Clinico-demographic Profile and Diagnostic Modalities in Patients with Pancreatobiliary Malignancy Undergoing Endoscopic Retrograde Cholangiopancreatography in a Tertiary Care Center of Nepal

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ABSTRACT

Background

Pancreatobiliary malignancies (PBM) are often diagnosed at an advanced stage, leading to poor outcomes. Studies on the clinical profile and diagnostic efficacy in research limited settings like Nepal are scarce.

Objective

To describe the clinico-demographic profile characteristic and evaluate the diagnostic yield of endoscopic techniques in-patient with suspected pancreatobiliary malignancy undergoing Endoscopic Retrograde Cholangiopancreatography.

Method

A retrospective, cross-sectional study was conducted at the endoscopy unit of a tertiary care center of Nepal from January 2017 to January 2023. We included 597 Patients over 18 years of age with suspected pancreatobiliary malignancy who underwent endoscopic retrograde cholangiopancreatography. Data on demographics, clinical presentation and diagnostic results (brush cytology and intraductal biopsy) were analyzed using descriptive statistics.

Result

Among 597 patients, the majority of patients (70.1%, n=419) were aged 50 years or older, with the highest proportion found in the 60-69 year age group. Significant cases were from the hilly region (52.9%) and Brahmin/Chhetri ethnic group (35.51%). In this study 52.4% were male and the most common presenting symptoms were obstructive jaundice (42.4%), abdominal pain (37.7%), and pruritus (22.8%). Endoscopic retrograde cholangiopancreatography was technically successful for biliary drainage in 93.6% (559/597), primarily using plastic stent (77.4%). Endoscopic retrograde cholangiopancreatography guided tissue diagnosis was done in 57.1% of patients (n=341) to establish histological diagnosis. The most frequent Endoscopic retrograde cholangiopancreatography finding was a distal common bile duct stricture (52.8%).

Conclusion

The diagnostic yield of Endoscopic retrograde cholangiopancreatography -guided tissue sampling remains suboptimal with biopsy proving superior to cytology. In a resource-constrained setting like Nepal, while considering the cost-effective and most sensitive diagnostic tool for pancreatobiliary malignancy, the preferred sequence for diagnostic tools is sonography, followed by CT scan for initial triage, and then Endoscopic retrograde cholangiopancreatography with brush and/or biopsy with drainage.

KEY WORDS

Bile duct, Cholangiocarcinoma, Endoscopic retrograde cholangiopancreatography, Nepal, Pancreatic neoplasm

INTRODUCTION

Pancreatobiliary malignancy (PBM) is a group of cancers affecting the pancreas and the biliary tract which includes intrahepatic and extrahepatic bile ducts and gallbladder.[1] PBM is often diagnosed late with fatal outcomes so early diagnosis and treatment are vital to increase the survival rate of patients.[2] Pancreatic cancer is currently the 3rd leading cause of cancer-related deaths in the United States. Pancreatic ductal carcinoma constitutes approximately 90% of all pancreatic cancer.[3] Worldwide pancreatic malignancy is the seventh leading cause of cancer-related death.[4]

Cholangiocarcinoma (CCA) or bile duct cancer is an epithelial cell malignancy of the biliary tree that arises from varying locations.[5] Extrahepatic is the most common and most treatable form of cholangiocarcinoma.[6-8] CCA is regarded as the second most frequent type of primary liver cancer which is diagnosed in the late decades of life with fatal outcomes.[9] Accounting for about 2% of all malignancies, CCA is considered a rare malignancy.[10] The Incidence of CCA has been increasing in Western countries during the last decades and increasing tremendously in Asian countries as well.[11-13]

For biliary obstruction caused by pancreatobiliary neoplasms, Endoscopic Retrograde Cholangiopancreatography (ERCP) with the placement of biliary plastic or metal stents is frequently utilized as palliative therapy to improve and maintain the quality of life in patients with advanced disease.[2] In this research, we studied the clinico-demographic profile along with the diagnostic methods in the patients with suspected PBM undergoing ERCP at a tertiary care center in Nepal.

METHODS

A descriptive cross-sectional study was conducted at the endoscopy unit of the Internal Medicine department of a tertiary care center from January 2017 to January 2023. Ethical approval was obtained from the respective Institutional Review Committee (IRC approval number: 39/23).

