gallbladder carcinoma but not significantly different between early and advanced group. Symptoms related to gallbladder cancer are usually nonspecific and include jaundice, abdominal pain, nausea, GB mass and weight loss. Due to non-specific symptoms, most of the patients present at an advanced stage with metastasis.¹⁴

In this study gallbladder carcinoma mainly presented with abdominal pain 30(71.43%) and jaundice 13(30.955), weight loss 9(21.43%), and GB mass 11(26.19%). Tumour markers such as CEA, and CA 19-9 have been widely used for the diagnosis of different types of cancer (e.g., liver, gastric, colorectal, and pancreatic) but inconsistent results were observed when these markers were used individually for the diagnosis of gall bladder carcinoma.⁵

In this study we observed that raised CA 19-9 24(57.14%) and CEA level 7(16.67%). As CA 19-9 is not specific for GBC and it should be combined with other imaging tests to diagnose GBC. Differentiation of the cause of gallbladder wall thickening remains a challenging task even with advances in imaging modalities. USG is sensitive for evaluation of the gallbladder mural thickening or mass and local extension into liver but its role in staging is limited as it is less reliable for detection of lymph nodes and peritoneal metastasis.⁸ Tumour location in the gallbladder is an important factor in producing symptoms before its progression to an advanced stage.¹⁴

In this study, gallbladder thickening was found in 11(26.19%) and gall bladder polyps in 11(26.19%) cases on USG of the abdomen. Gall bladder mass 20(47.62%), hepatic invasion 9(21.43%), enlarged porta hepatis lymph node 3(7.14%) in CECT of abdomen were our observations. Tumour located in the neck of the gallbladder produces symptoms at early stage and helps in early diagnosis of the disease.¹⁴

Conclusion

Delayed diagnosis of gallbladder cancer appears to be driven by both patient-related and diagnostic factors. Poor socioeconomic status, rural residence, and low educational attainment were common patient-related barriers, while poor awareness of early symptoms, the limited sensitivity of commonly used abdominal ultrasonography, and the low sensitivity of tumour markers also contributed to diagnostic delay. Addressing these modifiable factors through targeted interventions may shorten the time to treatment initiation and improve timely care for patients with gallbladder cancer.

References

1. W.Y. Yao et al. Preoperative lymphocyte to C-reactive protein ratio as a new prognostic indicator in patients with resectable gallbladder cancer. *Hepatobil Pancreat Dis Int* 2022;21(3):267-272
2. B.C. Jacobson et al. EUS-guided FNA for the diagnosis of gallbladder masses. *Gastrointest Endosc*. 2003; 57(2): 251-4.
3. R. Lam et al. Gallbladder disorders: a comprehensive review. *Dis Mon*. 2021; 67(7): 101-130
4. C.H. Fang et al. Impact of three-dimensional reconstruction technique in the operation planning of centrally located hepatocellular carcinoma. *J Am Coll Surg*. 2015; 220(1): 28-37.
5. Y. Okuda et al. Usefulness of operative planning based on 3-dimensional CT cholangiography for biliary malignancies. *Surgery*. 2015; 158(5): 1261-71.
6. Gorin SS, Heck JE, Cheng B, Smith SJ. Delays in breast cancer diagnosis and treatment by racial/ethnic group. *Arch Intern Med*. 2006;166:2244-52.
7. Salomaa ER, Sallinen S, Hiekkanen H, Liippo K. Delays in the diagnosis and treatment of lung cancer. *Chest*. 2005;128:2282-88.

8. Allgar VL, Neal RD. Delays in the diagnosis of six cancers: Analysis of data from the national survey of NHS patients: *Cancer. Br J Cancer*. 2005;92:1959-70.
9. Look M, Tan YY, Vijayan A, Teh CH, Low CH. Management delays for early gastric cancer in a country without mass screening. *Hepatogastroenterology*. 2003;50:873-76.
10. Amir Z, Kwan SY, Landes D, Feber T, Williams SA. Diagnostic delays in head and neck cancers. *Eur J Cancer Care (Engl)*. 1999;8:198-203.
11. Ghosh M, Sakhuja P, Singh S, Agarwal AK. p53 and betacatenin expression in gallbladder tissues and correlation with tumor progression in gallbladder cancer. *Saudi J Gastroenterol*. 2013;19: 34-39.
12. Glazer ES, Liu P, Abdalla EK, Curley SA. Neither neoadjuvant nor adjuvant therapy increases survival after biliary tract cancer resection with wide negative margins. *J Gastrointest Surg*. 2012; 16(9): 1666-1671.
13. Kumar S, Gupta P, Sharma V, Mandavdhare H, Bhatia A, Sinha S. Role of Ultrasound-Guided Fine-Needle Aspiration Cytology of Omentum in Diagnosis of Abdominal Tuberculosis. *Surg Infect (Larchmt)*. 2019; 20(1): 91-94.
14. Hundal R, Shaffer EA. Gallbladder cancer: epidemiology and outcome. *Clin Epidemiol*. 2014; 6: 99-109.