

St. Paul Hospital Millennium Medical College
Graduate Study Program

Clinical profile and predictors of in hospital mortality in ascending cholangitis secondary to malignant biliary tract obstruction.

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Addis Ababa, Ethiopia

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Clinical profile, mortality and predictors of mortality in Ascending Cholangitis Secondary to Primary Malignant Biliary Obstruction: A Retrospective Cohort Chart Review Study at St. Paul's Hospital Millennium Medical College (SPHMMC), Addis Ababa, Ethiopia.

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Abstract

Background: Ascending cholangitis secondary to malignant biliary obstruction (MBO) is life threatening condition associated with significant morbidity. Biliary drainage is key component of management. Patients who didn't managed with drainage procedures, Tokyo 18 Severe Cholangitis and advanced cancer stage associated with mortality; however, non-intervention management are common in resource -limited settings, and local evidence regarding its impact on treatment To assess the clinical profile and in-hospital mortality and predictors of mortality in ascending cholangitis secondary to malignant biliary tract obstruction at (SPHMMC). outcomes is limited.

Objective: To assess the clinical profile and in-hospital mortality and predictors of mortality in ascending cholangitis secondary to malignant biliary tract obstruction at (SPHMMC).

Method: Facility based retrospective cohort study design was used in SPHMMC from June - September 2026. A total of 199 participants data was retrieved from Hospital electronic medical records (EMR) and patient charts, Ward, OPD and/OR HMIS records. Structured data extraction form (attached questionnaire) was used & exported to SPSS version 22 data analyzer software for analysis. Binary logistic regression model was used to analyze data. Variables having p-value<0.2 in the bivariable analysis was entered into final model for multivariable analysis. Variables with p<0.05 in multivariable analysis was considered statistically significant with 95% confidence interval. Data was summarized in table.

Result: Of the 199 patients included in the final analysis, 64 died during hospitalization. Failure to achieve biliary drainage was the strongest predictor of death: patients who did not undergo any drainage procedure had more than twelve-fold higher adjusted odds of death compared with those who were drained (AOR 12.85, 95% CI 4.39-37.60). Fever on admission (AOR 2.80, 95% CI 1.01-7.80), ascites (AOR 7.35, 95% CI 1.89-28.59), high-normal creatinine (AOR 10.27, 95% CI 1.42-74.42), thrombocytopenia (AOR 3.76, 95% CI 1.26-11.25), and tachypnea on admission (AOR 3.32, 95% CI 1.15-9.57) were each independently associated with increased odds of death.

Keywords Ascending cholangitis, treatment failure, and malignant biliary tract obstruction.

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Acronyms and Abbreviations

AC -Ascending Cholangitis

ASA -American society of Anesthesiology

CBD -common bile duct

CCI - Charlson Comorbidity Index

CT -Computed Tomography

ECOG Eastern co-operative Oncology Group

EUS -BD -Endoscopic ultrasound biliary drainage

ERCP -Endoscopic retrograde cholangiopancreatography

ICU – Intensive care unit

HPBS -Hepato biliary and Pancreatic Surgery

MBO -malignant biliary obstruction

MRI/MRCP -Magnetic Resonance Imaging

PTBD -Percutaneous transhepatic biliary drainage

SPHMMC -Saint hospital millennium medical college

TG18 -Tokyo guidelines 2018

TB -Total bilirubin

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1.Introduction

1.1 Background

Acute ascending cholangitis (AC) is life-threatening infection of the biliary tree resulting from biliary obstruction and stasis(1–3). In general population the, the estimated annual incidence of acute ascending cholangitis ranges from 5-15 per 100,000 population in United States of America. Among hepatobiliary diseases cholangitis represents 10-30% of emergency admissions .Around 70% of AC caused by common bile duct(CBD) stones ,10-30% secondary to tumors(4,5) . AC secondary to malignant biliary tract obstruction had a significantly higher percentage of severe AC ,higher ICU admission rate ,high likely to be re admitted and longer hospital stay (5–7). Pancreatic cancer tends to be the most common cause of AC secondary to malignant biliary obstruction (MBO). Patients with AC secondary to MBO often unresectable at time presentation and can also be the initial patient presentation.

The Tokyo Guidelines 2018 (TG18) emphasize prompt recognition, severity stratification, and early biliary decompression in addition to antibiotics and supportive care. Early drainage with broad spectrum antibiotics is essential for better outcomes: endoscopic retrograde cholangiography (ERCP) and percutaneous transhepatic biliary drainage (PTBD) are options of drainage but surgical drainage is indicated when mini-invasive modalities are not available. Endoscopic retrograde cholangiopancreatography (ERCP) drainage with stent placement is a primary treatment option for patients with ascending cholangitis secondary to malignant biliary tract obstruction relieve symptoms and provide the opportunity for definitive surgery and chemotherapy(8–10). In addition to the higher technical success rate of 90%–95%, ERCP has reduced adverse events, hospitalization, and total costs. Additionally, it is associated with more prolonged survival than percutaneous transhepatic biliary drainage and surgical drainage. However, 10% of unresectable MBO patients do not respond to endobiliary stents. PTBD often has high technical success (many series 77–100%) and can achieve good biliary decompression when ERCP fails (2,9). Malignant biliary obstruction is technically more complex to relieve because of tumor infiltration, high-grade strictures, and multifocal disease(2,14). The mortality rate for AC secondary to MBO Surgical drainage more than 30% (10–15). Better outcomes of patients when drainage done within 24-48 hour of diagnosis of AC (2,9,10).

Mortality after early ERCP or PTBD drainage is 15-20% and delayed drainage double of risk of mortality to more than 20-40%**.** Mortality after surgical drainage varies from 32-60%(4) .Therapeutic failure can be clinical, radiological, or biochemical ; Non resolution of ascending cholangitis within 7 days of initial definitive drainage , evidenced by persistent fever, leukocytosis, hemodynamic instability, or failure of serum total bilirubin to decrease by ≥50%, or the need for repeat drainage or salvage surgery, Persistent or increasing biliary ductal dilatation, New or enlarging liver abscesses, lack of contrast flow into the duodenum or death within 30 days attributable to cholangitis(16,17) .

Data on predictors of mortality specifically in malignancy-associated cases remains scarce .Delayed drainage, septic shock or organ dysfunction advanced age, hypoalbuminemia, leukocytosis, or high bilirubin correlate with mortality risk and treatment failure (7,16). However, most studies evaluating outcomes in ascending cholangitis do not disaggregate data for malignant versus benign causes, limiting their utility in cancer-associated cholangitis (3,10,11,11–13). Data from low-resource settings are sparse and often use differing outcome definitions, but suggest a substantial burden of unfavorable outcomes.

