

Etiology of Common Bile Duct Strictures in Patients Presenting With Obstructive Jaundice at a Tertiary Care Military Hospital

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ABSTRACT

Objective: To assess common bile duct stricture etiology and its association with patient age, gender, and stricture location in patients presenting with obstructive jaundice.

Study Design: Cross-sectional analytical study

Place and Duration of Study: Pak Emirates Military Hospital, Rawalpindi, Pakistan, from Feb 24 to Jan 25.

Methodology: Patients with obstructive jaundice (n=96) and confirmed CBD strictures were included. Strictures were classified by location (proximal/mid/distal) and etiology (malignant/benign) using ultrasonography, CT, and ERCP. Inter-rater reliability was confirmed ($\kappa=0.85$). Data were analyzed using SPSS v27, and the Pearson chi-square test was used for associations ($p<0.05$).

Results: The mean age of patients was 55.28 ± 8.96 years, with the majority being male (59.4%). Distal strictures were most prevalent (56.3%), followed by proximal and general strictures (18.8% each), and mid-CBD strictures were the least common (6.3%). Malignancy was the leading cause, and specifically, cholangiocarcinoma was present in 31.3% of 62.6% of malignant cases. There were strong associations between stricture location and etiology ($p<0.001$), and age and stricture etiology ($p<0.001$).

Conclusions: The study found that malignant etiologies dominate CBD strictures, particularly in distal locations and older patients. Hence, early malignancy screening must be done for distal strictures, and age-specific diagnostic approaches must be designed for better health outcomes. Multicenter studies should be done to further validate the findings in diverse populations.

Keywords: Biliary Strictures, Stricture Etiology, Endoscopic Management, Cholangiocarcinoma

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INTRODUCTION

Liver and Biliary tract diseases have a significant contribution to global morbidity, with recent estimates of nearly 2 million deaths (4% of Global deaths) every year across World.¹ Jaundice is the most prevalent presentation of these diseases, characterized by a yellowish discoloration of the skin and mucous membranes. Jaundice is categorized into obstructive jaundice and non-obstructive jaundice. Obstructive jaundice is said to be present when there is hyperbilirubinemia due to an obstruction in the bile flow. It can occur due to obstruction at various anatomical sites, including the common bile duct (CBD), biliary tract, or ampulla of Vater.² Globally, 5-10% of patients with hepatobiliary cases suffer from obstructive jaundice, but the prevalence is higher in

South Asian countries like Pakistan (15-20%).³ Based on location, obstructive jaundice can be classified into intrahepatic and extrahepatic categories. Extrahepatic causes are more prevalent among the two subtypes and include gallstones, CBD strictures, biliary tract neoplasia, cholangitis, and pancreatic pathologies. Among these, CBD strictures present a significant clinical challenge with a 9.6% prevalence in Pakistan.⁴

The etiologies behind CBD strictures range from benign inflammatory conditions to aggressive malignancies⁵. Biliary stricture is a narrowing of the biliary tree caused mainly by malignant etiologies and 15-20% by benign etiologies. The most common malignant ones are adenocarcinoma of the pancreas, cholangiocarcinoma, duodenal carcinoma, ampullary tumors, gallbladder tumors, and metastatic disease⁶. Most of these pathologies present in a sinister manner and appear late in the disease. The standard of care in biliary stricture patients is draining bile and excluding

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malignancy, and the diagnosis may involve invasive and non-invasive modalities. Among these, the non-invasive modalities include Ultrasonography, computed tomography scan (CT), magnetic resonance imaging (MRI), and magnetic resonance cholangiopancreatography (MRCP).⁷ The invasive modalities include Endoscopic Retrograde Cholangiopancreatography (ERCP), Endoscopic Ultrasound Fine Needle Aspiration (EUS-FNAC), and percutaneous transhepatic cholangiography.⁸ ERCP is considered the gold standard modality as it allows for both diagnosis and treatment at the same time.⁹ The unavailability of diagnostic modalities in local settings and diverse etiologies complicate stricture diagnosis, which impacts disease prognosis and survival rates¹⁰.

