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Original Research Article

Clinical Profile &Etiological Spectrum of Extrahepatic Biliary Obstruction Cases Undergoing ERCP at an Indian Tertiary Care Centre

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Abstract

Background: Extrahepatic biliary obstruction (EHBO) is a common entity encountered in clinical practice. EHBO is a result of obstruction to bile flow anywhere from liver to duodenum.

Material and Methods: We retrospectively analyzed clinical, laboratory and endoscopic data of all the patients with features of EHBO who had undergone ERCP over a period of 1 year.

Results: 206 EHBO patients underwent ERCP. Mean age was 51.5 years. Majority were females (55.8%). However pancreatic head carcinoma (66.7%) and cholangiocarcinoma (100%) preferentially affected males. Benign causes were more common 65.5%. Choledocholithiasis was the most prevalent (56.8%) followed by benign biliary stricture (8.8%). Amongst malignant aetiologies gall bladder carcinoma (15.5%) was most common. Most of the patients presented with pain abdomen (58.2%). Mean bilirubin, raised alkaline phosphatase and renal dysfunction were more common in malignant cases though not statistically significant. However, anaemia (p=0.037) and deranged coagulation profile (p=0.041) was statistically significantly higher among malignant cases. Thrombocytopenia was statistically significantly higher among benign cases (p=0.044). Amongst choledocholithiasis 86.3% individuals had complete biliary clearance, while 8.5% underwent lithotripsy. Bismuth type 1, 2 & 3 benign biliary strictures were found in 72.2%, 16.6%, and 11.2%, respectively. In 83.3% of such patients biliary stenting was successful. Those with malignant strictures, 67.3% had block below hilum, 27.6% had hilar block, 5.1% had complex anatomy of block. Adequate endoscopic biliary drainage was achieved in 86.2%, while 13.7 % required percutaneous transhepatic biliary drainage after the failed ERCP. Self-expanding metallic stent was inserted in 11 patients. Overall, periampullary diverticula and needle knife were present in 5 and 18 cases respectively.

Conclusions: Contrary to previous Indian studies, benign causes were more common causes of EHBO undergoing ERCP than malignancy. Common benign and malignant aetiologies were choledocholithiasis and gall bladder carcinoma respectively.

Introduction

Extrahepatic biliary obstruction (EHBO) is the interruption of bile flow from the liver to the duodenum at extrahepatic biliary site. This obstruction may be intrinsic or as a result of external compression from a number of diseases. EHBO may result from benign or malignant diseases.

Young patients are frequently affected by benign causes such as choledocholithiasis, iatrogenic or sclerosing benign biliary strictures, and parasite infections such as ascaris, liver flukes, and hydatid cysts. Malignant aetiologies include tumours of the second part of the duodenum, ampulla of vater, head of pancreas & gallbladder carcinoma [1]. The most common causes of the malignant and benign aetiologies are gallbladder cancer (GBC) and common bile duct stone (CBD) respectively[2].

Most commonly patients with biliary tract obstruction present with either abdominal pain or jaundice. Other clinical features may include pruritus, fever, weight loss, abdominal lump and cholangitis. Tenderness is a commonest sign although malignant causes of EHBO are frequently associated with a painless progressive jaundice

with or without abdominal mass and weight loss [3].

EHBO cases are associated with deranged liver function test (LFT). Usually total, direct serum bilirubin and alkaline phosphatase levels are raised. Abdominal ultrasound is useful tool with the sensitivity of 94% and specificity of 96% [4].Although axial CT has role in obstructive biliary disease, it is less effective in defining the entire biliary anatomy. MRCP is investigation of choice for better delineation of biliary anatomy. It is non invasive technique with no radiation hazard. The sensitivity is nearly 90% and specificity of 94% in biliary mapping.

Direct cholangiography, including percutaneous transhepatic cholangiography (PTC) and endoscopic retrograde cholangio pancreatography ERCP, is still the gold standard for determining the presence and severity of biliary blockage [4]. ERCP is a gold standard procedure for evaluation of biliary tract lesions because of its high diagnostic accuracy. Additionally it offers the therapeutic advantage making it widely used in investigation for pancreaticobiliary diseases. Limited information is available from India regarding the demographics, clinical, laboratory, and endoscopic characteristics of patients with extrahepatic biliary obstruction (EHBO) who undergo ERCP. With this context, we carried out this study over a year and gathered data from indoor patient files, the hospital information system (HIS), and endoscopy software (Cutescopy Pro).