Patients over 18 years of age with suspected PBM with complete medical records who underwent ERCP were included in our study. Those with incomplete hospital records were excluded from the study. The study included those with confirmed pancreatobiliary malignancies, diagnosed through histopathology from ERCP, or Endoscopic Ultrasound (EUS), or Computerized tomography (CT) guided biopsy, and who underwent ERCP. Additionally, the study also included those with strong suspicions of malignancy confirmed by clinical, CT scan and EUS findings, and who also underwent ERCP. The choice of stent type (plastic and self-expandable metallic stent - SEMS) was determined for each patient based on the indication and technical aspects, following counselling. The study excluded those with suspected intrahepatic cholangiocarcinoma, who underwent percutaneous transhepatic biliary drainage. This study defined technical successes as the stents positioned above the hilar stricture, ensuring drainage of at least the hepatic lobe, observing main dilation on prior imaging, and visualizing segments filled with contrast during ERCP.

Total population sampling was performed from the medical records of patients fulfilling the inclusion criteria. All the eligible cases that were listed in the medical record of Dhulikhel Hospital from January 2017 to January 2023 were obtained manually. The tally considered patients undergoing multiple ERCP procedures as a single case. A sample of 597 patients was obtained. Self-structured proforma was used as a research tool for data collection based on a literature review. The patient's information was obtained from hospital records from the outpatient and inpatient department of Dhulikhel Hospital. Data regarding demography, clinical features, laboratory findings, investigations and complications were recorded in the proforma.

Data was collected and cleaned in Statistical Package for Social Sciences (SPSS) version 25.0 (IBM, Armonk, NY, USA) and the collected data was rechecked and validated before analysis for errors. Analysis was done using the same SPSS tool. The mean and standard deviation for continuous data and frequency and proportion for categorical data were calculated.

RESULTS

A total sample population of 597 patients was obtained. Among them, 313 (52.4%) were males while 284 (47.6%) were females. The sociodemographic characteristics of patients are detailed in table 1. Most of the patients included in our study were of age 60 to 70 years (24.3%) followed by 70 to 80 years (21.9%). Patients less than 30 years were the lowest (2.4%). Most of the participants were from the hilly region, 52.9%, followed by terai region (40.9%) and Himalayan region (6.2%). Brahmin/Chhetri ethnic groups were the most prevalent (35.5%) followed by Mongolian (26.8%), Newar (18.8%), Madhesi (13.9%) and Dalit (5.1%).

The clinical profile of the study participants has been given in the table below (Table 2). Most of the patients (19.1%) presented with cholangitis. 15.8% of patients suffered from choledocholithiasis whereas cholecystitis was found in 1.17% of the patients. They had chief complaints of Obstructive jaundice (42.4%), abdominal pain (37.7%), itching (22.8%), vomiting (17.6%), anorexia (15.8%) and weight loss (11.2%).

Findings from ERCP are given in the table below (Fig. 1). Among the neoplasms, 52.8% were distal cholangiocarcinoma, followed by 26.5% in hilar region, 12.1% in ampullary and peri-ampullary regions, 5.2% in pancreas and 3.5% in gall bladder.

Table 1. Sociodemographic characteristics of the patients undergoing ERCP (n=597)

Parameter	Study Participants (n)	Percentage (%)
Age group in years		
Less than 30	14	2.35
30-40	49	8.21
40-50	81	13.57
50-60	143	23.95
60-70	145	24.29
70-80	131	21.94
80-90	34	5.70
Address		
Hilly region	316	52.93
Himalayan Region	37	6.20
Terai region	244	40.87
Ethnicity		
Brahmin/Chhetri	212	35.51
Newar	112	18.76
Mongolian	160	26.80
Dalit	30	5.03
Madhesi	83	13.90

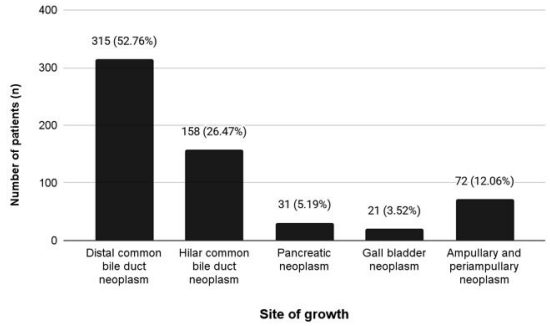

Figure 1. Endoscopic Retrograde Cholangiopancreatography findings (n=597)