Despite the clinical significance, in Pakistan most studies focus on gallstones or hepatitis-related liver failure, and limited studies explore the etiologies behind CBD strictures. Due to this gap, there is a lack of region-specific diagnostic and therapeutic guidelines. This descriptive cross-sectional study aimed to determine CBD stricture etiologies in patients who presented at Pak Emirates Military Hospital and to assess the associations of stricture etiologies with stricture location, patient age, and gender. The findings of this study can potentially help in early detection, refine diagnostic approaches, and contribute to better clinical decision-making.

METHODOLOGY

This research followed a cross-sectional analytical study design. After obtaining approval from the Ethical Review Board (reference number ERC/23/24 dated 01 Jan 2024), the study was conducted at Pak Emirates Military Hospital, Rawalpindi, Pakistan, from Feb 24 to Jan 25. An online software called OpenEpi Version 3 was used for the sample size calculation with the following assumptions: Two-sided significance level (1-alpha) = 95, Power (1-beta, % chance of detecting) = 80, Ratio of sample size, Unexposed/Exposed = 1, Odds Ratio = 8.1, and Risk/Prevalence Ratio = 6.11 The initial required sample size was 74 participants, but we included 96 patients who met the inclusion criteria according to non-probability consecutive sampling. The inclusion of more study participants was justified due to the sampling technique, which allowed the inclusion of all eligible patients presenting in the study period.

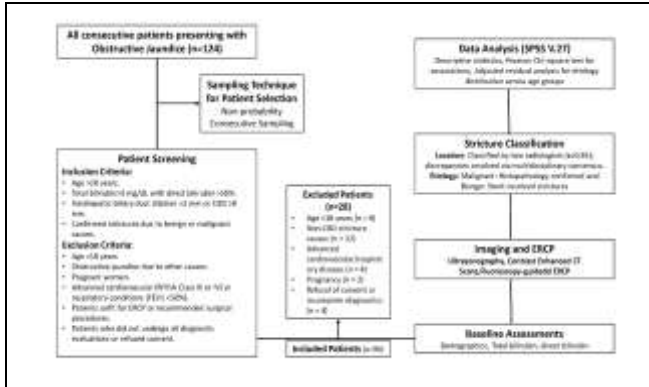
Inclusion Criteria: Patients of both genders who were over 18 years old and had clinical (total bilirubin>3 mg/dL with direct bilirubin>50%) and/or radiological

evidence of obstructive jaundice (intrahepatic biliary duct dilation>2 mm or CBD>8 mm on ultrasonography/CT). After diagnosis, patients who had strictures due to benign or malignant causes, such as cholangiocarcinoma, gallbladder carcinoma, pancreatic malignancy, benign strictures, iatrogenic factors, or post-surgical complications were included.

Exclusion Criteria: Patients aged below 18 years or with obstructive jaundice due to causes other than CBD strictures were excluded. Pregnant women, patients with advanced cardiovascular (NYHA Class III or IV) or respiratory (FEV1 less than 50%) conditions, or patients unfit for ERCP or recommended surgical procedures were excluded. Patients who did not undergo all diagnostic evaluations or refused consent were also excluded.

Data collection included patient demographics, location of the biliary stricture, underlying cause, and subsequent follow-up management. CBD strictures were confirmed through standardized radiological protocols: ultrasonography through Cardio 200 G machine (assessed ductal dilation with common hepatic duct more than 6 mm and CBD more than 8 mm and ruled out choledocholithiasis), contrast-enhanced CT scans (evaluated stricture extent, lymphadenopathy, and metastatic spread), and ERCP (Epik i7010 by Pentax Medical) with fluoroscopy (Siemens 3830259 V5070). The strictures were classified based on location by two independent radiologists with more than 5 years of hepatobiliary experience as: proximal (at or above hepatic duct bifurcation), mid (between cystic duct insertion and bifurcation), distal (near ampulla of Vater), and general (where specific anatomical locations were indeterminate). The discrepancies were resolved by multidisciplinary consensus (radiologist, gastroenterologist, and surgeon). Malignant etiologies were confirmed by histopathology (ERCP-guided biopsy or surgical specimen reviewed by two pathologists), and benign etiologies were defined by stricture resolution after stenting. Malignant strictures included cholangiocarcinoma (primary bile duct cancer), pancreatic or gallbladder cancer (causing external compression or direct invasion), and metastatic cancer (secondary malignancies affecting the bile duct). Moreover, the benign strictures included cholangitis (inflammatory narrowing due to infection), cholecystitis (secondary stricture formation from gallbladder inflammation), and surgical or iatrogenic causes (strictures resulting from previous

