Bangladesh Med J. 2024 Jan; 53(1)
DOI: https://doi.org/10.3329/bmj.v52i3.81058

Original Article

Early Gallbladder Carcinoma: Demographic Features, Associated Factors and Surgical Outcomes in Tertiary Care Hospitals of Bangladesh

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Abstract

Gall bladder carcinoma is the most prevalent biliary tract malignancy worldwide. It has no specific symptoms. Symptoms begin with the advancement of disease, and it terminates the life rapidly. Therefore, early diagnosis and intervention lead to positive results, and better outcomes could be assured following surgery. This cross sectional descriptive study was conducted among admitted patients, in the Department of Hepato-Biliary-Pancreatic Surgery and Liver Transplant (HBPS and LT) of BIRDEM General Hospital, Ibn Sina Specialized hospital and Crescent Gastro Liver and General Hospital in Dhaka City from January 2022 to June 2024, over a period of 2 years and 6 months. Most of the data (90%) were obtained from BIRDEM and rest 10% from above mentioned hospitals. The initial estimated sample size was 86; however, after applying the inclusion and exclusion criteria, only 40 cases were included due to data limitations. The study included all histopathologically verified early gallbladder carcinoma cases, but excluded those with signs of advanced malignancy. Cases were selected irrespective of age or sex, anatomical distribution, clinical features, risk factors, histological type, and surgical outcomes. After receiving ethical approval from the Ethical Committee and verbal consent from the patients, data were collected through face-to-face interviews and observations using a pre-testing questionnaire and check list specifically designed for the study by the researcher. The peak incidence of gallbladder carcinoma was observed in 5th and 6th decades of life with the mean age of the cases being 58.12±7.75 years and their age range was 35 to 80 years. Female was predominance; where, male female ratio was 1:2.34. Gall stone (80%) was the most common associated factor and mostly diagnosed incidentally (92.5%). Mostly done procedure was laparoscopic cholecystectomy and it was about 90% .Tumor involve fundus of the gallbladder in 55% cases and most of these were adenocarcinoma (90%). After surgery, wound infection rate was 7.5% and port site hernia was 5%, however there was no recurrence and survivability was 97.5% within the duration of study periods. Early surgical intervention brings good result in the management of early gallbladder carcinoma.

Keywords: *Early gallbladder carcinoma; risk factors; treatment outcome.*

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INTRODUCTION

Early gallbladder carcinoma (EGBC) is defined as cancer confined to the mucosa (pT1a) or muscularis (pT1b) according to the TNM classification. The incidence of gallbladder carcinoma in Bangladesh is 5.3%[1,2]. Clinical symptoms of EGBC can be non-specific and symptoms begin with the advancement of the diseases with a very gloomy outcome. It is unlikely many other malignancy of the body, this tumour does not respond well to the conventional chemo-radiotherapy and surgery is the only treatment option in early cases.

MATERIALS AND METHODS

This cross-sectional descriptive study was carried out in the Department of Hepato-Biliary-Pancreatic surgery and Liver Transplant (HBPS & $LT_{x)}$ in Bangladesh Institute of Diabetes, Endocrine and Metabolic Disorders (BIRDEM)

Hospital, Ibn Sina Specialized hospital and Crescent Gastro Liver and General hospital , from January 2022 to June 2024. Data were collected by using a questionnaire devised for the study by researcher himself. 90% data were obtained from BIRDEM and 10% from above mentioned hospital. Data processing and analysis were done using SPSS (statistical package for social sciences), version 26. The test statistics used to analyze the data were descriptive statistics

RESULT

Total patients of this study were 40 (male 12, female 28) and male female ratio was 1:2.34.

Table I states the distribution of the patients by their demographic characteristics; here, 70% of the patients were in age group 56-65 years and 15% were in age group 66-75 years. Mean age of the patients was 58.12 ±7.75 years.