Material and Methods

We retrospectively analyzed the hospital records of all patients who had undergone ERCP in the department of Gastroenterology, Mahatma Gandhi Medical College & Hospital, Jaipur, overa period of 1 year from January 2022 to December 2022.

Clinical and laboratory data of all the patients with features of EHBO were recorded. All subjects underwent blood investigations and imaging. The diagnosis of EHBO was further confirmed by fine needle aspiration cytology (FNAC), brush cytology or post surgical histopathology.

Blood investigations included complete hemogram (CBC), liver and renal function tests (LFTs& RFTs), random blood sugar, and coagulation profile (PT/INR). Imaging included ultrasonography (USG) or contrast enhanced computerized tomography [CECT] or magnetic resonance imaging (MRI)/ magnetic resonance cholangio pancreatography (MRCP).

ERCP was performed in the patients who met the following criteria. ERCP was done using Pentax scope under propofol sedation in prone or left lateral position [6].

1. Patients with clinical, biochemical or imaging data suggestive of biliary tract disease.
2. Choledocholithiasis on imaging
3. Sphincter of Oddi dysfunction (SOD) according to modified Milwaukee criteria
4. Stent placement across strictures and postoperative bile leak

Benign biliary stricture (BBS) was diagnosed on the basis of the history, serum indicators, imaging and brush cytology results [7, 8].On ERCP, benign biliary strictures had regular, symmetric, and short segment narrowing [9]. The biliary strictures were classified as 'Indeterminate stricture' when trans-abdominal imaging and ERCP with conventional brush cytology were nondiagnostic [10,11]. While malignant stricture was characterised with mass lesion along with elevated serum CA 19-9, carcinoembryonic antigen (CEA) and on ERCP were typically irregular, asymmetric with long segment constriction [12,13].

Bismuth classification was used to classify benign and malignant strictures. Benign strictures were classified as follows: Type 1- Low common hepatic duct (CHD) stricture (>2 cm distal to hilum), Type 2- Proximal CHD stricture (<2 cm distal to hilum), Type 3- Hilar involvement upto proximal extent of CHD, but confluence was preserved, Type 4- confluence involved, no communication between left and right ducts, Type 5- Type 1, 2 or 3 plus stricture of an isolated (aberrant) right duct. (Figure 1).

Malignant stricture classification included: Type 1- tumour distal to hepatic confluence, Type 2 – tumour involving hepatic confluence but preserved left and right duct communication, Type 3- tumour involving common hepatic duct (CHD) with right and left hepatic duct, Type 4- multicentric with right and left hepatic duct involvement.(Figure 2)

SPSS software version 24.0 (SPSS, Chicago, IL, USA), was used to conduct the statistical analysis. Descriptive statistics, such as mean and standard deviation was used for normally distributed numerical data.

Median and interquartile range were used for skewed numerical variables. Counts and percentages for categorical variables were computed. Numerical variables were compared by Student's independent samples t test, if normally distributed, or by Mann-Whitney U test, if otherwise.