An almost equal number of participants had hyperbilirubinemia and extreme hyperbilirubinemia (total serum bilirubin > 12 mg/dL) with 46.4% vs 46.9% respectively. Only 6.7% had normal bilirubin levels in their blood as shown in table below (Table 3). On measuring the liver enzymes of study participants, Alkaline Phosphatase (ALP) was deranged in 561 (93.9%), Gamma-glutamyl Transferase (GGT) was deranged in 555 (93%) indicating biliary pathology. However, Aspartate aminotransferase (AST) and Alanine Aminotransferase (ALT) were also deranged in 508 (85.1%) and 398 (66.7%) respectively signifying hepatocellular extension of the disease.

All patients underwent biliary drainage with ERCP with stent placement and technical success in stent placement was achieved in 559 (93.6%). Among them, in 462 patients, a plastic stent was kept while in the rest 135 patients, a metal stent was kept. The success rate of plastic stents was significantly higher than metal stents, $p < 0.01$. With the help

Table 2. Clinical profile of the patients (n=597)

Associated conditions	Study Participants (n)	Percentage (%)
Cholangitis	114	19.10
Cholecystitis	7	1.17
Choledocholithiasis	94	15.75
Symptoms		
Obstructive jaundice	253	42.38
Abdominal pain	225	37.69
Itching	136	22.78
Vomiting	105	17.59
Anorexia	94	15.75
Weight loss	67	11.22

Table 3. Bilirubin level in patients (n=597)

Grading	Study participants (n)	Percentage (%)
Within range	40	6.7
Hyperbilirubinemia	277	46.4
Extreme hyperbilirubinemia		
Grade 1 (12-14.9 mg/dL)	54	9
Grade 2 (15-19.9 mg/dL)	87	14.5
Grade 3 (20-29.9 mg/dL)	91	15.3
Grade 4 (≥ 30 mg/dL)	48	8.1

of ERCP, about 341 (57.1%) patients underwent different modalities for histological diagnosis of pancreatobiliary malignancy.

Among 597 study participants, Brush cytology were performed in 87 (14.6%) patients while the intraductal biopsy was done in 233 (39.0%) patients. The positive results of malignancy was found in 35 (5.86%) patients who underwent brush cytology and 142 (23.78%) patients who underwent intraductal biopsy. EUS was performed in 16 (2.68%) patients and Fine Needle Aspiration Cytology (FNAC) was positive in 7 (1.17%) patients. Furthermore, 5 (0.83%) patients underwent both intraductal biopsy and brush cytology, among which malignancy was confirmed in all patients (100%). 269 (45.05%) patients among the study participants had a probable high suspicion of malignancy but the tissue diagnosis was not attempted as the patients were unstable and needed only palliative care or they presented with cholangitis where immediate pus drainage was necessary. 24 (4.02%) of the total study participants had a negative tissue diagnosis despite high clinical suspicion.

DISCUSSIONS

Both pancreatic cancer and CCA are more prevalent in males with increasing incidence with age and both are found to affect people in their fifth to seventh decade of life.[14] Our study showed males were more commonly affected and more than 75% of the cases aged greater than

50 years with one quarter of the patients being younger than 50 years, 52.93% of cases were from the hilly region of Nepal followed by Terai (40.87%) and Himalayan (6.2%). This study did not demonstrate statistically significant association between age groups and either address categories (p=0.254) or ethnicity (p=0.106).

Neoplasms of both pancreatic and biliary origin can have a similar presentation as most patients can present with abdominal pain, nausea, jaundice, vomiting, and/or weight loss.[15] In our study, the PBM patients presented with obstructive jaundice and abdominal pain followed by itching, vomiting, anorexia, and weight loss.

Considering the biochemical tests, an elevation in ALP and bilirubin more than ALT and AST would characterize cholestatic pathology.[16] A patient suffering from a chronic mechanical obstruction of the biliary tract will have elevated "cholestatic" enzymes, ALP and GGT, and mildly elevated AST and ALT.[17] In our study, majority of the patients (93%) had shown reports of elevated ALP and GGT relating to the obstructive pathology of biliary tract.

