



ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCES,  
DEPARTMENT OF CLINICAL ONCOLOGY

CLINICAL CHARACTERISTICS, TREATMENT PATTERN AND SURVIVAL  
OF PATIENTS WITH BILIARY TRACT CANCER: A FIVE-YEAR  
RETROSPECTIVE COHORT STUDY AT TIKUR ANBESSA SPECIALIZED  
HOSPITAL, ETHIOPIA.

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Clinical characteristics, treatment pattern and survival of patients with biliary tract cancer: A five-year retrospective cohort study at Tikur Anbessa Specialized Hospital, Ethiopia.

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This is to certify that the thesis entitled “**Clinical characteristics, treatment pattern and survival of patients with biliary tract cancer: A five-year retrospective cohort study at Tikur Anbessa Specialized Hospital, Ethiopia**” is submitted in partial fulfillment of the requirements for the Specialization Certificate in clinical oncology to the department of clinical oncology, Addis Ababa University college of health science and has been carried out by Dr. Aklilu Sinte under my supervision.

Therefore, I recommend that the student has fulfilled the requirements and hence hereby can submit the Thesis to the Department

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**Declaration**

I hereby declare that this research thesis is my original work and has not been presented by any other investigator and all the source materials used for this thesis have been duly acknowledged

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## Abstract

**Background:-** Biliary tract cancers (BTCs); including intrahepatic and extrahepatic cholangiocarcinoma and gallbladder cancer—are rare but aggressive malignancies with rising global incidence and mortality. In low- and middle-income countries like Ethiopia, biliary tract cancer often presents at an advanced stage contributing to poor outcomes. To date, no published studies in Ethiopia have investigated treatment patterns and survival outcomes for biliary tract cancer patients

**Objectives:** This study aims to investigate the clinical characteristics, treatment patterns and survival of biliary tract cancer patients at Tikur Anbessa Specialized Hospital from January 01, 2020 to September 01, 2025 in Addis Ababa; Ethiopia.

**Methods:** A retrospective cohort study was conducted by reviewing medical records of adult patients diagnosed with biliary tract cancer from January 1, 2020 and September 01, 2025. Data on demographics, clinical characteristics, treatment modalities (surgery, radiotherapy, chemotherapy), and survival was collected using standardized data collection tools. All data was analyzed by using SPSS version 25. Descriptive statistics was used to describe demography, clinical characteristics, treatment modalities and survival pattern. Survival was estimated using Kaplan-Meier analysis. Uni-variant was performed to identify association of predictive factors (patient, disease and treatment related) with survival.

**Results:** A total of 50 patient were analyzed; the median age of diagnosis was 55.61 years old with  $SD \pm 12.77$ . Female patient accounted 56%. About 38% of the patient had underlying comorbidities, 70% of the patient presented with abdominal pain, in 90% of the patient diagnosis was made with tissue confirmation, 54% the patient had elevated CA19.9. CT scan was done for most of the patients. The most common site was gallbladder cancer accounting 44%, 68% presented with metastasis and the rest were locally advanced and adenocarcinoma was the frequent histologic type (68%). Surgery was done for 17 patients and of this 6 patient achieved complete resection. The most common first line systemic therapy was chemotherapy in 82% with cisplatin plus gemcitabine. About 22% (11) patient were found to have progressive disease following any first line therapy and 7 patients started second line systemic therapy with FOLFOX. By the time of data analysis about 70% patient were died with median overall survival of 6 month (95% CI, 4.85-7.14 months), and 1-, 2-, and 3-year overall survival of 28.6%, 11.4% and 2.9% respectively. Patient with underlying medical illness (Hypertension), first line chemotherapy with cisplatin plus gemcitabine who completed or received 6 cycles and who achieved partial response had better median and overall survival.

**Conclusions:** The survival outcomes of biliary tract cancer patients was very poor. Doublet chemotherapy is the commonest patterns of treatment. Being hypertensive and receiving 6 cycles of doublet systemic chemotherapy were associated with improved survival.

**Key word: Biliary Tract Cancer, Overall survival**

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## ***Abbreviations and Acronym***

<i>AAU</i>	<i>Addis Ababa University</i>
<i>AFP</i>	<i>Alpha-fetoprotein</i>
<i>AJCC</i>	<i>American Joint Committee on Cancer</i>
<i>BILCAP</i>	<i>BILIary CAPECitabine</i>
<i>BTC</i>	<i>Biliary tract cancers</i>
<i>CA19-9</i>	<i>carbohydrate antigen 19–9</i>
<i>CAPOX</i>	<i>Capecitabine Oxaliplatin</i>
<i>CCI</i>	<i>Charlson Comorbidity Index</i>
<i>CEA</i>	<i>Carcinoembryonic Antigen</i>
<i>DFS</i>	<i>Disease-Free Survival</i>
<i>EBRT</i>	<i>External beam radiotherapy</i>
<i>ECCA</i>	<i>Extrahepatic cholangiocarcinoma</i>
<i>ECOG</i>	<i>Eastern Cooperative Oncology Group</i>
<i>ERCP</i>	<i>Endoscopic retrograde cholangio-pancreatography</i>
<i>FNAC</i>	<i>Fine needle Aspiration</i>
<i>FOLFOX</i>	<i>Folinic acid Fluorouracil Oxaliplatin</i>
<i>GBC</i>	<i>Gallbladder cancer</i>
<i>GC</i>	<i>Gemcitabine and Cisplatin</i>
<i>GLOBOCAN</i>	<i>Global Cancer Observatory</i>
<i>HR</i>	<i>Hazard Ratio</i>
<i>ICCA</i>	<i>Intrahepatic cholangiocarcinoma</i>
<i>MRI</i>	<i>Magnetic resonant imaging</i>
<i>MRCP</i>	<i>Magnetic resonant cholangio-pancreatography</i>
<i>OS</i>	<i>Overall survival</i>
<i>RECIST</i>	<i>Response Evaluation Criteria in Solid Tumors</i>
<i>TASH</i>	<i>Tikur Anbessa specialized Hospital</i>
<i>USA</i>	<i>United state of America</i>

## CHAPTER 1. BACKGROUND

### 1.1. Introduction

Biliary tract cancers (BTCs); including intrahepatic, extrahepatic cholangiocarcinoma and gallbladder cancer are uncommon representing 1% of adult cancer and clinically heterogeneous tumors that differ in epidemiology, biology, presentation and outcomes across subtypes and region(1–3). The incidence of cholangiocarcinoma in western world is 0.35-2cases per 100000 annually; however highest in Asia and south America; China and Brazil respectively reaching 40 times higher than the study observed in UK(1,4–6). Gallbladder cancer (GBC) also shows striking geographic and sex disparities. GLOBOCAN 2018 estimated 219,420 new GBC cases and 165,087 deaths occurred worldwide in 2018, with particularly high rates among women in Chile, India, Poland and Pakistan; by contrast, incidence is generally stable or declining in many high-income countries, possibly related to routine cholecystectomy(7,8). Data from Africa remain sparse; a retrospective series from Khartoum, Sudan, reported that most GBC patients were female and presented with advanced disease(9). National data remain limited; for Ethiopia, a 2019 report recorded 520 BTC cases with a standardized incidence rate of 1.4, but subtype detail and completeness are insufficient(10,11).