In Ethiopia, SPHMMC and similar resource limited settings delays in access to ERCP or interventional radiology are common contributing to increased morbidity and mortality. There remains a lack of local data incidence and risk factors for hospital mortality among cancer patients with ascending cholangitis presenting to tertiary hospitals like SPHMMC. Identifying such predictors was guide local clinicians in selecting the optimal drainage strategy, anticipating complications, and allocating limited intensive care and interventional resources. Moreover, this evidence was providing a foundation for advocating investment in endoscopic services and training. This study aims to identify clinical and radiological predictors of mortality among patients presenting with ascending cholangitis secondary to biliary and peri ampullary tumors. Understanding these predictors will help optimize early management strategies, guide clinical decision-making, and improve patient outcomes in resource-limited settings. Such insights could guide early triage and intervention strategies, optimize resource utilization, and ultimately improve survival in a high burden context.

1.2 Statement of the Problem

Factors such as tumor type, level of obstruction (hilar vs distal), pre-existing cholangitis, and delayed intervention contribute to mortality. Despite advances in minimally invasive drainage procedures such as ERCP and PTBD, mortality remains major challenge, particularly in low resource settings. In Ethiopia and low- and middle-income countries, data on outcomes of minimally invasive biliary drainage and predictors of treatment failure in malignant biliary tract obstruction are scarce. Most available evidence originates from high income countries.

In Ethiopia, SPHMMC where advanced endoscopic and interventional radiology services are limited, surgical or percutaneous drainage remains the primary mode of biliary decompression for many patients. As St. Paul's Hospital Millennium Medical College (SPHMMC) is one of the country's major tertiary referral centers managing hepatobiliary and pancreatic malignancies, understanding these patterns is critical. There is critical need to identify factors associated with mortality among AC secondary to MBO. Quantifying treatment failure and identifying its predictors would provide valuable insights for improving management strategies, referral timing, and drainage technique selection, and ultimately reduce morbidity and mortality in this high-risk population. This knowledge will help optimize triage, prioritize urgent drainage, improve supportive management, and ultimately reduce mortality and morbidity in this high-risk group. Moreover, the study's findings will provide baseline local data to guide future prospective research and quality improvement initiatives in hepatobiliary care at SPHMMC.

1.3 Rationale and Significance of the study of the Research

Early prompt biliary drainage is essential to control infection and prevent multi-organ failure in AC patients secondary to MBO. In high-income countries, ERCP is the standard method for biliary decompression, significantly reducing morbidity and mortality. However, at St. Paul's Hospital Millennium Medical College (SPHMMC), ERCP is not routinely available, and patients are primarily managed with surgical or percutaneous drainage, which carries higher rates of complications, prolonged hospitalization, and mortality. Currently, there is no local data describing the frequency, clinical course, or predictors of treatment failure both clinical and

radiological in patients with ascending cholangitis due to malignant biliary obstruction at SPHMMC. This knowledge gap limits the ability of clinicians to identify high-risk patients, anticipate complications, and optimize management strategies in a resource-limited setting. Conducting this study will provide evidence-based insights into the predictors of treatment failure, helping to guide clinical decision-making, improve patient monitoring, and inform institutional planning, including the potential introduction of ERCP services. Ultimately, the study aims to improve clinical outcomes, reduce morbidity and mortality, and contribute to strengthening hepatobiliary care for patients with malignant biliary obstruction in Ethiopia.

2 Literature Review

2.1 Introduction

Malignant obstruction is an increasingly common cause of acute cholangitis; studies report worse outcomes (higher early mortality, more complications) when the underlying cause is malignant rather than benign stone disease. Survival after biliary drainage in malignant disease is often limited by the underlying cancer, but cholangitis itself contributes substantially to early mortality and prevents cancer-directed therapy (18).The incidence of cholangitis secondary to malignant obstruction has risen due to increase incidence and improved survival among cancer patients and the frequent use of biliary stents for palliation. Early drainage is main stay of treatment in this group of patients, preferably with ERCP or PTBD .Despite advances in endoscopic and percutaneous drainage, treatment failure—defined as persistent or recurrent cholangitis, sepsis, persistent biliary obstruction despite drainage requiring additional drainage procedures or surgery, persistent elevation bilirubin or early mortality despite technically successful drainage—remains common in AC secondary to MBO(19). Understanding the clinical and radiological predictors of treatment failure is essential to guide management, improve patient selection for drainage modalities, and enhance outcomes in resource-limited settings such as SPHMMC where advanced endoscopic interventions are not routinely available.

2.1.2 Pathophysiologic rationale for predictor selection

Treatment failure in MBO-associated cholangitis results from a combination of host factors (age, comorbidity, nutritional state, organ dysfunction), infection severity (bacteremia, septic shock), tumor-related factors (level and extent of obstruction, malignant invasion of

ampulla/duodenum or hepatic hilum, bilateral ductal involvement), and procedure-related factors (failed or delayed biliary decompression, stent dysfunction, technical inability to access ducts). Radiology defines the anatomical obstacles that determine technical success (e.g., high hilar strictures, intrahepatic ductal involvement). These mechanistic links explain why both clinical/laboratory and imaging variables predict failure. Several studies have demonstrated that patients with malignant obstruction experience higher morbidity, mortality, and re-intervention rates compared with those with benign disease .(20,21) Furthermore, advanced malignancy often coexists with malnutrition, immunosuppression, and cholestatic liver dysfunction, all of which impair the host response to infection and delay recovery after drainage.(18)

2.1.3 Clinical predictors of treatment failure

Age, comorbidity and performance status (frailty, high ASA/CCI, ECOG)

Advanced age and high comorbidity burden predict failure/mortality. Some studies use CCI/ASA and show association with 30-day mortality indicators. Poor performance status less likely to receive drainage procedures and increase risk of mortality.(12)

Severity of illness at presentation

Several retrospective studies identify disease severity on admission as the strongest determinant of outcome. Patients presenting with severe cholangitis according to Tokyo 18, septic shock, renal dysfunction, or elevated SOFA scores have significantly higher odds of mortality and persistent cholangitis. Early organ dysfunction reflects systemic inflammatory burden and often indicates delayed diagnosis or incomplete drainage. In a multicenter Japanese cohort, severe Tokyo Guidelines 2018 (TG18) grade III cholangitis predicted a three-fold increase in clinical failure even after technically successful drainage(23).

Delay to biliary drainage and mode of drainage.

The timing of biliary decompression strongly influences prognosis. Studies consistently show that drainage delayed beyond 48 hours after diagnosis results in higher mortality and longer hospital stay(24). Drainage commonly delayed because coagulation abnormalities, lack of minimal invasive interventions. In resource-limited hospitals without urgent ERCP availability, delays can exceed several days, further increasing risk of mortality. ERCP has high technical success rates (85–95%) and is associated with lower procedure-related morbidity compared to

PTBD and surgical drainage in distal MBO. PTBD has comparable short-term efficacy to ERCP in achieving biliary decompression but may have higher procedure-related morbidity**,** including bleeding, bile leak, and catheter-related infection.(25) .Mortality in patients with severe cholangitis is influenced more by timely drainage than by the choice of ERCP vs PTBD. Surgical drainage has high technical success, durable decompression, and lower risk of recurrent obstruction compared to endoscopic stenting(26). However, it is associated with higher perioperative morbidity and mortality**,** especially in patients with sepsis or poor performance status.

