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Original Article

EARLY GALLBLADDER CARCINOMA: DEMOGRAPHIC CHARACTERISTICS, ASSOCIATED FACTORS AND OUTCOME AFTER SURGERY OF 40 CASES, MANAGED IN BIRDEM AND OTHER TERTIARY CARE CENTERS OF BANGLADESH

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Abstract:

Background: *Gall bladder carcinoma is the most prevalent biliary tract malignancy worldwide. It has has no specific symptoms. Symptoms begin with the advancement of disease and it terminate the life quickly. Thus, early diagnosis and treatment brings good outcome after surgery.*

Method: *This was a cross sectional descriptive study was conducted in admitted patients, in the Department of Hepato-Biliary-Pancreatic surgery and Liver Transplant (HBPS &LT$_{X)}$ in BIRDEM General Hospital , Ibn Sina Specialized hospital and Crescent Gastro Liver and General hospital in Dhaka , over a period of 2 and 1/2 years , from January 2022 to June 2024. 90% data obtained from BIRDEM and 10% from above mentioned hospitals. An estimate sample size was 86. But due to limitation of time ,a total 40 cases had been taken, after considering the inclusion and exclusion criteria . All histopathologically proven early gallbladder carcinoma were included while carcinoma with features of advance malignancy were excluded. Cases were selected irrespective of age and sex , anatomical distribution, clinical presentation, risk factors, histological type and outcome after surgery. Having obtained ethical clearance from the Ethical committee and verbal consent from the the patients, data were collected from the patients, through face to face interview by using a questionnaire devised for the study by researcher himself.*

Result: *A total 40 cases were included in the study. 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 (range: 35-80) years . Male to female predominance 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 7.5%, port site hernia 5%, there was no recurrence and survivability was 97.5% within this 2$^{1/2}$ years of study periods.*

Conclusion: 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..

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 were 40 with female predominance (male 12, female 28). Mean age of the patients was 58.12 ±?7.75 years with majority (70%) being in 56-65 years group. The youngest and the oldest ages were 35 and 80 years respectively (Table I).

Among the associated disease ,cholelithiasis (90%) was the most common , other associated factors were obesity and gall bladder polyp 2 (5%) cases each ;choledochal cyst with anomalous pancreatico-biliary maljunctionand and positive family history 1 (2.5%) case each (Table II).

EGBC mostly diagnosed incidentally (92.5%). Preoperative suspicious was possible only in 7.5% cases(Table III)

Table-I

Distribution of the patients by their demographic characteristics (n=40)

Sex	No of cases	Frequency in age group(Years)					Mean age	Standard
	(n-40)	35-45	46-55	56-65	66-75	>76	(Years)	deviation
Male	12 (30%)	o	o	10 (25%)	1 (2.5%)	1(2.5%)	58.12	7.75
Female	28 (70%)	1 (2.5%)	3 (7.5%)	18 (45%)	5(12.5%)	1(2.5%)		

Table-II

Associated factors for of gall bladder carcinoma

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

Time of diagnosis of gall bladder carcinoma in relation with operation

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

Four type of surgical intervention was done and laparoscopic cholecystectomy (90%) was the most common surgical intervention and others 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 with Roux –en –Y hepatico-jejunostomy (Table IV).

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

Most common histological variant was adeno-carcinoma and it was about 36 (90%) cases , others were mucinous adenocarcinoma 2 (5%) cases ; papillary adenocarcinoma and adeno-squamous cell carcinoma 1 (2.5%) case each (Table V).

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).

Subsequent follow up and radiology showed no further evidence of recurrence. 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).

Table-IV

Types of procedure performed prior to diagnosis of gall bladder carcinoma

Types of procedure	Number 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

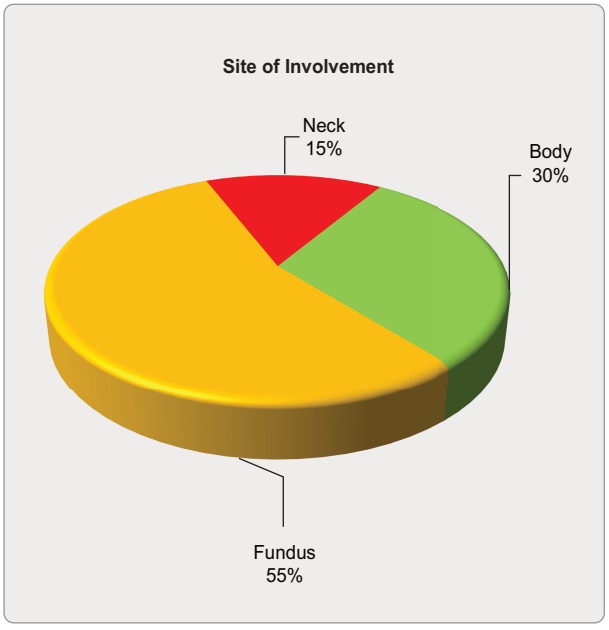

Figure 1: *Involving site of carcinoma in the gallbladder*

Table-V

Histopathological variant of gall bladder carcinoma.

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

Relation of tumor markers CA19-9 and CEA. With gallbladder carcinoma

		CA 19-9	
	No of cases	Level>37 U/mL	Level<37 U/mL
Pre-operative	7	2	5
Pre-operative	39	O	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

Outcome of 40 cases of early gallbladder carcinoma managed surgically.

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 the current 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 a 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] In this study , gall stone (90%) was the most common associated factors others were obesity (5%), gall bladder polyp (5%) ,anomalous pancreatico biliary mal junction (2.5%) and positive hamily 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 pancreaticobiliary maljunction with carcinoma of gallbladder and describe the pathological changes in anomalous junction.[5] Anomalous pancreaticobiliary 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 preoperatively, 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, most (55%) carcinoma originate from the fundus and most common histological variant was adenocarcinoma (90%) 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 and 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 tumour ,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 mentione 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.

Conflict of interest: Nothing to declare.

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