bile duct surgeries or interventions). The inter-rater reliability was ensured by the strong agreement of a third blind radiologist who reevaluated 20% of the cases ($\kappa=0.85$). To ensure consistency, PEMH hepatobiliary protocols were followed. During ERCP, stents were placed, pigtail catheters were passed, and biopsy samples were taken as needed.



The data were analyzed using the Statistical Package for the Social Sciences (SPSS, version 27). Descriptive statistics summarized patient demographics and stricture characteristics. Normality was confirmed for patient age (the only quantitative variable) through the Shapiro-Wilk test ($p=0.062$) and was reported as mean and standard deviation. The analysis of other categorical variables (stricture location, etiology, and age groups) relied on frequency distributions, so they were summarized as frequencies and percentages. Associations between categorical variables (stricture etiology, location, age groups) were analyzed using the Pearson Chi-square test ($\alpha=0.05$). Additionally, adjusted residual analysis after the Chi-square test identified specific cells that contributed most to the overall association between stricture etiology and age groups. Adjusted standardized residuals greater than ± 1.96 were considered statistically significant ($p \leq 0.05$). This indicated that the observed frequency in a cell was significantly higher or lower than expected under the null hypothesis.

RESULTS

A total of 96 eligible patients were included in this study. The ages ranged from 38 to 75 years, and the mean age was 55.28 ± 8.96 years. Most of the patients were male 57(59.4%), and females constituted 40.6% ($n=39$) of the cohort. The most prevalent strictures in the study population were distal strictures 54(56.3%). There were an equal number of patients

with proximal 18(18.8%) and general strictures 18(18.8%), while only 6 patients had mid-CBD strictures (6.3%). The etiologies behind these strictures are summarized in Table-I.

Table-I: Frequencies and Percentages of Stricture Etiologies in Patients (n=96)

Stricture Etiology	Frequency (%)
Malignancy	30(31.25%)
Mass with unconfirmed Malignant or Benign Nature	6(6.25%)
Cholangiocarcinoma	30(31.25%)
Benign Mass	6(6.25%)
Cholangitis	6(6.25%)
Cholecystitis	6(6.25%)
Previous Surgery	6(6.25%)
Iatrogenic Cause	6(6.25%)

Malignancy (31.25%) and cholangiocarcinoma (31.25%) were the leading causes. Other etiologies (each 6.25%) included unconfirmed masses, benign masses, cholangitis, cholecystitis, prior surgery, and iatrogenic causes. Moreover, malignancies clustered in proximal ($n=12$) and distal strictures ($n=18$), and cholangiocarcinoma was localized to proximal ($n=6$) and distal ($n=24$). Cholangitis ($n=6$) and iatrogenic causes ($n=6$) were exclusive to general and distal strictures, respectively.

Moreover, as Table-II shows, malignancies clustered in proximal ($n=12$) and distal strictures ($n=18$), and cholangiocarcinoma was localized to proximal ($n=6$) and distal ($n=24$) locations. Cholangitis ($n=6$) and iatrogenic causes ($n=6$) were exclusive to general and distal strictures, respectively.