In suspected pancreatobiliary malignancy, abdominal imaging is warranted which includes CT scan, Magnetic Resonance Imaging (MRI), Magnetic resonance cholangiopancreatography (MRCP) and/or EUS before invasive procedure e.g. ERCP.[15] These investigations are employed for the diagnosis and staging of pancreatobiliary malignancy. Histopathological diagnosis of pancreatobiliary malignancy can be done with brush cytology and intraductal biopsy or EUS guided FNAC/Fine Needle Aspiration Biopsy (FNAB). Studies have shown the sensitivity and specificity of brush cytology up to 87% and 90% respectively and that of intraductal biopsy as 48.1% and 99.2% respectively.[18,19] Contrary to this, biopsy had more success rates than brush cytology in our study among 325 (54.4%) patients.

Biliary and pancreatic duct strictures, which can be caused by pancreatobiliary malignancy, can be evaluated with brush cytology.[20] Intraductal biopsy is the only method to obtain a true tissue specimen for histological diagnosis, however, it requires technical expertise and sphincterotomy for access.[21] Also, studies have shown that intraductal biopsy and brush cytology are comparable although both have low sensitivity in the detection of PBM.[22] In our study tissue sampling was also done with the help of EUS. EUS was significantly more sensitive for the detection of pancreatobiliary malignancy as compared to CT, angiography, and ultrasound.[23] In comparison to ERCP, EUS-based tissue sampling was also found to be more sensitive and accurate in the case of intrinsic biliary stricture in the distal bile duct.[24] In our setting, 44% of the fine needle probes were positive which suggests EUS can be considered better for the detection of malignancy but not for confirmation in comparison to biopsy (61% positive) during ERCP.

Technical success of ERCP has been reported to be between 90-100%.[25,26] In our study, biliary drainage using ERCP with stent placement was the primary treatment modality and technical success was present in 94.75% of cases. Based on a study by Park et al. symptomatic improvement was present in more than 90% of patients undergoing ERCP stent placement for malignant biliary obstruction.[25] However, in our study, due to a lack of data on follow-up, we couldn't assess the impact of stent placement. Among 559 patients with successful cannulation, in 462 (82.65%) patients, a plastic stent was kept while in the rest 135 (24.15%) patients, a SEMS was kept. SEMS are more expensive but have longer patency with longer patient survival and lower reintervention rate as compared to plastic stents.[27] However, as most of our patients couldn't afford SEMS, they opted for plastic stents.

For the evaluation of the PBM, ERCP is a sensitive tool but recommended as a therapeutic tool in treatment due to risk of post-ERCP pancreatitis.[15] In a country like Nepal with limited financial resources, the order of diagnostic tool could be Sonography followed by CT-scan then ERCP with brush and/or biopsy, as EUS may not be available in most of the hospital. As ERCP can be used for both diagnosis and intervention of PBM in the same setting in our study, it is significantly preferred. Recent guidelines recommend ERCP-guided biliary sampling for an unresectable mass when biliary decompression is also required, whereas EUS-guided fine needle biopsy is preferred for surgically resectable masses or when ERCP tissue collection has failed.[28] As most pancreatobiliary malignancies present late as an unresectable mass in our setting, ERCP-guided biliary decompression is the preferred modality of drainage.

The study was limited to clinical settings and relied completely on the medical records and imaging findings which might have underrepresented and underreported the findings of the study. Further studies adapting strong study design and approaches can further strengthen the findings of the study. Due to a lack of data on follow-up, the effect of biliary drainage for clinical relief couldn't be evaluated; hence future studies may consider adding follow up data.

CONCLUSION

This study provides crucial insights into the demographic and clinical profile of pancreatobiliary malignancy (PBM) in Nepal, revealing higher disease burden in hilly regions and among the Brahmin/Chhetri group with obstructive jaundice, abdominal pain and weight loss as hallmark presentations. For clinicians, the key takeaway is the validation of cost effective, staged diagnostic algorithms for resource limited setting starting from sonography followed by CT scan and ERCP which is emphasized as for both diagnosis (via brush/biopsy) and immediate biliary drainage with high success. This research is first of its kind in Nepal and can serve as a critical reference point for conducting further researches.

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