Both gallbladder cancer and cholangiocarcinoma frequently manifest with non-specific systemic symptoms such as weight loss, anorexia and fatigue(3,6,9). Jaundice; a marker of advanced disease caused by intrinsic or extrinsic biliary obstruction from tumor, nodal enlargement or liver metastases is reported in roughly 21-72%% of cases, with variation by primary site (3). Because early symptoms are vague, many patients present late: 50-80% have locoregionally advanced or metastatic disease at diagnosis, a pattern also noted in African cohorts(3,9).

The diagnosis of Biliary tract cancer integrates clinical assessment of patient condition, liver function tests, cross-sectional and cholangiographic imaging and tumor markers. Abdomen and pelvic CT-scan; the most common imaging used for diagnosis and staging, has overall accuracy of 87% and MRI/MRCP which also provide detailed anatomy and characterization of lesion and vascular relation to assess resectability and ERCP allows ductal visualization, biliary drainage and tissue sampling (brushings cytology and/or biopsy; sensitivity ~74%, specificity ~70%). CA19-9 lacks diagnostic specificity but can assist with prognostication and treatment response once a diagnosis is established(12–14).

Prognosis varies by subtype and stage at presentation and in some studies, there was also variation in survival based on performance status and sex of the patient. A population based retrospective study from Iceland, Canada and Thailand showed five-year survival rate of 15% and 24% for male and female respectively with worst prognosis seen in advanced stage(<2%) and intrahepatic cholangiocarcinoma(15–18). No sufficient data were available in Africa; with some single center study showed 5year overall mortality rate of 56% in early-stage gallbladder cancer who under gone radical surgery(9). And retrospective chart review from European study also showed poor survival in this malignancy with 5year survival rate of <2%(18).

Management is complex and ideally guided by a multidisciplinary team. Surgical resection offers the only chance of cure for resectable tumors, with operative strategy determined by primary site(18–22). Despite curative-intent surgery, recurrence is common and pattern of recurrence differ by subtype: GBC is more prone to distant failure, while extrahepatic cholangiocarcinoma more often recurs locoregionally(21,22). High recurrence rates warrants the use of adjuvant therapy to improve relapse-free and overall survival while preserving quality of life which is supported by observational and prospective study and different national guideline's and experts recommended different kind of adjuvant therapies (23–29).

Most patients present with unresectable or metastatic disease and only both systemic and palliative local therapy improves survival over best supportive care(29–39). In advanced setup liver transplantation offer long term survival in retrospective studies(37–39).

In low- and middle-income countries, including Ethiopia, late presentation is compounded by constrained access to advanced imaging, endoscopy, pathology, systemic therapy and complex surgery or transplantation. Regional studies document high proportions of advanced-stage presentation, reliance on palliative treatment and high mortality(10,29).

## 1.2. Statement of the Problem

Biliary tract cancers (BTCs), including intrahepatic and extrahepatic cholangiocarcinoma as well as gallbladder cancer, are uncommon malignancies accounting for only about 1% of adult cancers globally(1). Despite their rarity, they are highly aggressive, clinically heterogeneous, and associated with poor prognosis(4,6). The global burden is unevenly distributed: while incidence remains low in most high-income countries, exceptionally high rates are reported in parts of Asia and Sout(1,5,8,11). Gallbladder cancer in particular shows striking geographic and sex disparities, disproportionately affecting women in countries such as Chile, India, and Pakistan[8].

In Africa, however, data on BTC remain very limited. The few available studies, such as those from Sudan, suggest that most patients present late with advanced disease(9,29). Similarly, in Ethiopia, from Addis Ababa cancer registry data from 2019 reported only 520 BTC cases with a standardized incidence rate of 1.4, but lacked essential detail on subtypes, stage at presentation, clinical features, and outcomes(10). This scarcity of reliable data hinders accurate estimation of the true burden of BTC in the region and prevents development of evidence-based prevention and management strategies.

Compounding the problem, BTCs often present with vague and non-specific symptoms such as anorexia, fatigue, and weight loss, which delay diagnosis until advanced or metastatic stages in about 50-72% of cases(3,6,9). Even when surgical resection is feasible, recurrence rates remain high, and adjuvant therapies are inconsistently applied(21–23). In resource-constrained settings such as Ethiopia, challenges are further amplified by limited access to advanced imaging, histopathology, endoscopy, systemic therapies, and specialized surgical or transplant services. Specifically in Ethiopia no national or local studies are available regarding patient presentation, clinical characteristics, pattern of treatment and their outcome.

In conclusion, BTCs represent a neglected but fatal cancer disease in Ethiopia. The combination with late presentation, inadequate diagnostic facilities, limited treatment options, and scarcity of robust epidemiological data creates a major gap in understanding the disease burden and outcomes. Without comprehensive local studies, efforts to design targeted prevention, timely diagnosis, and effective management strategies remain severely compromised. This study aims to address and provide valuable insights into the patterns of presentation, treatment approaches, and outcomes of BTC patients in Ethiopia.

### **1.3. Significance of the study**

This study is significant as it sheds light on the real-world characteristics, clinical presentation, treatment approaches, and outcomes of patients with biliary tract cancer. It also explored the common challenges related to disease presentation, adherence to treatment guidelines, and gaps in existing studies. By addressing these issues, the study aims to provide valuable insights into treatment strategies, survival outcomes, and other critical aspects of managing this cancer type. Ultimately, the findings can help inform clinical practice and support evidence-based decision-making for healthcare professionals in Ethiopia and beyond.

## **CHAPTER 2. LITERATURE REVIEW**

### **2.1. Demography of biliary tract cancer patient**

Biliary tract cancers are diverse group of malignancy that differ in age, sex and underlying comorbidities(3–5,7,9,15,16). These disparities also depend on the anatomic location of the tumor origin in the biliary trees. In western countries; the peak age incidence of cholangiocarcinoma is the seventh decade of life with slight male predominance and rarely occurs before fourth decade of life(4,7). Age at diagnosis for biliary malignancy was consistently lower in men compared to women, specifically for extrahepatic cholangiocarcinoma in men. Intrahepatic cholangiocarcinoma was diagnosed at a younger age in both sexes(15). Patient in their seventh to eighth decade of life has also 5-10times higher mortality rate(3,5). Unlike cholangiocarcinoma, gallbladder cancer is more common females with 2:1 ratio(3,9,16). Underlying comorbidities are very common in biliary tract malignancy occurring one third of cases and meta-analyses and population studies consistently link type II diabetes to an increased risk of both iCCA and eCCA, with a particularly strong association observed for iCCA(3,4). Patient with underlying chronic illness had poor tolerance to both medical and surgical treatments which require optimization of systemic therapy and operability(3,18).