Table-II: Etiologies Concerning Stricture Types (n=96)

Etiology	Proximal n (%)	Mid n (%)	Distal n (%)	General n (%)
Malignancy	12(66.66)	0(0)	18(33.33)	0(0)
Cholangiocarcinoma	6(33.33)	0(0)	24(44.44)	0(0)
Benign	0(0)	0(0)	0(0)	6(33.33)
Cholecystitis	0(0)	0(0)	6(11.11)	0(0)
Cholangitis	0(0)	0(0)	0(0)	6(33.33)
Mass (unconfirmed)	0(0)	0(0)	6(11.11)	0(0)
Previous Surgery	0(0)	6(100)	0(0)	0(0)
Iatrogenic	0(0)	0(0)	0(0)	6(33.33)

Then we analyzed the associations using the Pearson Chi-square test ($\alpha=0.05$) (Table-III), with adjusted residual analysis (cutoff: ± 1.96) to identify significant cell contributions. While SPSS flagged that 37.5% of cells had expected frequencies < 5 (exceeding the 20% threshold), the test was applied cautiously because it remains conservative for large datasets even with sparse cells. Adjusted residuals were prioritized

for interpreting specific associations like mid-CBD strictures and iatrogenic causes. Statistical associations were analyzed further as shown in Table-III.

A strong association was found between the stricture location and etiology ($\chi^2=202.6, p<0.001$). Moreover, a strong association between age and stricture etiology was also found ($\chi^2 = 134.0, p < 0.001$). Adjusted residual analysis further gave the distribution of etiologies in different age groups, as shown in Table-IV.

Table-III: Association of Stricture Etiology with Location and Age (n=96)

Parameters	Study Groups		p-value
	Group A Malignant (n=60)	Group B Benign (n=36)	
Location n (%)			
Proximal	18 (18.7%)	0 (0%)	<0.001
Mid	0 (%)	6 (6.2%)	
Distal	42 (25%)	12 (21.8%)	
Generalized	0 (0%)	18 (18.7%)	
Age n (%)			
30-40 years	0 (%)	6 (6.2%)	<0.001
40-50 years	0 (%)	18 (18.7%)	
50-60 years	42 (43.75%)	13 (13.54%)	
>60 years	18 (18.7%)	6 (6.2%)	

Table-IV: Distribution of Etiologies across Age Groups (n=96)

Age Group (Years)	Etiology	n	Adjusted Residual	p-value
30-40	Cholangitis	3	4.6	<0.001
	Benign Causes	3	4.6	<0.001
40-50	Iatrogenic Causes	6	5.3	<0.001
	Cholecystitis	6	5.3	<0.001
50-60	Malignancy	24	4.0	<0.001
More than 60	No significant associations	-	-	-

These findings highlighted the increasing prevalence of malignant strictures with advancing age, which contrasts with younger cohorts where benign or indeterminate pathologies prevail.

DISCUSSION

This study found that 62.6% of CBD strictures in our cohort were malignant, with cholangiocarcinoma (31.3%) and other malignancies (31.3%) constituting most cases. A strong association was observed between stricture location and etiology ($p<0.001$). Distal strictures (56.3%) were predominantly linked to malignancies, but mid-CBD strictures were all benign. Age also significantly correlated with etiology ($p<0.001$), and malignancies dominated in older age groups.

The prevalence of CBD strictures is increasing with the increasing prevalence of the etiologies behind

them. Interestingly, male patients predominated (59.4%) in this study cohort, which implies that CBD strictures are more prevalent in the male population. This notion is also reported by Pratyusha *et al.*, in a similar study conducted at a tertiary hospital in Telangana, India. Malignancy accounted for 31.3%, and specifically cholangiocarcinoma accounted for another 31.3% of the causes of CBD strictures. This implies that more than half (62.6%) of the population had strictures due to malignant causes.¹¹ The adjusted residual analysis highlighted that malignancy was significantly prevalent in the 50- 60-year age group also found by Shukla *et al.*¹² However, in the 40- to 50-year age group, iatrogenic causes and cholecystitis caused more strictures. In patients aged more than 60 years, no single etiology dominated over the others. These findings indicate that age-specific diagnostic considerations should also be considered while evaluating biliary strictures.