Table- I: Distribution of the patients by their demographic characteristics (n=40)

Sex	Male	Female
No of cases	12 (30%)	28 (70%)
Frequency in age group (Years)		
35-45	0	1 (2.5%)
46-55	0	3 (7.5%)
56-65	10 (25%)	18 (45%)
66-75	1 (2.5%)	5(12.5%)
>76	1(2.5%)	1(2.5%)
Mean age (Years)	58.12	
Standard deviation	7.75	

Table II shows the associated factors of gall bladder carcinoma; among the associated disease, 36 (90%) had cholelithiasis, other associated factors were obesity and gall bladder polyp 2 (5%) cases each; choledochal cyst with anomalous pancreatico-biliary maljunction and positive family history 1 (2.5%) case each.

Table- II: Associated factors of gall bladder carcinoma (n=40)

Factors	Frequency	Percentage
Gall stone	36	90
Silent /asymptomatic+symptomatic	29+7	80.6+19.4
Obesity	2	5
Gall bladder polyp	2	5
Choledochal cyst with anomalous pancreatico-biliary maljunction	1	2.5
Family history	1	2.5

Table III contains the time of diagnosis of gall bladder carcinoma in relation with operation EGBC; study finds that 37 (92.5%) diagnosed incidentally after surgical procedure (post-operative diagnosis) and preoperative suspicious was possible only in 7.5% cases.

Table- III: Time of diagnosis of gall bladder carcinoma in relation with operation (n=40)

Time of diagnosis	No of cases	Percentage
Pre- operative diagnosis (Suspicision on imaging)	3	7.5
Gall bladder polyp(size >2cm)	2	5
Cholecystitis(irregular wall thickening)	1	2.5
Post-operative diagnosis		
(Specimen showed malignancy)	37	92.5
Cholelithiasis with cholecystitis	36	90
Choledochal cyst with Pancreatico-biliary maljunction	1	2.5

Table IV describes the types of surgical procedures performed prior to diagnosis of gall bladder carcinoma; here four types of surgical intervention was done and 36 (90%) surgical interventions were done by laparoscopic cholecystectomy. Others 4 (10%) surgical interventions were open procedure. Among the open procedure 2 (5%) cases underwent laparoscopic cholecystectomy followed by frozen section biopsy, 1 (2.5%) case underwent limited hepatic bisegmentectomy (frozen section facility not available) and 1 (2.5%) case underwent cholecystectomy and total excision of choledochal cyst with Roux –en –Y hepatico-jejunostomy.

Table- IV: Types of procedure performed prior to diagnosis of gall bladder carcinoma (n=40)

Types of procedure	No of cases	Percentage
Laparoscopic procedure (lap. Cholecystectomy)	36	90
Open procedure	4	10
Frozen section biopsy	2	5
Hepatic bisegmentectomy (frozen section facility not available)	1	2.5
Cholecystectomy with total excision of choledochal cyst with Roux-en-Y hepatico-jejunostomy	1	2.5

Figure 1 illustrates the site of origin of tumour in gall bladder; here 22 (55%) cases carcinoma originate from the fundus, 12 (30%) cases from body, and 6 (15%) cases from neck.

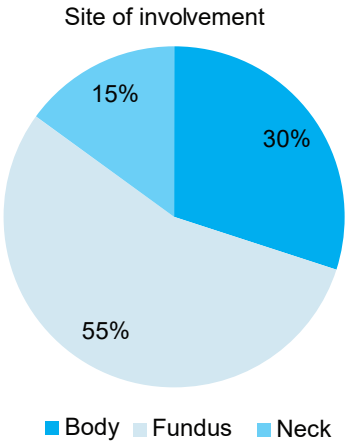

Figure- 1: *Pie chart of involving site of carcinoma in the gallbladder (n=40)*

Table V exhibits the histopathological variant of gall bladder carcinoma; among the various histological variant adenocarcinoma was found in 36 (90%) cases, others were mucinous adenocarcinoma 2 (5%) cases; papillary adenocarcinoma and adeno-squamous cell carcinoma 1 (2.5%) case each.