Baseline hepatic reserve and comorbidity

Patients with WBC > 11000 or < 4000, elevated bilirubin (bilirubin > 14) TB increment or cannot decrease more than 50% from baseline within 2 weeks of drainage, albumin < 3mg/dl mg/dl, prolonged INR, or underlying chronic liver disease exhibit reduced ability to clear infection and recover after drainage. Preexisting cirrhosis and hepatic atrophy have been independently associated with treatment failure. Similarly, comorbidity indices such as the Charlson Comorbidity Index (CCI) and high ASA physical status correlate with poor outcomes. Frailty, advanced age, and malnutrition also contribute to impaired physiological reserve. (5,23,27,28)

Microbiological factors and previous interventions

Malignant obstruction often involves chronic indwelling stents or prior biliary instrumentation, predisposing to polymicrobial or multidrug-resistant (MDR) infections. Bacteremia, especially with extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae, correlates with persistent cholangitis and re-infection .(29,30) Prior antibiotic exposure and repeated ERCPs further alter biliary flora, reducing treatment efficacy. Patients with recurrent stent occlusion or prior percutaneous biliary drainage have significantly higher recurrence rates. Biofilm formation and tumor ingrowth around uncovered metal stents lead to incomplete bile clearance, creating a reservoir for infection. Each re-intervention carries incremental risk of cholangitis recurrence, emphasizing the need for predictive modeling to optimize initial drainage strategies.(17).

2.1.4 Radiological predictors of treatment failure

Level and extent of obstruction

Radiologic imaging (CT, MRI/MRCP) plays a central role in predicting outcomes. Intra hepatic bile duct obstruction, Hilar and multifocal obstructions (Bismuth types II–IV) are consistently associated with lower drainage success and higher rates of persistent cholangitis compared with distal common bile duct obstruction. Complete biliary drainage is main stay of treatment .Incomplete drainage of separate biliary segments often results in residual sepsis even when one lobe is decompressed. (3,23,31) .Korean study demonstrated that drainage of less than 50 % of functional liver volume doubled the risk of treatment failure.

Volume of undrained liver and lobar atrophy

CT volumetry and MRCP can estimate the volume of undrained bile ducts. The greater the undrained portion, the higher the likelihood of infection persistence. Lobar atrophy and segmental exclusion indicate chronic obstruction and poor functional recovery even after drainage. These imaging markers therefore serve as surrogates for "functional drainage adequacy."(32)

Local complications and tumor characteristics

Radiologic features such as liver abscess, or portal vein involvement are negative prognostic indicators. Tumor vascular encasement often limits stent patency and predisposes to recurrent obstruction. Moreover, periductal infiltration and irregular ductal morphology increase technical difficulty and reduce stent efficacy. Tumor size > 3 cm and liver metastasis associated with poor prognosis. Peritoneal carcinomatosis. distant metastasis, stage of pancreatobiliary tumor associated with 90 days mortality.(27, 32).

Type and configuration of drainage

Imaging also guides the choice of unilateral versus bilateral stenting in hilar lesions. Studies comparing both approaches suggest that bilateral drainage of ≥50 % of liver volume improves biochemical and clinical outcomes, but at the cost of greater technical complexity. Conversely,

unilateral stenting may suffice for distal obstructions with intact contralateral drainage. Radiological assessment of ductal anatomy is therefore a key determinant of both strategy and prognosis.(16, 23, 26).

Procedural and device-related factors

Technical and procedural variables interact with patient and imaging factors to determine clinical outcomes. Incomplete or non-functional drainage, even after apparent technical success, is a leading cause of persistent cholangitis. Stent characteristics—metal versus plastic, covered versus uncovered—also influence patency and infection recurrence. Meta-analyses report higher short-term patency but increased cholangitis risk with uncovered metal stents due to tumor ingrowth. Institutional factors are equally important: high-volume centers demonstrate better technical and clinical success rates, likely reflecting procedural expertise and access to multidisciplinary management (14,31).

3 Objectives

3.1 General Objective

To examine the clinical profile and predictors of treatment failure among patients with ascending cholangitis secondary to malignant biliary tract obstruction at SPHMMC, Adis ababa, Ethiopia, 2026.

3.2 Specific Objectives

1. To describe the demographic characteristics, clinical presentation, laboratory and imaging findings of ascending cholangitis secondary to malignant biliary tract obstruction.
2. To describe management strategies employed.

3. To determine magnitude and factors associated with in hospital mortality among patients with ascending cholangitis secondary to malignant biliary tract obstruction

4 Methodology

4.1 Study Design

Retrospective cohort study, reviewing medical records of adult patients diagnosed with AC secondary MBO managed at SPHMMC.

4.2 Study Period

The study period was from June 2026 to September 2026.

4.3 Study setting

St Paul Hospital Millenium Medical College (SPHMMC) is a major tertiary referral hospital in Addis Ababa, Ethiopia, serving catchment population of over 5 million. The HPB surgery unit includes experienced HPB surgeons and fellows. Available drainage procedures include PTBD and surgical by pass ERCP not routinely available.

4.4 Source and Study Population

All patients who were diagnosed with ascending cholangitis secondary to malignant biliary tract obstruction and managed in SPHMMC during the study period.

4.5 Inclusion Criteria

All adult patients (> 18 years of age) admitted at SPHMMC with ascending cholangitis secondary to malignant biliary obstruction during study period.

4.6 Exclusion criteria

Patients with an incomplete medical record (missing key variables for outcome or major predictors).

4.7 Sample Size Determination

Consecutive sampling method was used. Sample size was calculated using Epi Info version 7 (StatCalc) for retrospective study .Assuming 95% confidence interval ,80% power and 1:2 patients with drainage /no drainage, the expected rate of patients rate of treatment failure is among patients without drainage was 40% .Risk ratio of 0.5 assumed to detect clinically significant reduction in treatment failure among patients who underwent drainage .Based on this sample size was 197.After adding 10% to account incomplete medical records sample size was set 207.

4.8 Variables

4.8.1 Dependent Variable

After drainage or start of antibiotics

- Death during hospitalization

4.8.2 Predictors

Clinical predictors.

- Age (years)
- Sex
- Comorbidities: diabetes mellitus, HTN

- Vital signs at presentation: temperature, heart rate, blood pressure (hypotension defined as SBP <90 mmHg)
- Organ dysfunction at presentation: renal failure (creatinine), respiratory failure.
- Laboratory: albumin, total bilirubin, direct bilirubin, ALT/AST, alkaline phosphatase, WBC count, platelets, INR

Radiological predictors (CT/MR findings).

Radiological Predictors

- Level of obstruction.
- Radiological Resectability.

Treatment related predictors

Drainage procedure

- ✓ ERCP
- ✓ PTBD
- ✓ Surgical
- ✓ Cholecstojejunostomy
- ✓ Hepaticojejunostomy
- ✓ Intrahepatic hepaticojejunostomy, segment 3 by pass.
- ✓ Managed conservatively with antibiotics.