### **2.2. Clinical presentation of biliary tract cancer patient**

BTC presents unique challenges and clinical presentation depends on anatomic location of tumor, stage of the disease and underlying liver condition(3–5,7). Gallbladder cancer may be incidental finding during or after cholecystectomy for benign disease or may present with abdominal pain or bloating (66%), nausea and vomiting(20-49%) (6,7). Both gallbladder and cholangiocarcinoma also present with non-specific symptom such weight loss, anorexia, and fatigue(6,7,9). Jaundice; sign of advanced disease; observed in around 60%cases with some variation based on site of tumor origin and caused by extrinsic or intrinsic compression of bile duct by the tumor, enlarged lymphadenopathy and liver metastasis from extrahepatic cholangiocarcinoma or gall bladder carcinoma(9).

### **2.3. Diagnosis of biliary tract cancer patient**

Significant number of patient present with non-specific symptom making the diagnosis at early stage difficult and 80% are locoregional advanced or metastatic disease(3,6,9). In gallbladder cancer patient may be asymptomatic and malignancy is identified incidentally, through detection of deranged liver function or imaging for unrelated scenarios(9). Medical history, liver function test, various imaging technique and tumor markers are used to make diagnosis, stage and predict the prognosis(12–14). Transabdominal ultrasound is the first imaging choice for evaluation of gallbladder anatomy and space occupying mass in the liver with limited accuracy for staging. CT- can be the main modality in diagnosing, and staging of both cholangiocarcinoma and biliary tract cancer with overall accuracy of 87%, specificity of 75-91% and determining resectability sensitivity of 37-73% and it can also evaluate potential peritoneal implants and distant metastasis

to the liver and other visceral organs(12). Magnetic resonant imaging(MRI), can also provide more anatomic details of liver, bile duct and gallbladder and characterization of cancer, differentiation of hepatocellular carcinoma vs intrahepatic carcinoma, as well as evaluation of vascular invasion with sensitivity of 91% and specificity 87%(13). Endoscopic retrograde cholangio-pancreatography (ERCP) with additional benefit of biliary dilatation and acquisition of brush cytology and biopsy is well established modality to assess biliary tree and having sensitivity and specificity 74% and 70% respectively(13,14). Elevation of Serum carbohydrate antigen 19.9 (CA19.9), on the background of established diagnosis of biliary tract cancer it provide information on response to treatment and prognosis and because of low specificity not used for diagnosis

#### **2.4. Survival outcome of biliary tract cancer patient**

Five-year survival rates are highly variable, depending on the specific type of BTC (intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma, or gallbladder cancer), stage the disease, sex and performance of the patient at diagnosed(8,9,15,17,18,20,27–29,38). These rates range from 2% to 30% for cholangiocarcinoma and 2% to 70% for gallbladder cancer, with significantly better outcomes for patients diagnosed at earlier stages((28,29). Intrahepatic cholangiocarcinoma (iCCA) generally carries the poorest prognosis, while distal extrahepatic cholangiocarcinoma tends to have the most favorable outcome. The presence of distant metastases at diagnosis dramatically reduces survival; five-year survival drops to as low as 2-3%(15–19,26–29). Older individuals above the age of 75years and poor performance status( $\geq 2$ ) are also higher mortality rate with shorter median overall survival across all tumor subtype(5,18). Most reported data had similar survival rate in both gender with non-statistically significant difference(5,15,16). Patient treated with surgery with complete resection and without recurrence had better long-term outcome(17,21–24).

#### **2.5. Treatment pattern of biliary tract cancer patient**

Treatment of biliary tract cancer is complex which depends on patient related factors(performance status, presence of comorbidities such as hypertension, diabetes mellitus), cancer related variables (tumor stage) and availability of expertise; and typically managed with involvement of specialties on having multidisciplinary discussion to improve outcome of treatment(18–20,26,27). Surgery is the only curative treatment modality for resectable disease and the approach depends on primary location of the cancer(18,28). Surgery is also modality of palliative option as biliary drainage in advanced disease to palliate obstructive jaundiced symptoms by making bypass surgery(22,28,29).

Despite having curative resection, most biliary tract cancer will have recurrence either systemic or locoregional; gallbladder cancer more prone to distant recurrence, while extrahepatic cholangiocarcinoma is more likely to recur locally, in the region surrounding the initial tumor site(21–25,28). Supplementary treatment is required and aims to improve both relapse-free and overall survival while preserving the patient's quality of life(21–25,27,28).

The currently available research is focused on evaluating adjuvant therapy to enhance outcomes for biliary tract cancers. This includes comparing different chemotherapy regimens to observation alone and investigating the effectiveness of chemoradiation (a combination of chemotherapy and radiation therapy)(21–25,37,39).

BILCAP trial showed adjuvant capecitabine chemotherapy for six months after radical surgery for early-stage disease significantly improved overall survival(25). Given that cholangiocarcinoma often recur locally, additional local treatment strategies like radiation therapy after surgery may be beneficial(37). Because gallbladder cancer tends to involve extensive local and regional spread as well as a high likelihood of distant metastasis, both radiation and chemotherapy may be valuable in the adjuvant setting for both gallbladder and cholangiocarcinoma(29,37).

Unresected locally advanced or distant metastatic patient have poor outcome with median survival of ranging 1-3months without treatment(6,15,19,20,29). For individuals with advanced BTC, systemic therapy offers a survival advantage compared to supportive care alone(26,29–35). For the past decade, the combination of gemcitabine and cisplatin (GC) has been the standard of care, based on robust evidence from clinical trials. This regimen significantly improved median overall survival compared to single-agent gemcitabine(34). However, the survival benefit associated with GC remains modest, underscoring the need for more effective treatment options. Recent progress in chemotherapy combinations, immunotherapy, and targeted therapies based on specific genetic markers holds considerable promise(34–36). Recent phase III trial (TOPAZ-1) demonstrated a statistically significant improvement in overall survival for patients with advanced BTC who received durvalumab combined with chemotherapy compared to those treated with chemotherapy alone(36). This finding offers hope for enhanced patient outcomes

There are also promising treatment option now adays such as neoadjuvant chemoradiation followed by liver transplantation, external beam radiotherapy, radioembolization, and chemoembolization for locally advanced BTC(37–39). Liver transplantation offers a potentially curative option for unresectable hilar cholangiocarcinoma, with studies reporting favorable long-term survival rates. One study showed a 5-year survival rate of 82% in transplant recipients, compared to only 21% in patients who underwent surgical resection(38).