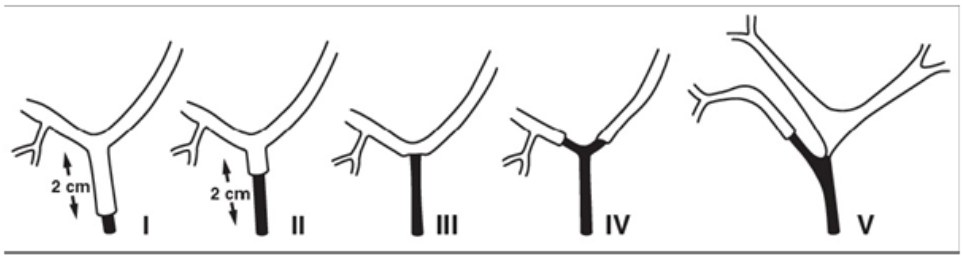

Figure 1: Bismuth classification of benign stricture

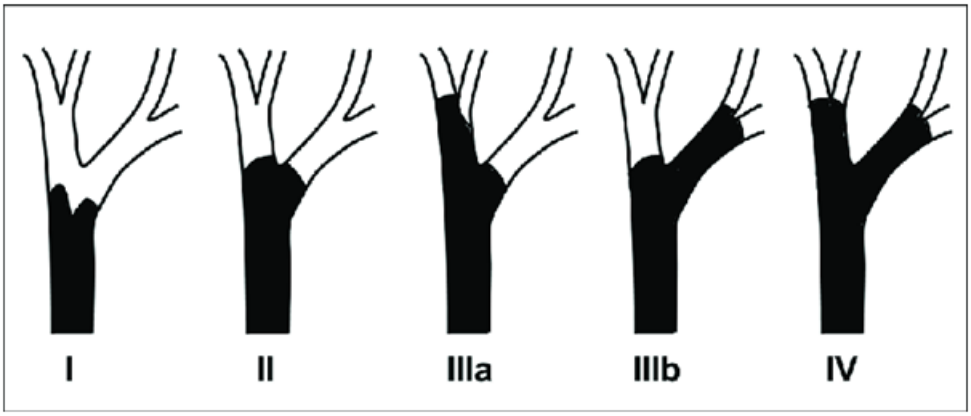

Figure 2: Bismuth classification of malignant stricture

Results

206 patients underwent ERCP during the study period of 1 year. The mean age of patients undergoing ERCP was 51.5(15.1) year. Most of them were females (n= 115, 55.8%). Choledocholithiasis (males- 40.2%, females- 59.8%), gall bladder carcinoma (males- 31.2%, females- 68.8%) and periampullary carcinoma (males- 36.3%, females-63.7%) were seen predominantly in females. However pancreatic head carcinoma (66.7%) and cholangiocarcinoma (100%) preferentially affected males. (Table 1).

Benign causes were seen in 65.5% of all cases, which included choledocholithiasis as the most prevalent cause (n=117, 56.8%) followed by benign biliary stricture in 18 (8.8%). Malignant aetiologies included gall bladder carcinoma (GBC) (n=32, 15.5%), cholangiocarcinoma in 6 (2.9%) patients (hilar cholangiocarcinoma in 4, and distal cholangiocarcinoma in 2 patients), periampullary carcinoma in 11 (5.3%) patients and pancreatic head carcinoma in 9 (4.3%) patients. Other causes like bile leak (n=8), choledochal cyst (n= 5) were seen in 13 (6.3%) patients. (Table 1).

Most of the patients presented clinically with pain abdomen (58.2%), followed by jaundice seen in 57.7%, cholangitis in 27.6%, pruritus and weight loss in 18.9 %. Fever was present in 14.5% of all the patients. Pain, jaundice, fever, pruritus, and cholangitis were present in 85 (52.7%), 54 (46.1%), 19 (16.2%), 13 (11.1%), and 30 (25.6%) respectively, in those with CBD stricture. In malignant strictures pain, jaundice, fever, pruritus and cholangitis were present in 23 (39.6%), 46 (79.3%), 7 (12%), 18 (31%) and 15 (25.8%) cases respectively. The majority of patients with malignant stricture (n=33, 56.8%) had weight loss. Pain, jaundice, fever, pruritus, and cholangitis were present in 8 (44.4%), 12 (66.7%), 2, 5 (27.8%), and 7 (12%) respectively in patients with benign and indeterminate strictures. (Table 2).

Laboratory investigations revealed 133(64.5%) cases were anaemic with haemoglobin<12 g/dl. 49 (23.7%) cases had leucocytosis (total leucocyte counts >12000), 17 (8.3%) cases had thrombocytopenia, 46 (20.3%) cases had abnormal coagulation profile, 8 (3.8%) cases had deranged RFTs and 118 (57.3%) cases had raised alkaline phosphatase.