Table- V: Histopathological variant of gall bladder carcinoma (n=40)

Histological type	No of cases	Percentage (%)
Adenocarcinoma	36	90
Mucinous adenocarcinoma	2	5
Papillary adenocarcinoma	1	2.5
Adeno squamous cell carcinoma	1	2.5

Table VI states the relation of tumor markers CA19-9 and CEA with gallbladder carcinoma; CA19-9 (cut off value 37 U/mL) and CEA (cut off value 10 ng/mL) were done before surgery in 7 cases and 4 cases respectively and after surgery these level were done in every cases and these level were below normal in every cases.

Table- VI: Relation of tumor markers CA19-9 and CEA with gallbladder carcinoma (n=40)

	CA 19-9		
	No of cases	Level >37 U/mL	Level <37 U/mL
Pre-operative	7	2	5
Pre-operative	39	0	39
	CEA		
	No of cases	Level >10 ng/mL	Level <10 ng/mL
Pre-operative	3	1	2
Post-operative	39	0	39

Table VII displays the subsequent follow up and radiology showed no further evidence of recurrence; here, 3 (7.5%) patients had experienced wound infection, 2 (5%) patients had port site hernia and survivability was 97.5% within 2.5 years of the study period.

Table- VII: Outcome of 40 cases of early gallbladder carcinoma managed surgically (n=40)

Surgical out comes	Frequency	Percentage (%)
Wound infection	3	7.5
Open procedure	2	5
Laparoscopic cholecystectomy	1	2.5
Hernia (port site)	2	5
Recurrence	0	0
Survivability	39	97.5

DISCUSSION

In this study, the mean age at diagnosis was 58.12±7.75 years and female were diagnosed more and male-to- female ratio was 1:2.34. In an Indian study, conducted by Dutta U, Bush N, Kalsi D, Popli P, Kapoor VK et al. showed that the mean age of presentation of GBC in Indian subcontinent is younger than their counterparts in the USA and western European countries[2,3]. In their study, they also mentioned that women of this region are exposed to higher levels of estrogen and progesterone during their lifetime which promotes benign and malignant diseases of gallbladder [2,3]. Here, gall stone was the most common (90%) associated factors others were obesity (5%), gall bladder polyp (5%), anomalous pancreatico-biliary maljunction (2.5%) and positive family history of gall