## 2.6. Conceptual frame work

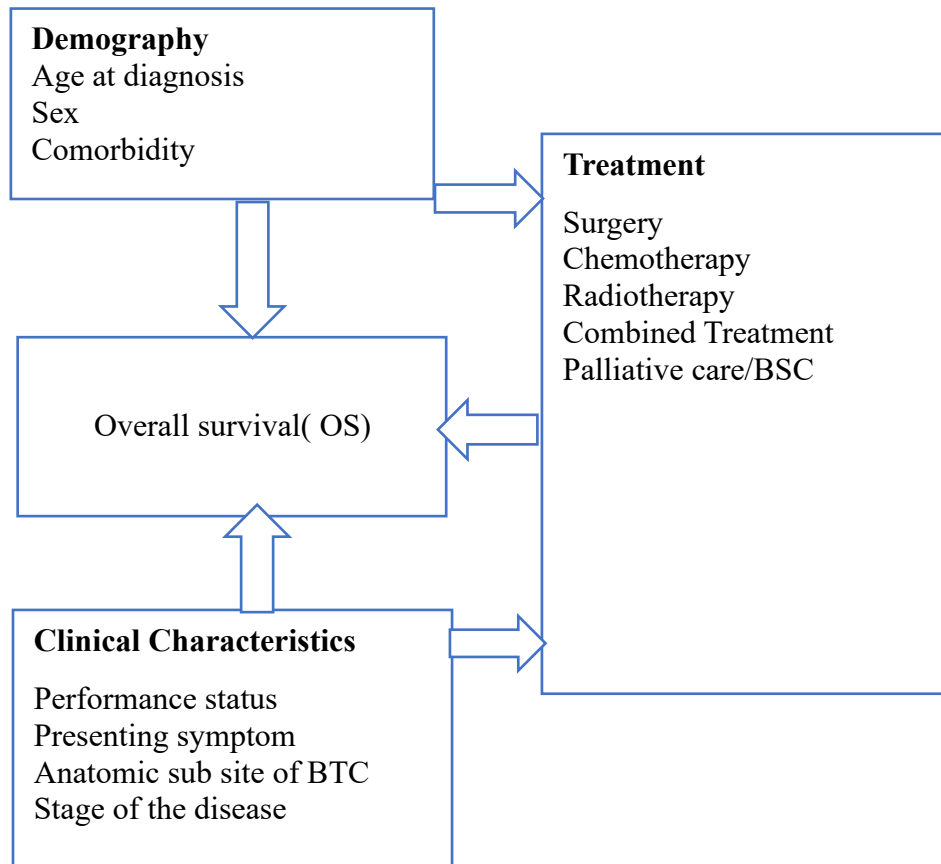


Figure 1:-Conceptual frame work indicating possible relation between dependent and independent variables( newly developed)

## **CHAPTER 3. OBJECTIVES**

### **3.1. General Objective**

- ✓ To investigate the clinical characteristics, treatment approaches and survival of biliary tract cancer (BTC) patients at Tikur Anbesa Specialized Hospital, over a five-year period (between January 1, 2020 and September 01, 2025)

### **3.2. Specific objectives**

- ✓ To describe the clinical characteristics of patients diagnosis with biliary tract cancer
- ✓ To evaluate the treatment modalities used for biliary tract cancer at Tikur Anbesa Specialized Hospital
- ✓ To estimate the survival of patients with biliary tract cancer

## **CHAPTER 4. MATERIALS AND METHODS**

### **4.1. Study Area and Period**

The study was conducted from January 01, 2020 – September 01, 2025 at Tikur Anbessa Specialized Hospital oncology department in Addis Ababa, Ethiopia. Addis Ababa is the capital city of Ethiopia. Tikur Anbessa specialized Hospital is one of Ethiopia's leading tertiary care centers, serving as a national referral hospital for complex cases and providing specialized care to patients from across the country, with a population of over 120 million. The Hospital provides health services for approximately 25 thousand inpatients and 400 thousand outpatients in a year with a bed capacity of 755. Most of the cases of biliary tract cancer diagnosed at TASH are linked to oncology for evaluation and treatment. Oncology department has its own ward with 28 inpatient and outpatient 12 bed for chemotherapy, radiotherapy services with both External beam radiotherapy(EBRT) and Brachytherapy, which was serving more than 10,000 patient per year for more than two decades.

### **4.2. Study design**

- ✓ Institutional retrospective cohort study was conducted.

### **4.3. Population**

#### **4.3.1. Source population**

- ✓ All biliary tract cancer patients who was treated and on follow up at Tikur Anbessa Specialized Hospital during study period.

#### **4.3.2. Study population**

- ✓ All biliary tract cancer patients who meet the inclusion criteria

### **4.4. Data collection period:**

- ✓ From October 01, 2025 to October 30,2025

### **4.5. Inclusion and Exclusion criteria**

#### **4.5.1. Inclusion criteria**

- ✓ Biliary tract cancer diagnosed with either imaging and tumor marker with or without biopsy
- ✓ Adequate staging documentation
- ✓ Patients diagnosed within the specified study period.

#### **4.5.2. Exclusion Criteria**

- ✓ Patient with incomplete records
- ✓ Non-volunteers who cannot provide any medical information up on phone calls for survival status.

#### **4.6. Sample size and Sampling technique.**

- All biliary tract cancer patients who fulfilled the inclusion criteria during the study period.

#### **4.7. Study Variables**

##### **4.7.1. Independent Variables**

- Age, sex, place of residency
- Comorbidities
- ECOG Performance Status
- Anatomic location of tumor
- AJCC stage of Biliary tract cancer
- Treatment pattern

##### **4.6.2. Dependent variable/ outcome**

- Survival

#### **4.8. Data collection procedures**

The data was collected by trained oncology residents from patient's medical record available on their I-CARE number registered on electronic card numbering system, which contained key details of the patients name, age, diagnosis, treatment and follow up. Data collection began with extracting electronic card number from new patient registrations, results and follow up forms. Initially 62 patients were extracted. While reviewing 12 patients were removed (7 non-biliary tract malignancy, 5 incomplete data). For the rest 50 cases; data was collected with standardized data collection tools. To supplement existing records and address data gaps, patients or their families were contacted by phone to determine survival status. Of 50 cases, 42 cases were reached successfully and the rest couldn't be contacted because their phone numbers were nonfunctional.

#### **4.9. Data management and Statistical analysis.**

All collected data were anonymized to protect patient confidentiality. Double data entry and data cleaning procedures were implemented before running the analysis to ensure data accuracy and exported to SPSS version 25. Normality tests were performed using visual inspections of histograms, Q-Q plots, and Shapiro-Wilk tests. Descriptive Statistics were used to summarize patient demographics, clinical characteristics, treatment patterns, and survival outcomes. Median and overall survival (OS) was estimated using Kaplan-Meier analysis. Uni-variate cox regression was used to identify and analyze the association between predictors of survival.