Anaemia was statistically significantly higher in malignant cases (79.3% vs 58%) as compared to benign causes (p=0.037). Alkaline phosphatase was also raised in malignant cases (62% vs 55 %) in benign causes but the results were not statistically significant (p=0.07).

Thrombocytopenia (16.7% vs 6.9%; p= 0.044) was significantly higher in malignant cases while deranged coagulation profile (INR>1.2) (34.5% vs 16.6%; p=0.041) was statistically significantly higher in malignant cases. Renal dysfunction was seen in 12% (n=7) malignant cases compared to 5.5%(n=1) benign stricture. Mean bilirubin (11.5 mg/dl ± 3.5 versus 4.6 mg/dl ± 2.1; p = 0.75)and direct bilirubin (5.9 ± 1.2 versus 3.1 ± 1.1; p= 0.69) were higher in malignant as compared to benign stricture. (Table 3).

75% of the patients with choledocholithiasis also had cholelithiasis. In 59% of patients, multiple common bile duct calculi (>2) were found. Failed cannulation was seen in 9 (7.7%) patients. Lithotripsy was used in 10 (8.5%) of cases. 101 (86.3%) individuals had complete biliary clearance. Failure of biliary clearance with balloon sweeping was attributed to large stones >15 mm in size (n=11/117, 9.4%), biliary stricture (n=2/117, 1.7%), impacted stones in (n=2/117, 1.7%), and altered anatomy in (n=1/117, 0.85%) patients. Cases with failed biliary drainage with a stent in situ underwent surgical intervention. (Table 4).

Bismuth type 1, 2 & 3 benign biliary strictures were found in 72.2%, 16.6%, and 11.2%, respectively. In 83.3% of patients biliary stenting was successful. Failure of biliary stenting was due to tight biliary strictures that prevented guidewire passing across the strictures. (Table 5).

Among those with malignant strictures, 39 (67.3%) had block below hilum (Type1), 16 (27.6 %) had hilar block (Type 2), 3(5.1%) case had complex anatomy of block (Type 3). Adequate endoscopic biliary drainage was achieved in 50 (86.2%). However 8 (13.7 %) required percutaneous transhepatic biliary drainage (PTBD) after the failed ERCP. Tight biliary strictures in 6 patients & gastric outlet obstruction in 2 patients were causes of the failure of endoscopic biliary drainage.Self expanding metallic stent (SEMS) was inserted in 11 patients (18.9%)(Table 6).During ERCP, periampullary diverticulae were present in 5 (2.4%) cases and needle knife was used in 18 (8.7%) cases. (Table 7).

Table 1: Aetiological spectrum along with age and sex distribution of EHBO cases undergoing ERCP

Cause of EHBO	Number (%)	AGE (years) Mean (SD)	Gender, n (%)
Choledocholithiasis	117 (56.8%)	50.1 (16.0)	M[#]- 47 (40.2), F[@]- 70 (59.8)
Benign/ Indeterminate Strictures	18 (8.8%)	49.9(17.7)	M- 10 (55.5), F- 08 (44.5)
Malignant strictures	58 (28.1%)	57.3(10.2)	M- 26 (44.8), F- 32 (55.1)
GB carcinoma	32 (15.5%)	56.1(10.7)	M- 10 (31.2), F- 22 (68.8)
PACA*	11(5.3%)	57.3 (7.7)	M- 04 (36.3), F- 07 (63.7)
Pancreatic head carcinoma	09(4.3%)	59.1 (11.6)	M- 06 (66.7), F- 03 (33.3)
Cholangiocarcinoma	06(2.9%)	64.3(8.4)	M- 06 (100), F- 00 (00)
Others	13 (6.3%)	39.8 (4.7)	M- 8 (61.5), F- 5 (38.5)
Total	206 (100%)	51.5 (15.1)	M- 91 (44.1), F- 115 (55.8)