Other studies also reported malignancies as the most common cause of obstructive jaundice, especially in older populations.¹³ Research has established that age plays a significant role in the risk of developing malignant biliary strictures.¹⁴ This study also found a strong association between age and stricture etiology ($p<0.001$), indicating that age plays a role in stricture development. Tariq *et al.*,¹⁵ reported that cholangiocarcinoma is rising among malignancies that affect hepatobiliary outcomes. This study also reiterates this notion, as 31.3% of the patients had strictures due to cholangiocarcinoma.

Distal strictures prevailed in 56.3% of the total in our study cohort. Dorrell *et al.*, concluded that patients with distal strictures often present with advanced-stage disease, and these strictures are attributed to the encroachment of malignancies.¹⁶ In distal stricture patients, the most predominant causes were cholangiocarcinoma (44.4%) and malignancy (33.3%). Khan *et al.*, also indicated that tumors that affect the pancreatic head and lower CBD are the primary causes of distal obstruction.¹⁷ Moreover, strictures due to benign causes were only 6.3% of the total and were associated with cholangitis or cholecystitis in our study population. Hence, benign conditions existed in our cohort but did not contribute significantly to obstructive jaundice. However, studies like Kordeni *et al.*, reported contradictory findings in different cohorts, some stating benign conditions to be the major cause of obstructive jaundice while others stating malignant conditions to be the major cause.¹⁸

This study found a strong association between the location of strictures and the underlying cause with a chi-square value of 202.6, $p < 0.001$, and a high likelihood ratio (145.5). A study by Simoes *et al.*, also discussed the nature of malignancies affecting distal regions¹⁹. Moreover, in this study, most of the proximal strictures were due to malignancy (66.6%), and interestingly, mid-CBD strictures were exclusively linked to previous surgeries. This highlighted a distinct pattern in post-surgical biliary complications. However, significant variations were observed in the stricture etiologies across age groups.

During ERCP, etiologies were inquired about, and interventions were done or planned based on the status of the strictures. Most of the patients (75%) received stent placements during the procedure. The placement of stents in most of the patients highlights the importance of ERCP as a primary palliative measure in malignant strictures. It has also proven effective in other settings to manage malignancies where subsequent stenting alleviated biliary obstructions.²⁰ For our cohort, subsequent surgery was planned for 7.3% of patients, including Whipple's procedure (4.2%) and other advanced surgeries (3.1%). Hence, surgical options were less explored and less favored for advanced malignancies. ERCP also aided in percutaneous drainage in 6.3% of the patients through pigtail catheter insertion. This aspect highlighted the importance of individualized management strategies in biliary stricture cases.

Future research should employ a multicenter approach and include larger and more diverse patient populations to validate the findings. Furthermore, prospective studies that use techniques like cholangioscopy and tissue sampling may be considered to provide more detailed insights into the pathological processes underlying CBD strictures. Prospective multicenter studies are needed to address the single-center design and small mid-CBD subgroup (6.3%) and refine regional management protocols.

LIMITATION OF THE STUDY

The limited sample size reflected the scarcity of eligible patients during the study period. ERCP assessed benign and malignant etiologies, but tumor markers and significant postoperative assessments were not used. The cross-sectional design precluded causal inference and longitudinal assessment of outcomes and disease progression. As a single-center study, its findings have limited generalizability.

CONCLUSION

Malignant etiologies dominated CBD strictures, including cholangiocarcinoma and pancreatic or gallbladder

malignancies. It was concluded that distal strictures were strongly associated with malignancy, supporting early malignancy screening. Malignancies peaked at 50–60 years, whereas benign or iatrogenic causes were more common in younger patients. Gender was not significantly associated, supporting equitable diagnostic approaches. ERCP was central to diagnosis and management, with stenting relieving obstruction in 75% of cases

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MEW & MNAK: Data acquisition, data analysis, critical review, approval of the final version to be published.

IA & MAHS: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MFS & MSS: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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