4.9 Operational definitions

1. Ascending cholangitis **-**diagnosis based on Tokyo guidelines (TG18) criteria.

2. Malignant biliary obstruction -radiologically or histologically confirmed malignancy causing biliary tract obstruction.

3. Treatment failure occurrence of the following

A. Mortality after started on management of cholangitis

4.10 Data Sources and Collection Procedures

Data was retrieved from: Hospital **electronic medical records (EMR)** and patient charts, Ward, OPD and OR HMIS records. Structured data extraction form (attached questionnaire) was used.

4.11 Data Quality Assurance

Data quality assurance was optimized and checked by Training of data collectors and pilot testing on 10 randomly selected charts, double entry and cross-verification of data, Periodic data consistency checks and outlier screening, and de-identification of all patient records before analysis

4.12 Handling of Missing Data

Describe the pattern of missingness. Use complete -case analysis if < 5 %: multiple imputation (MICE) if > 5% with sensitivity analysis.

4.13 Data Processing and Statistical Analysis

Descriptive Analysis

- Categorical variables summarized as frequencies and percentages.

Bivariate Analysis

- Compare predictors between treatment success and failure groups using Chi-square for categorical variables.

Multivariable logistic regression Analysis

- Predictors with $p < 0.20$ in bivariate analysis was enter a multivariable logistic regression model
- Adjusted odds ratios (AOR) with 95% confidence intervals was reported

4.14 Ethical Considerations

Ethical clearance was obtained from the SPHMMC Institutional Review Board (IRB). Patient identifiers are removed, and data stored securely in password-protected files accessible only to the research team. As a retrospective chart review, the requirement for informed consent was waived per institutional policy.

CHAPTER FIVE

5. RESULTS AND DISCUSSION

Table 1 result of demographic data

Variable		Frequency	Percent
Age	Less than 40 years	26	13.1
	41 to 60 years	93	46.7
	Above 61	80	40.2
Sex	Male	101	50.8
	Female	98	49.2
Co-morbidity	No	144	72.4
	Yes	55	27.6
Types of co-morbidities	DM	24	12.1
	Other	10	5

According to the data the predominant population were middle-aged to elderly (86.9% are >40 years old), with an almost equal sex distribution (50.8% male, 49.2% female). About 27.6% have comorbidities, primarily Diabetes Mellitus (12.1%) and Hypertension (10.6%).

This shows the typical age of onset for pancreatobiliary malignancies. The presence of comorbidities in over a quarter of the research is clinically significant, as DM and HTN are

known to impair microvascular healing and increase the risk of sepsis and acute kidney injury, thereby elevating the baseline risk of mortality.

5.2 Result of other clinical information of the participant

Table 2 Result of other clinical information of the participant

Variable		Frequency	Percent
Severity of cholangitis	Moderate	128	64.3
	severe	71	35.7
Duration of hospital stay(days)	Acute	35	17.6
	prolonged	114	57.3
	chronic	50	25.1
Co-morbidity	No	144	72.4
	Yes	55	27.6
Types of co-morbidities	HTN	21	10.6
	DM	24	12.1
	Other	10	5
Malignancy primary site	Pancreatic head	65	32.7
	Distal cholangiocarcinoma	28	14.1
	Ampullary cancer	13	6.5
	Gallbladder	13	6.5
	Hilar cholangiocarcinoma	63	31.7
	Intrahepatic cholangiocarcinoma	8	4
	HCC & other	9	4.5
Metastasis diseases at presentation	No	167	83.9
	Yes	32	16.1
Site of metastasis	Liver	29	14.1
	Lung	4	2
Previous history of biliary drainage	No	174	87.4
	Yes	25	12.6
Mode of drainage	ERCP	5	2.5
	PTBD	14	7
	Surgery	6	3

According to the study finding no mild case was found all 100% of the reported patients was presented with either Moderate (64.3%) or severe (35.7%) cholangitis. Furthermore, 57.3% experienced a "prolonged", more than 2 weeks hospital stay, and 25.1% had a "chronic" more than 1 month hospitalization.

The result of the absence of "mild" cases in a tertiary referral hospitals like SPHMMC is common since most of the patents in Ethiopia present at late stages and where the hospital is the only the most severe, complicated cases are transferred. The fact that over one-third (35.7%) presented with severe cholangitis (likely meeting TG18 Grade III criteria with organ dysfunction) is a major red flag. According to the TG18 and the cited literature (e.g., the Japanese multicenter cohort), severe cholangitis at presentation is the strongest independent predictor of hospital mortality. The high rate of prolonged hospitalization (57.3%) directly reflects the morbidity burden and the strain on hospital resources when definitive drainage is delayed or unavailable in the country.

The other most common primary malignancies in the study participants were Pancreatic head tumors (32.7%) and Hilar cholangiocarcinoma (31.7%), together calculated nearly 65% of cases. Most patients (83.9%) did not have distant metastasis at presentation, though when present, the liver was the most common site (14.1%).

However, the high proportion of hilar cholangiocarcinoma (31.7%) is a critical prognostic factor. As stated in the literature review, hilar obstructions (Bismuth types II–IV) are technically more complex to drain than distal obstructions. Incomplete drainage of separate biliary segments in hilar tumors is a radiological predictor of repeated sepsis and mortality.

The other most clinical finding is only 12.6% of patients had a previous history of biliary drainage: PTBD (7%), Surgery (3%), and ERCP (2.5%).

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5.3 Clinical Presentation of Study Participants at Admission

Table 3 Clinical presentation of study participants at admission

Variable	Category	Frequency	Percent
RUQ pain	No	20	10.1
	Yes	179	89.9
Jaundice	No	10	5
	Yes	189	95
Duration of jaundice	Acute	80	40.2

	Chronic	119	59.8
Fever	No	67	33.7
	Yes	132	66.3
Blood pressure	Hypotension	30	15.1
	Normal	145	72.9
	Hypertension	24	12.1
Icteric conjunctiva	No	18	9
	Yes	181	91
Ascites	No	124	62.3
	Yes	75	37.7
Peripheral edema	No	149	74.9
	Yes	50	25.1
Pleural effusion	No	164	82.4
	Yes	35	17.6

According to the data almost all patients was presented with the classic features of biliary obstruction such as right upper quadrant pain was present in 89.9% and jaundice in 95% of participants, with icteric conjunctiva was confirmed on physical examination in 91%. Regarding the variable fever which is one of Tokyo Guidelines criterion for cholangitis, was documented in 66.3% of patients, and 15.1% were hypotensive at presentation. The study participants which are more than one-third of participants (37.7%) had ascites, and more than one fourth of the patients had peripheral edema (25.1%) or pleural effusion (17.6%) at the time of admission.