PACA*- Periampullary carcinoma, M[#]- Male, F[@]- Female

Table 2: Clinical presentation of patients with EHBO undergoing ERCP

Symptom	Stones (n = 117)	Benign (n =18)	Malignant (n =58)	Others (n= 13)	Total cases (n= 206)
Jaundice	54 (46.1%)	12 (66.7%)	46 (79.3%)	7 (53.8%)	119 (57.7%)
Pain Abdomen	85 (52.7%)	8 (44.4%)	23 (39.6%)	4 (30.7%)	120 (58.2%)
Pruritus	13 (11.1%)	5 (27.8%)	18 (31.0%)	3 (23.0%)	39 (18.9%)
Cholangitis	30 (25.6%)	7 (38.9%)	15 (25.8%)	5 (38.4%)	57(27.6%)
Weight loss	2 (1.7%)	3(16.7%)	33 (56.8%)	1 (7.7%)	39 (18.9%)
Fever	19 (16.2%)	2 (11.1%)	7 (12.0%)	2 (15.3%)	30 (14.5%)

Table 3: Laboratory investigations of patients with EHBO undergoing ERCP

Laboratory parameter	Stones (n = 117)	Benign stricture (n =18)	Malignant stricture (n =58)	Others (n= 13)	Total cases (n=206)	p value
Anaemia (Haemoglobin< 12 gm/dl)	68 (58%)	13 (72.2%)	46 (79.3%)	6 (46.1%)	133(64.5%)	0.037*
Leucocytosis (TLC >11000 cells/mm^3)	28 (24.0%)	4 (22.2%)	15(25.8%)	2 (15.4%)	49 (23.7%)	0.41
Thrombocytopenia(Platelets <1.5 lac/mm^3)	10 (8.5%)	3(16.7%)	4 (6.9%)	0 (0.0%)	17 (8.3%)	0.044*
Total Bilirubin in mg/dl Mean (SD)	3.5 (1.6)	4.6 (2.1)	11.5 (3.5)	5.3 (1.9)	-	0.75
Direct bilirubin in mg/dl Mean (SD)	1.8 (0.4)	3.1 (1.1)	5.9 (1.2)	2.8 (0.9)	-	0.69
Raised Alkaline phosphatises(U/L)	67 (57.2%)	10 (55.6%)	36 (62.0%)	5(38.4%)	118 (57.3%)	0.07
Total protein (gm/dl)	8.02 (0.65)	7.52 (0.53)	6.80 (0.73)	7.91(0.45)	-	0.13

Albumin (gm/dl)	4.10 (0.35)	4.02 (0.47)	3.78 (0.50)	4.05(0.55)	-	0.46
INR>1.2	17 (14.5%)	3 (16.6%)	20 (34.5%)	2 (15.3%)	46 (20.3%)	0.041*
Deranged RFT (serum Creatinine >1.5mg/dl)	0 (0.0%)	1 (5.5%)	7 (12.0%)	0 (0.0%)	18 (3.8%)	

*: statistically significant, letters with different letter indicate statistically significant difference

Table 4: ERCP findings in EHBO patients (N=117) with choledocholithiasis

No of calculi (N=117)	**Single - 48 (41.0%)** **Multiple - 69 (59.0%)**
Cholelithiasis	88/117 (75.2%)
Stone size	<1cm: 92 (78.6%) >1cm: 25 (21.4%)
Cannulation achieved	Yes = 108 (92.3%) No† = 09 (7.7%)
Use of lithotripsy 30 (10.45%)	Yes = 10 (8.5%) No = 107 (91.5%)
Clearance of stones	Partial: 11 (9.4%) Complete: 101 (86.3%) No clearance: 05 (4.3%)
Reason for failure of stone extraction by balloon	Large stones (>15 mm in 11/117 = 9.4%) Associated biliary stricture in 2/117 (1.7%) Impacted stones in 2/117 (1.7%) Altered anatomy in 1/117 (0.85%)

Table 5: ERCP findings in patients with benign biliary stricture (N=18) undergoing ERCP

Type of stricture (Bismuth classification)	Type 1 = 13 (72.2%) Type 2 = 3 (16.6%) Type 3 = 2 (11.2%)
Successful biliary stenting	Yes = 15 (83.3%) No = 3 (16.6%)

Table 6: ERCP findings in patients with malignant stricture (N=58) undergoing ERCP