bladder carcinoma (2.5%). A study conducted in Germany, in 2019, by Søreide K, Guest RV, Harrison EM, Kendall TJ, Garden OJ, Wigmore SJ et al. showed that 70 to 90% of GBC patients have cholelithiasis and it is presumed that chronic mucosal irritation by calculi leads to dysplasia and eventually develop carcinoma[3]. The Cancer Prevention Study II Nutrition Cohort, the relative risk of gallbladder cancer was 1.8 (95% confidence interval [CI], 1.1 to 2.9) in obese men with a BMI of 30.0 to 34.9 compared to men with a normal BMI (18.5 to24.9)[3]. Alvi AR et al. showed in his study that several factors are signs of potential malignant growth of polyp: polyps greater than 10 mm, rapidly increasing polyps, solitary or sessile polyps, association with gallstones, patients over 50 years of age.[4] In his study he also evaluated the risk of anomalous pancreatico-biliary maljunction with carcinoma of gallbladder and describe the pathological changes in anomalous junction.[5] Anomalous pancreatico-biliary maljunction potentially allowing pancreatic secretions to regurgitate into the biliary system and gallbladder, and so leading to malignant changes in the mucosa.[5] The histological subtype in such cases is usually a papillary carcinoma.[9] Our study was correspond to this international study[4,5] In current study , most of the cases (92.5%) were diagnosed incidentally and suspicious cases underwent open procedure. A similar finding was reported by some other researchers in patient with GBC[8]. According to Blumgart`s Surgery of the Liver, Biliary Tract and Pancreases , authors advocate when a EBGC suspected pre-operatively, it is contraindicated to do a laparoscopic cholecystectomy to prevent perforation of the gallbladder wall and the spillage of bile into the abdominal cavity (15-45% of patients) which tends to result in dissemination and significantly worsens the prognosis[16,17]. In this current study , majority (55%) of the carcinoma originate from the fundus and most common (90%) histological variant was adenocarcinoma which are similar to other international study[9,12]. In current study, CA 19-9 and CEA were used to assess the residual diseases and recurrence after surgery. Ashish Sachan, Sundeep Singh Saluja, Phani Kumar Nekarakanti et al. conducted a study in Department of Gastrointestinal Surgery, Govind Ballabh Pant Institute of Post Graduate Medical Education and Research, Jawahar Lal Nehru Marg, New Delhi, 2020, India to evaluate the role of tumor markers-carbohydrate antigen 19–9 (CA19–9) and carcinoma embryonic antigen (CEA) in patients with GBC. They included 176 patients in their study they advocate that higher levels of CA 19-9 and CEA, may not mean that anyone have carcinoma, conditions other than cancer can cause higher level. These conditions include an infection or inflammation in pancreases, liver disease, gall stone and cystic fibrosis [14]. In this study wound infection rate in laparoscopic procedure was 2.5% and in open procedure 5%. Agaba EA, Rainville H, Wemulapali P et al reported in their study that the incidence of SSI rates ranged from 2.5% to 41.9% [18.] In this study, port site hernia was 5% (2 cases).We didn't observe any hernia in open procedure. Hernias at the port insertion site have been reported in many papers with the incidence between 0.14% and 22[18]. Study period was 18 months and there was no recurrence observed during this period. Patients were assessed clinically and biochemically including liver function test and tumor marker and USG of whole abdomen at 3 months interval during first 3 months and 6 months interval in later years. Recurrence depends on tumor size, tumor morphology resection margin ,hepatic versus peritoneal side involvement and portal vein involvement[20].According to Blumgart`s Surgery of the Liver, Biliary Tract and Pancreases, authors report that in case of T1a tumor, simple cholecystectomy is appropriate and curative in 90% cases and 1 year OS of 100% for patient with T1a tumours[16,17]. In current study, out of 40 cases, 1 patient died due to sudden myocardial infraction on 4th post-operative day, following laparoscopic cholecystectomy and this patient was already discharged from hospital. In this study 1 year survivability was 97.5%. The study period was short to follow up the survivability of early gall bladder carcinoma. In this study another observation was, follow up period was short to be significant. According to international study, there is a cumulative survival rate by stage. T1a stage cancers (infiltration limited to the mucosa) require only a cholecystectomy, provided that the margin of the cystic duct is free from cancer[18]. The prognosis for this group of patients is very good and according to some reports a 5-year survival reaches 100% [18,19]. Prognosis depends mainly on the stage of the disease and the possibility of R0 resection [20]. The tumor biology seems to play a key role and it largely determines the course of the disease [20]. The least advanced cancers (T1a) allow for almost a 100% 5-year survival after only laparoscopic cholecystectomy[21]. Therefore, patients with incidentally detected cancer have significantly better prognosis[21]. In this study most of the cases were incidentally diagnosed and their prognosis were good.

Having summarized the above mentioned discussion, it is evident that early-stage gallbladder carcinoma is most

commonly an incidental finding in patients who have undergone cholecystectomy for inflammatory disease of the gallbladder. However, if detected early in young patient with early stage (T1a tumor), has better overall 5 years survival rates.

CONCLUSIONS

This study finds that early gallbladder carcinoma was detected more frequently in female; where male female ratio was 1:2.34 and highest incidence (70%) was found in age group 56-65 years. Time of diagnosis of in relation with operation EGBC; Most of the (92.5%) gall bladder carcinoma diagnosed incidentally after surgical procedure. The only challenge is early diagnosis of gall bladder carcinoma prior to surgical intervention.

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