#### **4.10. Ethical consideration**

Ethical clearance and approval for the study was obtained from Institutional Ethics Review Board of college of health science, Addis Ababa University. Ethical clearance was obtained from TASH;

Permission was obtained from Chief Executive Director of the hospital and unit leaders and privacy was maintained. Patient confidentiality was maintained

#### 4.11. Operational definition

- **Patient Demography** :- Characteristics of the patient population, including age, sex, ethnicity, and socioeconomic status
- **Performance Status**:- Performance status refers to a patient's general well-being and ability to carry out daily activities, assessed using the Eastern Cooperative Oncology Group (ECOG) Performance Status Scale.
  - ECOG 0: Fully active without restriction.
  - ECOG 1: Restricted in strenuous activity but can perform light work.
  - ECOG 2: Ambulatory and capable of self-care, but unable to do work activities; up more than 50% of waking hours.
  - ECOG 3: Capable of limited self-care; confined to bed or chair more than 50% of waking hours
  - ECOG 4: Completely disabled; cannot do self-care; confined to bed or chair.
- **Clinical Characteristics**:- Medical conditions and features of the disease, such as tumor stage, grade, histology, and presence of comorbidities
  - **Tumor Stage**: The anatomical extent of disease according to the AJCC 8th edition TNM staging system.
  - **Tumor Grade**: The level of cellular differentiation on a standardized **1–3scale** (G1: well-differentiated; G2: moderately differentiated; G3: poorly differentiated /undifferentiated)
  - **Histology**: The specific tissue type and cellular pattern classified according to the World Health Organization (WHO) Classification of Tumors.
  - **Comorbidities**: individual who had one or more listed comorbidities in the **Charlson Comorbidity Index (CCI)**.
- **AJCC Stage of Biliary Tract cancer**:- The extent of the disease based on the size of the tumor, the involvement of lymph nodes, and the presence of metastasis.
- **Adequate staging**:- Determining the extent of disease which consisting of primary tumor size or invasion of adjacent organs, presence of lymph node and distant metastasis, with minimum of contrast enhanced abdominal CT, chest x ray, CA 19 9 and liver function tests
- **Treatment Pattern**:- The specific regimen or combination of therapeutic interventions administered to biliary tract cancer patients.
- **Overall survival**:- The duration of time from the date of diagnosis to the date of death from any cause.
- **Median overall survival**:- The time from the date of initial biliary tract cancer (BTC) diagnosis until the point at which 50% of the patient population is expected to have died from any cause.

#### **4.12. Dissemination plan and use of the result**

The findings of this study will be presented to the Department of Clinical Oncology as part of the thesis defense. A summary report will be submitted to Addis Ababa University (AAU). In addition, the results will be shared with clinicians involved in the treatment of biliary tract cancer to help identify key areas for improving patient outcomes in this setting. Efforts will also be made to publish the findings in peer-reviewed journals to contribute to the broader scientific community and support evidence-based practice

## 5. RESULT

### 5.1. Sociodemographic characteristics

A total of 62 patient chart were extracted and reviewed from I-CARE; an electronic patient data documentation system. Twelve cases were excluded for analysis due 7cases had non biliary tract cancer(pancreatic cancer=3 and hepatocellular carcinoma=4) and 5 cases for incomplete data. A total of 50 case was analyzed for survival. About 35(70%) of the patient died during data analysis (95% CI, 0.57-0.83) and the remaining 30% were censored.

The median age of diagnosis was 55.61(SD±12.77)years ranging from 32 -79 years old. Female patient account 56% of the study. Seventy percent of the patient were populated in Urban area and about 44% of patients was from Addis Ababa and 26% from Oromia. In about 38% (n=19) of the cases underlying chronic illness was observed. Among these, hypertension and diabetes mellitus were identified as the most common co-morbidities.

Table 1:*Sociodemographic and Clinical Characteristics of biliary tract cancer patient; TASH, January 1, 2020 -September 01, 2025*

Variable	Category	Frequency(N)	Percent(%)
<b>Age(years)</b>	31-45	12	24.0%
	46-59	18	36.0%
	60-75	16	32.0%
	>75-80	4	8.0%
<b>Gender</b>	Male	22	44.0%
	Female	28	56.0%
<b>Region</b>	Tigray	2	4.0%
	Afar	2	4.0%
	Amhara	4	8.0%
	Oromia	13	26.0%
	Benishangul	1	2.0%
	SNNP	6	12.0%
	Addis Ababa	22	44.0%
<b>Residency</b>	Rural	15	30.0%
	Urban	35	70.0%
<b>Educational Status</b>	No Education	20	40.0%
	Less than high school	8	16.0%
	High School Diploma	7	14.0%
	Degree and above	15	30.0%
<b>Underlying medical history</b>	No	31	62.0%
	Yes	19	38.0%
<b>Type of Underlying medical history</b>	Hypertension	9	18.0%
	Diabetes Mellitus	3	6.0%
	Chronic Kidney Disease	1	2.0%
	Cardiac Disease	1	2.0%
	Chronic Liver Disease	2	4.0%
	Retroviral infection(RVI)	3	6.0%

## 5.2. Clinical presentation of patients

A vast majority of the participants (96%) reported symptoms upon presentation, with only 4% being asymptomatic. The predominant initial symptom by far was abdominal pain, affecting 70% of the total sample. Jaundice and abdominal bloating were the next most common specific symptoms, each accounting for 8% of cases. The duration of these symptoms varied significantly among the 48 symptomatic patients; exactly half of these individuals experienced symptoms for longer than 90 days (41.7% of the symptomatic subgroup). Majority of the patient(80%) received their diagnosis at TASH.

*Table 2: Clinical Presentation and place of diagnosis of biliary tract cancer patient; TASH, January 1, 2020 -September 01, 2025*

Variable	Category	Frequency(n)	Percent(%)
Symptom at presentation?	No	2	4.0%
	Yes	48	96.0%
Initial Symptom	Abdominal pain	35	70.0%
	Dyspepsia	1	2.0%
	Jaundice	4	8.0%
	Abdominal bloating	4	8.0%
	Pruritus	1	2.0%
	Combination of symptoms	3	6.0%
Place of initial diagnosis	Hospital other than TASH	5	10.0%
	TASH	40	80.0%
	Private clinic	5	10.0%
Duration of symptom (Days)	<30 days	8	16.60%
	30-90 days	20	41.7%
	>90 days	20	41.7%

## 5.3. Diagnosis

The definitive diagnosis was established through biopsy (84.0%). Gallbladder was the most frequent primary cancer site (44.0%), followed by intrahepatic (ICCA) and extrahepatic cholangiocarcinoma (eCCA) each responsible for 34.0% and 22.0% cases respectively. Histologically, adenocarcinoma was the most common pathology (68.0%). The majority of patients presented with advanced disease; 60.0% were classified as T4 stage, 76% lymph node involvement (N1/N2) and 68.0% had metastasis (M1), predominantly to the liver (36.0%) and peritoneum (20.0%). Large proportion of patients maintained a good performance status, with 80.0% having an ECOG PS of 0 or 1. For CA19-9, 18.0% of patients had levels below the normal threshold of 37 U/mL, while 34.0% had elevated levels ( $\geq 37$  U/mL). A notable 28.0% of CA19-9 results were listed as unknown. CEA and AFP was less frequently tested biomarkers; only 14% and 10% of the patient had elevated respectively.