Type of stricture	Type 1 = 39 (67.3%) Type 2 = 16 (27.6%) Type 3 = 3 (5.1%)
Adequate biliary drainage achieved	50 (86.2%)
Self-expanding metallic stent (SEMS)	11 (18.9%)
Percutaneous transhepatic biliary drainage (PTBD)	8 (13.7%)
Reason for failure of endoscopic biliary drainage (N=8)	Tight stricture = 6 (75%) Gastric outlet obstruction = 2 (25%)

Table 7: ERCP findings of EHBO cases

Periampullary diverticulae	05 (2.4%)
Use of needle knife	18 (8.7%)

Discussion

Our study focussed on the spectrum of clinical features, and the usefulness of ERCP as a therapeutic or palliative modality in EHBO cases. Similar to the previous study conducted in our institute by Upadhyay et al. we found benign causes were more common compared to malignant aetiologies of EHBO. Choledocholithiasis (56.8%) and carcinoma of gall bladder (15.5%) were the most common benign and malignant causes of EHBO respectively. [14].

In contrast to our study, data from AIIMS Delhi (75.3% vs. 24.7%), Madhuet al (63.3% and 36.6%) and Verma et al (62.7% vs 37.2%)found that the prevalence of malignant causes were higher than benign. Overall, similar to our study, the most frequent benign and malignant aetiologies were choledocholithiasis (12.4%) and GBC (28.7%) respectively [15, 16, 17]. However in study by Selvasekaran et al periampullary carcinoma (34%) was the commonest malignancy [18]. These contrasting findings could be explained as, our research was an analysis of laboratory profile of EHBO cases undergoing ERCP rather than population based study that recorded only clinical profile of patients that presented as EHBO.

Similar to studies by Upadhyay et al(57.7%) and Madhu et al(65.6%), we found that EHBO predominantly affected females (55.8%)[14,16].

Common causes of benign and malignant aetiologies such as choledocholithiasis (F=59.8%), gall bladder carcinoma (F= 68.8%) respectively were frequently seen in females comparable to global data. However pancreatic head carcinoma (66.7%) and cholangiocarcinoma (100%) preferentially affected males like other studies[19].

Jaundice (57.7%) and abdominal pain (58.2%), were observed in 66-88% and 51 to 66% of cases, respectively. Patients with malignancy usually presented with jaundice, mean bilirubin of 11.5 mg/dl± 3.5 vs 4.6 mg/dl ± 2.1 and direct bilirubin of 5.9 ± 1.2 versus 3.1 ± 1.1 md/dl [14,17].

Those with malignant strictures had incidence of abnormal coagulation profile and anaemia. The mean bilirubin level in choledocholithiasis of 3.5 mg/dl was consistent with previous studies.

However, the mean bilirubin and ALP levels were greater in malignant EHBO cases than benign. Therefore, in patients with obstructive jaundice, greater bilirubin levels may be a sign of malignant disease[20]. Similar to our previous study by Upadhyay et al, in cases of choledocholithiasis, single calculus was found in 41%. We could achieve complete biliary clearance via ERCP in 86.3% cases[14].

Failure of biliary clearance via balloon were the presence of large (≥15 mm) or impacted stones, tight biliary stricture, and altered anatomy. In 66.7% of cases of benign biliary stricture the biliary stenting for was successful. The predominant reason for failed biliary stenting was tight biliary stricture.

Majority of the patients had block below hilum in cases of malignant strictures.

This could be because with ERCP it was difficult to get views for block at hilum and complex blocks due to complex anatomy. In 75.8 % case of GBC successful endoscopic biliary drainage was accomplished, while the others needed percutaneous transhepatic biliary drainage (PTBD). The major reason for requirement of PTBD were tight biliary stricture and gastro-duodenal infiltration.

Conclusion

Our study highlights that choledocholithiasis were the predominant cause of extra-hepatic biliary obstruction and the endoscopic therapy is reassuring in such cases. While, gallbladder carcinoma was commonest aetiology of malignancy in EHBO cases. Such EHBO cases usually present with end stage disease and endoscopic palliation is at the most can be offered. Endoscopic palliative therapy has promising results in most of these patients while PTBD remains a good alternative.

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