These results indicate that the majority of patients in this cohort presented late with signs of disease course: third-spacing of fluid (ascites, edema, effusion) rather than early, uncomplicated biliary obstruction. The predominance of chronic (more than 4 weeks) over acute (less than 4 weeks) duration of jaundice (59.8% vs 40.2%) is consistent with the high proportion of hilar and pancreatic head tumors described above.

5.4 Laboratory Investigation Findings

Table 4 Laboratory profile of study participants

Variable	Category	Frequency	Percent
Creatinine	Low (<0.5mg/dl)	27	13.6
	Low-normal (0.5-0.5mg/dl)	22	11.1
	Normal (0.8-1.1mg/dl)	105	52.8
	High-normal (1.2-1.3)	10	5
	High(>1.3 mg/dl)	35	17.6
Leukocytosis	No	46	23.1
	Yes	153	76.9
CRP	Moderate to high	103	51.8
	Very high	96	48.2
Total bilirubin	Moderate	31	15.6
	Severe	168	84.4
Direct bilirubin	Moderate	24	12.1
	Severe	175	87.9
ALP	Normal	5	2.5
	High	194	97.5
AST	Normal	14	7
	High	185	93
ALT	Normal	21	10.6
	High	178	89.4
INR	Normal	34	17.1
	Mildly elevated	94	47.2
	Moderately elevated	28	14.1
	Severely elevated	43	21.6
Anemia	No	101	50.8
	Yes	98	49.2
Hypoalbuminemia	No	32	16.1
	Yes	167	83.9
Thrombocytopenia	No	167	83.9

	Yes	32	16.1

The study participants laboratory findings showed severe cholestasis and systemic inflammation in most of the participants. Total and direct bilirubin was in the severe range in 84.4% and 87.9% patients respectively and alkaline phosphatase was elevated in 97.5% patients consistent with high grade biliary obstruction. Transaminases were often raised also (AST 93%, ALT 89.4%) indicating hepatocellular injury. The other laboratory finding leukocytosis which is a major criterion of the Tokyo Guidelines was present in 76.9% of the patients, and C-reactive protein was moderately and very highly elevated in practically all the patients (51.8% and 48.2%, respectively).

The finding of markers of impaired hepatic synthetic function and coagulopathy were also common: hypoalbuminemia was present in 83.9% of patients, and INR was mildly, moderately, or severely elevated in a combined 82.9% of the study. The laboratory result of renal function test of the study participants were variably affected, with 17.6% of patients showing high creatinine values suggestive of acute kidney injury or hepatorenal compromise. Nearly half of the participants (49.2%) was anemic and 16.1% had thrombocytopenia, both of which may reflect chronic disease, malignancy-related bone marrow suppression, or portal hypertension in patients with advanced hepatobiliary disease.

Over all these findings show that the majority of participants presented with severe biochemical derangement rather than mild, early obstruction, a pattern consistent with the high proportion of severe cholangitis, delayed presentation, and eventual treatment failure observed in this cohort.

4.5 Radiological and Imaging Findings

Table 5 Imaging and radiological findings

Variable	Category	Frequency	Percent
Imaging modality used	CT scan	160	80.4
	MRI/MRCP	10	5
	CT & Ultrasound	9	4.5

	Ultrasound & MRI/MRCP	9	4.5
	CT & MRI/MRCP	11	5.5
Resectability on imaging	No	128	64.3
	Yes	71	35.7
Site of obstruction	Distal extrahepatic	108	54.3
	Hilar	91	45.7

Regarding imaging computed tomography (CT) was the most frequently used imaging modality, which is performed alone in 80.4% of patients, while the remainder underwent a combination of CT, ultrasound, and MRI/MRCP for further anatomical characterization. On imaging, most tumors were assessed as unresectable (64.3%), reflecting the generally advanced stage at presentation already suggested by the high rates of hilar and pancreatic head involvement. The result show that site of obstruction was distal extrahepatic in 54.3% of patients and hilar in 45.7%.

The distal and hilar obstruction is clinically important because, as discussed in the literature review, hilar strictures (Bismuth types II-IV) are technically more difficult to drain completely and carry a higher risk of incomplete decompression and persistent cholangitis than distal common bile duct obstruction. The result of almost half of the cohort having hilar disease, and nearly two-thirds taken as unresectable.

5.6 Management and Treatment Received

Table 6 Management and treatment received

Variable	Category	Frequency	Percent
Treated with antibiotics	No	0	0
	Yes	199	100
Drainage done	No	70	35.2
	Yes	129	64.8
Mode of drainage (n=129)	ERCP	13	6.5
	PTBD	46	23.1

	Surgical drainage	70	35.2
Type of surgical procedure (n=74)	Cholecystojejunostomy	36	18.1
	Hepaticojejunostomy	30	15.1
	Whipple procedure/segment III bypass	8	4

The majority of patients (85.4%) were treated with antibiotics for cholangitis. Slightly less than two-thirds (64.8%) go through some form of biliary drainage procedure. Of these patients who underwent drainage, surgical drainage was used most commonly (35.2% of entire sample), followed by PTBD (23.1%); ERCP was used for only 6.5% of patients.

In the patients who had a surgical drainage procedure, cholecystojejunostomy (18.1%) and hepaticojejunostomy (15.1%)were the most common, whereas only 4% of patients had a Whipple procedure or segment III by-pass.

This proportion reflects resource issues outlined above, where lack of ERCP has lead to the increased reliance on a surgical bypass, and percutaneous management as the best available methods of biliary decompression. Both surgery and percutaneous management carry a greater risk of procedure associated mortality than ERCP. More than a third (35.2%) received no drainage intervention: likely because of clinical performance status, unresectable disease, late diagnosis, or death before a drainage could be organized reasons.

5.7 Magnitude of Treatment Failure

Table 7 Overall treatment outcome

Outcome	Frequency	Percent
Survived	135	67.8
Died (treatment failure)	64	32.2
Total	199	100

Of the 199 patients included in the final analysis, 64 died during hospitalization, giving an overall in-hospital mortality, or treatment failure rate, of 32.2%. This falls within the range of 15% to 40% reported in the literature for treatment failure following drainage of malignant biliary obstruction, but sits toward the upper end of that range, consistent with the advanced disease stage, high proportion of hilar involvement, and limited access to timely endoscopic drainage described in the preceding sections.

5.8 Factors Associated with Treatment Failure: Bivariate and Multivariable Analysis

Binary Logistic regression analysis was carried out to determine the association between independent variables and dependent variable. Predictors with a p-value < 0.20 on bivariate analysis were entered into a multivariable logistic regression model to identify independent predictors of treatment failure (death).

Table 4.8 presents the crude odds ratio (COR) from bivariate analysis alongside the adjusted odds ratio (AOR) from the multivariable model, both with 95% confidence intervals; the reference category for each variable is marked "1", and adjusted associations that remained statistically significant (95% CI excluding 1) are marked with an asterisk (*).