Table 3: Tumor Characteristics and Staging of biliary tract cancer patient; TASH, January 1, 2020 -September 01, 2025

Variable	Category	Frequency	Percent
Diagnostic Tools	Tissue (Biopsy/FNAC)	43	86.0%
	Imaging (CT/MRI)	5	10.0%
	Following surgery for other purpose	2	4.0%
Primary Cancer Site	Gallbladder	22	44.0%
	ICCA	17	34.0%
	eCCA	11	22.0%
Histology Type	Cholangiocarcinoma	6	12.0%
	Undifferentiated	2	4.0%
	Papillary carcinoma	1	2.0%
	Adenocarcinoma	34	68.0%
	Squamous Cell Carcinoma	2	4.0%
T-Staging	T2	2	4.0%
	T3	17	34.0%
	T4	30	60.0%
	Tx	1	2.0%
N-Stage	N0	7	14.0%
	N1/N2	38	76.0%
	Nx	5	10.0%
Group Stage	Early stage(T2N0M0)	1	2.0%
	Locally advanced	15	30.0%
	Metastasis(M1)	34	68.0%
Site of metastasis	Liver	18	36.0%
	Lung	3	6.0%
	Bone	2	4.0%
	Peritoneum	10	20.0%
Performance status(ECOG)	0 & 1	40	80.0%
	≥2	10	20.0%
Level of CA19.9(U/mL)	<37	9	18.0%
	≥37	17	34.0%
	Unknown	24	48.0%
Level of CEA(ng/mL)	<5	16	32.0%
	≥5	7	14.0%
	Unknown	27	54.0%
Level of AFP(ng/mL)	<20	13	26.0%
	≥20	5	10.0%
	Unknown	32	64.0%

#### 5.4. Treatment pattern

The primary first-line treatment approach varied, with chemotherapy being the most frequent choice (58.0%, n=29), followed by surgery (34.0%, n=17), best supportive care (6.0%, n=3), and radiotherapy (2.0%, n=1). The time gap between diagnosis and treatment initiation was began treatment within 6 weeks in most of the patients( 80.0% n=40). For those undergoing surgery, the intention was largely curative (26.0% n=13), while a smaller fraction (8.0%) received palliative

surgery. But post-surgical outcomes indicated that complete R0 resections were achieved in only (12.0%;n=6). Chemotherapy was predominantly administered with a palliative intent (78.0%, n=39). The specific chemotherapy regimen of choice was cisplatin combined with Gemcitabine, used in (80.0% n=40) of treated patients. Regarding the treatment course, (40% n=20) of patients successfully completed their full course of chemotherapy (6 cycles, n=20), while more than half (50%,n=25) did not complete the planned regimen. The main reasons of not completion were poor performance status (26.0%, n=13) and disease progression (14.0%, n=7), while a few individuals (4.0%, n=2) were still on treatment and the remaining (4.0%, n=2) were died while on chemotherapy.

*Table 4: Pattern of first line treatment and outcome of biliary tract cancer patient; TASH, January 1, 2020 -September 01, 2025*

Category	Category	Frequency	Percent (%)
Type of First Line Treatment	Surgery	17	34.0%
	Chemotherapy	29	58.0%
	Radiotherapy	1	2.0%
	Best Supportive Care	3	6.0%
Planned surgery	Palliative	4	8.0%
	Curative	13	26.0%
Outcome of surgery	Complete resection(R0)	6	12.0%
	Gross residual (R2)	11	22.0%
Intent of chemotherapy	Adjuvant	4	8.0%
	Palliative	39	78.0%
	Neoadjuvant	2	4.0%
	No Chemotherapy	5	10.0%
Type of 1 <sup>st</sup> line Chemotherapy	Capecitabine	1	2.0%
	Carboplatin + paclitaxel	2	4.0%
	Cisplatin+ Gemcitabine	40	80.0%
	Gemcitabine	2	4.0%
Cycles of Chemotherapy Received	<3 cycles	9	18.0%
	3-5 cycles	16	32.0%
	6 cycles	20	40.0%
Completion status of 1 <sup>st</sup> Line Chemotherapy	Yes	20	40.0%
	No	25	50.0%
Reason for not completion of chemotherapy.	Poor PS	13	26.0%
	Disease Progression	7	14.0%
	Unknown	1	2.0%
	Death	2	4.0%
	Still on Chemotherapy	2	4.0%
Time Gap of 1 <sup>st</sup> Line Treatment initiation after the diagnosis	<6 weeks	40	80.0%
	6-12 weeks	5	10.0%
	>12 weeks	2	4.0%

#### **5.4.1. Response evaluation and Outcome**

Responses to treatment were evaluated after three cycles of chemotherapy. Responses were calculated by response evaluation criteria in solid tumors RECIST version1.1(Response Evaluation Criteria in Solid Tumors version 1.1). The primary method for assessing treatment

response was Imaging (CT/MRI) (40% of patients), followed by a combination of imaging and tumor markers (22%). The outcome of this first-line therapy varied, with the highest frequency patient had a progressive disease ( 22%, n=11), while only 6% achieved a Complete Response.

A specific analysis of the 11 patients whose disease progressed revealed that progression was most frequently locoregional (8%) and typically identified via mid-cycle imaging (14%). Of these 11 patients, 7 went on to receive a second line of treatment, commonly using the FOLFOX regimen (8%). A notable observation is that most of these patients did not complete the subsequent therapy; only 2 of the 7 individuals finished their second line of treatment.

*Table 5: Response to First-Line Therapy and Subsequent Treatment Patterns of biliary tract cancer patient; TASH, January 1, 2020 -September 01, 2025 .*

Variable	Category	Frequency(N)	Percent (%)
Response Assessment Modality of first line therapy	Imaging(CT/MRI)	20	40.0%
	Imaging(CT/MRI) and Tumor Marker	11	22%
	Not Assessed	11	22%
	Unknown	3	6%
Outcome of First Line Therapy	Partial Response	10	20%
	Complete Response	3	6%
	Stable Disease	7	14%
	Progressive Disease	11	22%
Site of progression	Locoregional	4	8%
	Lung	3	6%
	Liver	2	4%
	Bone	1	2%
	Combination(locoregional and liver)	1	2%
Timing of pression	Mid Cycle Imaging	7	14%
	End Cycle Imaging	4	8%
Second line treatment	No	4	8%
	Yes	7	14%
Type of second line chemotherapy	FOLFOX	4	8%
	CAPOX	1	2%
	Cis/Gemcitabine	2	4%
Completion of second line treatment	Yes	2	4%
	No	5	10%

## 5.5. Survival Analysis

The Kaplan–Meier estimator was used to estimate survival curves for categorical predictors. Factors/predictors such as the presence and type of underlying comorbidities, type and total cycle of chemotherapy received, completion rate of systemic therapy, reason of discontinuation and outcome of first line treatment was statically significant with univariate analysis of P-value <0.05 with Kaplan-Meier method compared with long-rank test.

*Table 6: Univariate Analysis of Factors Associated with Overall Survival (OS) and 1-2-, and 3year overall survival of biliary tract cancer patient; TASH, January 1, 2020 -September 01, 2025*

Variable	Category	Median OS (month)	p-value	95% CI(month)		1year OS	2year OS	3year OS
Comorbidity	Yes	9	0.004	1.42	16.57	45%	20%	6.7%
	No	5		3.97	6.03	10.5%	5%	0.0%
Type Comorbidity	Hypertension	17	0.007	11.15	22.84	55.6	44%	11%
	Type2 Diabetes mellitus	13		.00	27.40	33%	0.0%	0.0%
	No chronic illness	5		3.97	6.03	10.5%%	5%	0.0%
Type of 1st line chemotherapy	Carboplatin/Paclitaxel	3	0.024	-	-	-	-	-
	No chemotherapy	2		0.92	3.07	15%	0%	-
	Cisplatin+ Gemcitabine	7		4.15	9.84	34.6%	15.4%	3.8%
	Gemcitabine	2		-	-	-	-	-
Cycles of chemotherapy received	< 3 cycles	3	0.000	0.22	5.77	0%	-	-
	3-5 cycles	6		4.32	7.67	25%	0%	-
	6 cycles	15		0.00	33.59	60%	40%	10%
Patient completed 1st line chemo	Yes	15	0.003	0.00	33.59	60%	40%	10%
	No	5		4.14	5.85	10%	0%	-
Reason of discontinuation	Poor PS	5	0.004	3.88	6.11	8.3%	0%	-
	disease progression	9		0.41	17.58	20%	0%	-
Outcome of 1 <sup>st</sup> line therapy	Partial response	16	0.000	.00	37.60	50%	33%	3%
	Stable disease	7		4.85	9.14	20%	0%	-
	Progressive disease	9		3.15	14.84	33%	11%	-
	Unknown	2		.	.			
	Not assessed	5		4.38	5.62	10%	0%	-
<b>Overall</b>		6		4.87	7.12	28.6%	11.4%	2.9%

Patient with underlying comorbidities had significantly higher median overall survival of 9months (95% CI: 1.42–16.57 months,  $p=0.004$ ) and better 1-, 2-, and 3-year survival rates of 45%, 20%, and 6.7%, respectively as compared to those patients without comorbidities median OS of 5 months (95% CI: 3.97–6.03 months). From these comorbidities; individual with hypertension had the longest median OS (17 months, 95% CI: 11.15–22.84,  $p=0.007$ ), achieving high 1-year (55.6%) and 2-year (44%) survival rates. In contrast, those with T2DM had a median OS of 13 months (95% CI: 0.00–27.40), but both types 2 diabetes mellitus and those individual without chronic illness had poor long-term outcomes none of the patient survived up to 3years.

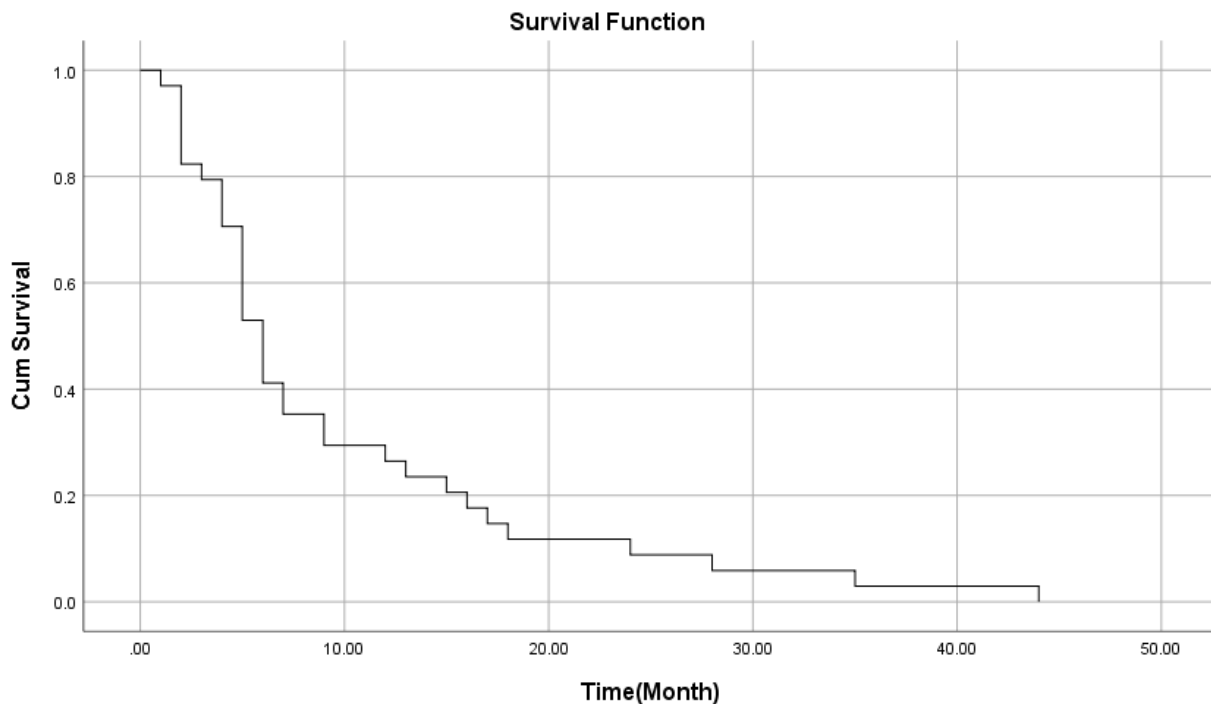
The type of first-line chemotherapy also demonstrated varied effectiveness. Patient who received cisplatin plus gemcitabine had better median OS of 7 months (95% CI: 4.15–9.84months,  $p=0.024$ ) and 34.6% surviving at 1 year, 15.4% at 2 years, and 3.8% at 3 years. In contrast; patient who were on less frequent systemic therapy(gemcitabine monotherapy, carboplatin plus paclitaxel) or who did not receive any systemic therapy had shorter median survival and poor 1year overall survival.

The cycle of chemotherapy received had also significant prognostic for survival. Patient receiving 6cycle had the best outcome: a median OS of 15 months (95% CI: 0.00–33.59months, p=0.000), with 60%, 40%, and 10% survival at 1, 2, and 3 years, respectively. Patient receiving <3cycle had the worst median overall survival of 3months(95% CI:0.22-5.77months) and almost all patient did not survive up to one year.

Similarly; patients who completed their first-line chemotherapy regimen had a median OS of 15 months (95% CI: 0.00-33.59months, p=0.003) the highest survival rates compared to just 5 months for those who did not complete the regimen. Reasons for discontinuation systemic therapy were also analyzed. Discontinuation due to poor performance status resulted in a shorter median OS of 5 months, while discontinuation due to disease progression had a better median OS of 9 months(95% CI:0.41-17.58months, p=0.004).