Table 8 multivariable logistic regression analysis of factors associated with treatment failure

Variable	Categories	Treatment outcome (death)		COR(95%)	AOR(95%)
		No	Yes		
Severity of cholangitis	Moderate	101	27	1	1
	Severe	34	37	4.071(2.168-7.645)	1.226(0.378-3.979)
Duration of hospital stay	Acute	14	21	1	1
	Prolonged	86	28	0.217(0.098-0.483)	0.368(0.113-1.198)
	Chronic	35	15	0.286(0.115-0.708)	0.338(0.087-1.314)
Fever on admission	No	54	13	1	
	Yes	81	51	2.615(1.299-5.264)	2.802(1.006-7.799)
Ascites	No	97	27	1	1
	Yes	38	37	3.498(1.878-6.515)	7.345(1.887-28.593)*
Peripheral edema	No	108	41	1	1
	Yes	27	23	2.244(1.157-4.351)	0.185(0.044-0.769)*

Pleural effusion	No	119	45	1	1
	Yes	16	19	3.14(1.486-6.637)	3.19(0.679-15)
Creatinine	Low	21	6	1	1
	Low-normal	17	5	1.029(0.267-3.963)	1.868(0.347-10.075)
	Normal	81	24	1.037(0.376-2.862)	1.62(.444-5.909)
	High-normal	5	5	7.636(2.408-24.222)	10.272(1.418-74.415)*
	High	11	24	3.5(0.753-16.263)	4.197(0.954-18.473)
Drainage	No	23	47	13.463(6.596-17.478)	12.848(4.39-37.602)*
	Yes	112	17	1	1
Type of surgical drainage	Cholecystojejunostomy	29	7	1	1
	Hepaticojejunostomy	29	1	0.21(0.48-1.211)	0.146(0.016-1.302)
	Whipple/segment 3 bypass	4	4	0.034(0.003-0.391)	13.876(2.539-75.839)*
Shock	No	123	48	1	1
	Yes	12	16	3.417(1.506-7.753)	2.921(0.919-9.288)
Altered mental status	No	128	53	1	1
	Yes	7	11	3.795(1.583-18.137)	0.445(0.058-3.434)
Hypolbuminemia	No	27	5	1	1
	Yes	108	59	2.95(1.079-8.064)	1.13(0.305-4.186)
Thrombocytopnea	No	120	47	1	1
	Yes	15	17	2.894(1.337-6.261)	3.761(1.257-11.253)*
Temperature	Normal	122	43	1	1
	Fever	13	21	4.583(2.113-9.939)	
Saturation	Low	8	10	2.94(1.1-7.854)	1.061(0.124-9.096)
	Normal	127	54	1	1
Respiratory rate	Normal	122	42	1	1
	Tachypnea	13	22	4.916(2.276-10.618)	3.321(1.152-9.571)*

COR = crude odds ratio; AOR = adjusted odds ratio; CI = confidence interval; 1 = reference category; * statistically significant at $p < 0.05$ (95% CI excludes 1).

On multivariable analysis, several factors remained independently associated with treatment failure. Failure to achieve biliary drainage was the strongest predictor of death: patients who did not undergo any drainage procedure had more than twelve-fold higher adjusted odds of death compared with those who were drained (AOR 12.85, 95% CI 4.39-37.60). Fever on admission (AOR 2.80, 95% CI 1.01-7.80), ascites (AOR 7.35, 95% CI 1.89-28.59), high-normal creatinine (AOR 10.27, 95% CI 1.42-74.42), thrombocytopenia (AOR 3.76, 95% CI 1.26-11.25), and tachypnea on admission (AOR 3.32, 95% CI 1.15-9.57) were each independently associated with increased odds of death after adjustment.

Peripheral edema showed increased odds of death on bivariate analysis (COR 2.24) but a paradoxical, statistically significant protective association after adjustment (AOR 0.19, 95% CI 0.04-0.77). This counter-intuitive finding most likely reflects confounding by other variables already in the model, such as ascites and drainage status, and residual collinearity among the fluid-overload indicators, and should be interpreted with caution rather than as a genuine protective effect. Similarly, the very wide confidence interval around the Whipple procedure/segment III bypass category (AOR 13.88, 95% CI 2.54-75.84) reflects the very small number of patients in this subgroup and should also be interpreted cautiously.

Severity of cholangitis, duration of hospital stay, pleural effusion, shock, altered mental status, and hypoalbuminemia were significantly associated with death on bivariate analysis but did not retain statistical significance after adjustment, suggesting that their effect on outcome may be mediated through, or confounded by, drainage status and the other severity markers retained in the final model.

5.9 Discussion of Key Findings

This study set out to describe the clinical profile of ascending cholangitis secondary to malignant biliary obstruction at SPHMMC and to identify predictors of treatment failure. The findings show a cohort that is predominantly middle-aged to elderly, presents late with the classic features of biliary sepsis (jaundice, fever, right upper quadrant pain) with systemic compromise (ascites, hypoalbuminemia, coagulopathy), and is affected by pancreatic head and hilar cholangiocarcinoma in roughly two-thirds of cases.

The overall hospital mortality rate is 32.2% is consistent with, though at the higher end of, previously reported ranges, and mirrors the pattern described in the literature review whereby AC secondary to malignant obstruction carries a substantially worse prognosis than cholangitis due to benign stone disease. As anticipated from the pathophysiologic rationale outlined in Chapter One, mortality resulted from a combination of host factors (age, comorbidity, nutritional and hepatic reserve), infection severity (fever, leukocytosis, shock), and procedure-related factors, of which failure to achieve biliary drainage emerged as by far the strongest and most consistent predictor of death.

This finding has direct clinical and policy relevance for SPHMMC and similar resource-limited settings. Because ERCP is not routinely available, most patients who are drained undergo PTBD

or surgical bypass, which is more invasive and carry higher procedural risk than endoscopic drainage; yet even so, patients who received no drainage at all had by far the worst outcomes. This underscores that the priority for reducing mortality in this population is less about which modality of drainage is used, and more about ensuring that some form of timely biliary decompression is achieved at all, in line with the Tokyo Guidelines recommendation for drainage.

The independent association of ascites, elevated creatinine, thrombocytopenia, and tachypnea with death reflects the importance of baseline physiological reserve and organ dysfunction in determining outcome, consistent with prior studies linking hepatic and renal impairment, and markers of the systemic inflammatory response, to mortality in cholangitis. The unexpected protective adjusted association for peripheral edema is most plausibly explained by confounding within the multivariable model rather than a true biological effect, and highlights a limitation of working with a moderate sample size and a relatively large number of candidate predictors; this warrants further exploration in future, larger studies.

Taken together, these findings address the objectives set out for this study: they describe, for the first time in this setting, the clinical, laboratory, radiological, and management profile of AC secondary to MBO at SPHMMC; they quantify the magnitude of mortality ; and they identify clinical predictors, chief among them lack of biliary drainage, that could be used to triage patients for urgent decompression and closer monitoring in a resource-limited environment.

CHAPTER SIX

5. SUMMARY, CONCLUSION AND RECOMMENDATION

5.1 Summary of Major Findings

A total of 199 patients diagnosed with ascending cholangitis secondary to malignant biliary obstruction were included in the final analysis. The main findings are summarized below.

- Demographic profile: the cohort was predominantly middle-aged to elderly (86.9% were over 40 years), with an almost equal sex distribution (50.8% male, 49.2% female) and comorbidities, mainly diabetes mellitus and hypertension, in 27.6% of patients.
- Disease characteristics: more than one-third of patients (35.7%) presented with severe cholangitis, and most experienced a prolonged or chronic hospital course. Pancreatic head tumors (32.7%) and hilar cholangiocarcinoma (31.7%) were the leading primary malignancies, and 16.1% of patients had metastatic disease at presentation, most commonly to the liver.
- Clinical presentation: nearly all patients presented with jaundice (95%) and right upper quadrant pain (89.9%); fever was present in 66.3%, and features of systemic compromise such as ascites (37.7%), peripheral edema (25.1%), and hypotension (15.1%) were common.
- Laboratory and radiological profile: severe hyperbilirubinemia (84.4%), elevated alkaline phosphatase (97.5%), leukocytosis (76.9%), hypoalbuminemia (83.9%), and coagulopathy (82.9%) were frequent. On imaging, most tumors were unresectable (64.3%) and nearly half of patients (45.7%) had hilar obstruction.
- Management: 100% of patients received antibiotics and 64.8% underwent a biliary drainage procedure, most commonly surgical drainage (35.2%) or PTBD (23.1%); ERCP was used in only 6.5% of patients, and 35.2% received no drainage procedure at all.
- Magnitude of in hospital mortality: in-hospital mortality, the study's primary measure of treatment failure, occurred in 64 of 199 patients, an overall treatment failure rate of 32.2%.
- Predictors of mortality: on multivariable analysis, failure to achieve biliary drainage was the strongest independent predictor of death (AOR 12.85), followed by ascites (AOR

7.35), high-normal creatinine (AOR 10.27), thrombocytopenia (AOR 3.76), tachypnea (AOR 3.32), and fever on admission (AOR 2.80). Severity of cholangitis, prolonged hospital stay, shock, altered mental status, and hypoalbuminemia were associated with death on bivariate analysis but were not independently significant after adjustment.

5.2 Conclusion

The research general and specific objectives of the study were attained. The study documented demographic, clinical, laboratory, radiologic, and treatment characteristics of patients presenting with secondary ascending cholangitis from biliary malignant obstruction to SPHMMC, measured mortality rate and determined the factors predicting treatment failure as an independent outcome. The disease presentation with dominant pancreatic head and hilar cholangiocarcinoma, prevalent of severe cholangitis and high proportions of unresectable, locally advanced tumors observed in the cohort are consistent with findings from the global literature.

However, compared to patient cohorts in the high-income setting, patients at SPHMMC were at the later stages of their diseases, had more systemic compromise at presentation and underwent ERCP less frequently for biliary decompression.

An overall mortality rate of 32.2%, an upper limits of previous reports, highlights the substantial burden of local disease and limitation of timely decompression. Perhaps the most critical and addressable of the observations in this study is the finding of an order of magnitude increased mortality risk for those who did not receive biliary drainage. This demonstrates that even when access to routine ERCP is limited, timely biliary decompression-whether by PTBD or surgical interventions- is paramount for survival, greater than the specific technique employed. Additionally, the presence of ascites, renal compromise, and a low platelet count, tachypnea, and fever at presentation identify a subset of patients at elevated risk who should be monitored and aggressively managed more aggressively.

6.3 Recommendations

Based on these findings, the following recommendations are made:

- Recommendations To clinicians at SPHMMC, managing cases of ascending cholangitis:

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- Wherever ERCP is unavailable, proceed straight to either PTBD or surgical bypass, instead of simply waiting without decompression as absence of decompression instead of technique was found to be of importance.
- Patients having these additional features: ascites, tachypnea, fever, thrombocytopenia or impaired renal function, at presentation, were found to be at higher mortality and would ideally have escalated to a higher level.

➢ To management of SPHMMC and hospital:
- Increase capacity of ERCP and interventional radiology to minimize need of surgical bypassing for biliary drainage.
- Use standardized pathway or algorithm for management and triage for suspected ascending cholangitis, arising secondary to obstruction secondary to neoplasia to decrease delay for definitive drainage.
- Improve MDT working to faster staging, surgery of pancreatobiliary malignancies.

➢ To Policy makers and MoH:
- Foster access to training and equipment of interventional endoscopy SPHMMC as evidence show importance of access for decompression to save patient lives.
- Use standardized, prospective multi-hospital registration of the cholangitis outcomes.

6.4 Limitations of the Study

This study should be viewed in the context of some limitations. First, as a retrospective chart review study, its results are limited to the accuracy and completeness of the data available in our medical records; a certain degree of uncaptured or misclassified data could have occurred although data validation checks described in Chapter Three were used. Second, this was a single-institution study performed at a tertiary referral medical center that may receive more critically and complicatedly affected cases than do lower-level hospitals and its results might not be wholly applicable to other institutions or systems.

Third, although our overall sample size of 199 was sufficient for primary analysis, the number of outcome events was insufficient compared to number of potential predictor variables utilized in multivariable analyses, potentially yielding inflated standard errors/wide confidence intervals in

some smaller subgroup categories (e.g., those for the Whipple procedure/segment III bypass, and the paradoxically observed adjusted relation between peripheral edema and mortality).

6.5 Suggestions for Future Research

- Prospective, multi-center cohort studies across Ethiopian referral hospitals to improve generalizability and statistical power for detecting predictors of treatment failure.
- Studies that evaluate the effect of introducing or expanding ERCP services on treatment failure and mortality in malignant biliary obstruction.
- Development and external validation of a simple bedside clinical risk-prediction score for mortality in ascending cholangitis secondary to malignant biliary obstruction, suitable for use in resource-limited settings.
- Studies that analyze time-to-drainage as a continuous variable to better quantify the dose-response relationship between delay in decompression and mortality.
- Cost-effectiveness analysis comparing ERCP, PTBD, and surgical drainage in this population, to inform resource allocation decisions.
- Further investigation, in larger samples, of the unexpected adjusted association between peripheral edema and outcome observed in this study.

6.6 Practical Implications

The findings of this study have practical implications for several groups. For clinicians, the results provide a locally derived set of warning signs, ascites, tachypnea, fever, thrombocytopenia, and renal impairment, that can be used at the bedside to identify patients who need urgent drainage and closer monitoring. For hospital administrators, the strong association between the absence of drainage and mortality provides a clear, evidence-based rationale for prioritizing investment in interventional radiology and endoscopy services. For patients and their families, the findings reinforce the importance of early presentation and prompt acceptance of recommended drainage procedures. For health policy makers, the study contributes local evidence to support the case for expanding interventional endoscopic services at tertiary hospitals as a means of reducing mortality from malignant biliary obstruction in Ethiopia.

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ANNEX

Annex I Questionnaire

1. General information

1.1. Study ID: -------

1.2. Hospital MRN: -------

1.3. Date of data extraction: YYYY-MM-DD--------

2.1 Diabetes mellitus: 0=No, 1=Yes

2.2 Hypertension: 0=No, 1=Yes

2.3 Chronic liver disease / cirrhosis: 0=No, 1=Yes

2.4 chronic kidney disease: 0=No, 1=Yes

2.5 Cardiac disease 0=no 1 =Yes

2.4 Malignancy primary site: 1=Pancreatic head, 2=Periampullary, 3=Cholangiocarcinoma (intrahepatic/extrahepatic — specify), 4=Gallbladder, 5=Metastatic from other, 6=Unknown/other

2.6 Known metastatic disease at presentation: 0=No, 1=Yes

2.6 Previous biliary intervention (ERCP/PTBD/stent/Surgery) before this admission: 0=No, 1=Yes (specify: ERCP/PTBD/surgery)

3 Clinical presentations

3.1Fever on admission 0=No 1= yes

3.2 Right upper quadrant pain: 0=No, 1=Yes

3.3 Jaundice: 0=No, 1=Yes

3.4 Systolic blood pressure (mmHg) at presentation: __

3.5 Heart rate (bpm) at presentation: __

3.6 Respiratory rate (per min): __

3.7 SpO2 (%) on room air: __

3.8 Ascites

3.9 Peripheral edema

3.10 Pleural effusion

4 Laboratory results

4.1 White blood cell count (×10^9/L)

4.2 Hemoglobin (g/dL):

4.3 Platelet count (×10^9/L):

4.4 Serum bilirubin (total, mg/dL):

4.5 Alkaline phosphatase (IU/L):

4.6 AST (IU/L):

4.7 ALT (IU/L):

4.8 Serum creatinine (mg/dL):

4.9 INR

5 Severity of cholangitis

5.1 Mild

5.2 Moderate

5.3 Severe

6 Radiological

6.1 **I**maging modality for diagnosis: 1=Ultrasound, 2=CT Abdomen, 3=MRI/MRCP,

6.2 Level of biliary obstruction: 1=Extrahepatic (distal), 2=Hilar, 3=Intrahepatic, 4=Multiple levels

6.3 Metastatic lesions on imaging: 0=No, 1=Yes (specify sites)

7 Treatment and timing

7.1 Empiric antibiotics started: 0=No, 1=Yes

7.2 Biliary drainage: 0=No, 1=Yes

7.3 Type of drainage**:** 1=ERCP with stent, 2=Percutaneous transhepatic biliary drainage (PTBD), 3=Surgical biliary bypass, 4=None

Outcomes

7.4 In-hospital mortality: 0=No 1 yes

7.5 . ICU care & supportive measures

Annex II TG18 diagnostic criteria for acute cholangitis

A. Systemic inflammation

A-1. Fever and/or shaking chills

A-2. Laboratory data: evidence of inflammatory response

B. Cholestasis

B-1. Jaundice

B-2. Laboratory data: abnormal liver function tests

C. Imaging

C-1. Biliary dilatation

C-2. Evidence of the etiology on imaging (stricture, stone, stent etc.)

Suspected diagnosis: one item in A + one item in either B or C

Definite diagnosis: one item in A, one item in B and one item in C

Annex III TG18 severity assessment criteria for acute cholangitis

Grade III (severe) acute cholangitis

"Grade III" acute cholangitis is defined as acute cholangitis that is associated with the onset of dysfunction at least in any one of

the following organs/systems:

1. Cardiovascular dysfunction: hypotension requiring dopamine ≥5 lg/kg per min, or any dose of norepinephrine

2. Neurological dysfunction: disturbance of consciousness

3. Respiratory dysfunction: PaO2/FiO2 ratio <300

4. Renal dysfunction: oliguria, serum creatinine >2.0 mg/dl

5. Hepatic dysfunction: PT-INR >1.5

6. Hematological dysfunction: platelet count <100,000/mm3

Grade II (moderate) acute cholangitis

"Grade II" acute cholangitis is associated with any two of the following conditions:

1. Abnormal WBC count (>12,000/mm3, <4,000/mm3)
2. High fever (≥39°C)
3. Age (≥75 years old)
4. Hyperbilirubinemia (total bilirubin ≥5 mg/dl)
5. Hypoalbuminemia (< 3mg/dl)

Grade I (mild) acute cholangitis

"Grade I" acute cholangitis does not meet the criteria of "Grade III (severe)" or "Grade II (moderate)" acute cholangitis at initial diagnosis.

Annex IV **Assurance of Principal Investigator**

I the undersigned agree to accept all responsibilities for the scientific and ethical conduct of the Research project. I will provide timely progress report to my advisor and seek the necessary Advice and approval from my primary advisors in the course of the research. I will communicate Timely to my advisors all stakeholders involved in the study including any source of funding for This research.

Name of the student: _____

Signature: _____

Date: _____

Approval of the Primary Advisor

Name of the primary advisor: _____

Signature: _____

Date: _____

Approval of the Co-Advisor

Name of the primary advisor: _____

Signature: _____

Date: _____

Annexes V Work plan of the Research

Table 1 time frame of the research

Protocol Development and Ethical Clearance	Develop proposal draft, review by advisor, and submit to IRB for approval	Principal Investigator, Advisors	2 months	March - Aprill 2026
Preparation for Data Collection	Design data extraction form, pilot testing, and train data collectors	Data collectors	2 weeks	May 2026

Data Collection	Retrieve patient charts, radiology reports, and extract data	Data collectors	1 month	May 2026
Data Entry and Cleaning	Enter and verify data using EpiData	Data Clerk	1 month	June 2026
Data analysis	Conduct descriptive and multivariable analysis	Investigator	2 weeks	July 2026
Drafting of Research Report	Write results, discussion, and conclusion	Investigator	2 weeks	July 2 2026
Advisor Review and Revision	Submit draft to advisors and finalize report	Investigator and , Advisors	2 weeks	July 2026
Defense and Dissemination	Prepare presentation and defense before panel	Investigator	1 month	August 2026

Annexes VI Budget for Research Proposal

Table 2 Budget of proposal

No	Budget item	Description	Quantity	Unit cost	Total
1	Data collection				
1.1	Data collectors	Chart review and data extraction (2 months)	2	3500	7000
1.2	Data Entry Clerk	Data entry and cleaning (1 month)	2	3500	7000
	Subtotal				14000

2	Materials and Supplies	Data collection forms, IRB documents	2000	10	20000
2.1	Printing and Photocopying	Pens, files, staplers, envelopes, etc.			1500
	Subtotal				21500
3	Data management and analysis				
3.1	Software & Statistical Analysis	Software consultation	Lump sum	10000	10000
3.2	Data backup	Flash drives, cloud storage	Lump sum	6000	6000
	Subtotal				16000
4	Dissemination Of results				
4.1	Printing and Binding Final Report	3 bound copies of research	3	500	1500
5	Contingency ,10%	To cover unexpected costs			7000
	Total				25000