Finally, the outcome of the first-line therapy strongly predicted survival. Patients achieving a partial response had the best prognosis, with a median OS of 16 months(95% CI: 0.00-37.6months, p=0.000). and survival rates of 50%, 33%, and 3% at 1, 2, and 3 years.

By the time of data extraction about 70% patient were died with median overall survival of 6month(95% CI, 4.85-7.14months), 1- 2- and 3-year overall survival of 28.6%, 11.4% and 2.9% respectively. Multivariate analyses were performed, using a Cox proportional hazards model, to explore how underlying comorbidities, type and cycle of first line chemotherapy, their completion status, reason for discontinuation and the response rate of treatment. All the predictors were not associated the outcome of the study(Median overall survival).



**Figure 2:- Overall survival of biliary tract cancer(Median OS 6month (95% CI, 4.85-7.14)**

## 6.DISCUSSION

Single-center institutional studies are scarce. This retrospective study provides views on clinical presentation, treatment patterns, and survival outcomes. Fifty patients were analyzed. Most patients were aged 46–59; with the median age at diagnosis of 55.61 years (range 31–79). This is consistent with two Indian retrospective studies with a median age of 57(30,31). Unlike this in Western population-based and SEER database analyses, the median age was ranging 60–70 years(9,15–21).

In our study, more than half of the patients were female (56%), consistent with most reported data's(9,16,19–21,26,31); however, some European and population-based studies still report a male predominance(3)(18,31).

More than one third (38%) of patients had comorbidities. Specifically, hypertensive cases showed statistically significant median and overall survival rates. This contradicts with most studies, where comorbidities hindered treatment initiation and lowered overall survival(3,18,20,26,35). Better outcomes in our study may result from comorbid patients seeking earlier care and radical treatment. Additionally, our small sample size complicates detecting differences, and our participants were younger, with a median age of 55.61, compared to other studies(9,15–21).

The most common presentation of symptomatic patients was abdominal pain in 70%. This was very similar to findings from a study in Sudan where it occurred in 66% of patients(9). Unfortunately, in this study jaundice was less frequent despite advanced disease; this finding differs significantly from European and Canadian studies, where over 50% of patients had jaundice or elevated bilirubin(3,18,19,26). The low frequency of jaundice observed in our patient population is likely attributable to several factors. Primarily, the study had a limited sample size, which was a constraint inherent to the research design. Additionally, the lack of data regarding serum bilirubin levels meant this key indicator could not be thoroughly assessed. At diagnosis majority(80%) of the patient had good performance status(ECOG-0&1) which determined their treatment pattern; consistent to other studies(3)(16,18,26,33).

With few exceptions; most of our patients(90%) were diagnosed by tissue based either preoperative biopsy or FNAC, which was mandatory to make a diagnosis of biliary tract cancer. In about 5 patients; diagnosis was made based on symptom plus image finding. This was not standard methods; but sometimes for various reason patient may not have definitive tissue diagnosis. There was retrospective study in Thailand that they diagnosed patients with imaging for treatment of cholangiocarcinoma although they did not mention the possible reasons(17).

Consistent with other studies, gallbladder cancer was the most frequent primary site (45%), followed by intrahepatic cholangiocarcinoma(15,16,20,26,30). In some studies, intrahepatic cholangiocarcinoma unexpectedly appears more frequently than gallbladder cancer (3)(18,19,33,35). In this study, more than two-thirds of the patients had metastasis at diagnosis, which was a common clinical scenario consistent with other evidence(3,15,16,26,30,31).

Similarly, 38% of our study patients presented with locally advanced disease, due to either regional nodal metastasis or advanced T stage, which was comparable to reports from Icelandic and Canadian multicenter studies reporting 38% and 37.2%, respectively(15,16).

Only three patients received best supportive care; the remainder (94%, n=47) started at least one line of therapy, unlike other reports where about one-third of patients received supportive care(3,15–19,26,30,32). Among these treated patients, 95.7% began treatment within 90 days of diagnosis, while only 4.3% experienced delays. This is similar to a five-country European multicenter study where 7.8% of patients started treatment more than three months after their diagnosis(18,19).

Only a small number of patients in our study underwent surgery, and just 12% achieved R0 resection. This contrasts with a French study that reported higher R0 resection rates of 58% for ampulla cancer, 50% for gallbladder cancer, and 22% for ECC.(3). There were many reasons for this great variation in achieving a better surgical outcome: a multicenter design, a large sample size, a longer study period, a higher proportion of non-metastatic disease (48% versus 32%), and an advanced setup for surgery. In our study, data regarding the survival status for patients who had R0 resection was not possible to report because they were either few in number or lost to follow-up, unlike the French study where patients had a three-year overall survival of 63%(3).

In our study, chemotherapy with cisplatin plus gemcitabine was the most common first-line systemic therapy, used in 80% of patients, followed by gemcitabine monotherapy in 4%, which is consistent with other studies(16,18–20,26,30,31,34,35). The median overall and 1year overall survival of patient who received platinum doublet chemotherapy therapy in our study was 7months(95% CI, 4.15-9.8months) and 34.5% respectively; which had similar finding from SEER data analysis in 2023 and single institution retrospective study in Indian reporting cisplatin plus gemcitabine was used for 80.2% of patients and they had median overall survival of 8.1months (95% CI, 7.4–8.9 months) and one year overall survival of 33.9%(20,30). In our study, patients who completed a full course of cisplatin plus gemcitabine achieved better survival outcomes. This is similar to a US retrospective study evaluating this combination, which reported a median overall survival of 18 months (95% CI: 13–26 months). The discrepancy in median survival may be because patients in that study allowed to receive more than eight chemotherapy cycles if tolerated (35)

Response evaluation per RECIST criteria was feasible for 31 patients (62%). Disease progression occurred in 22% (n=11), while 36% had a combined response (20% partial response; 16% stable disease). The progression rate is consistent with two Indian retrospective studies (26.3–36.4%), yet the combined response rate differs (36% vs 61.4–73.4%), possibly due to their larger cohorts and longer study periods(30,31). Patients who achieved a partial response had better survival outcomes compared to those with other response types. This finding is consistent with other studies, although some reports did not determine specific survival rates(30,31,35)

Following progression in 22% (n=11) of the patients, 14% (n=7) initiated second-line chemotherapy, using FOLFOX in 10% (n=5) and cisplatin plus gemcitabine in 4% (n=2). The selection of second-line regimens in this study was consistent with other reports(18,20,26,31,33,35).

By the time of data analysis, approximately 70% of study patients had died. The median overall survival was 6 months (95% CI: 4.85–7.14), with 1-, 2-, and 3-year survival rates of 28.6%, 11.4%, and 2.9%, respectively. These findings are similar to those of institutional and population-based studies conducted in Europe, India, Korea, Turkey, Japan, Iceland, Canada, and the USA(3,6,15–20,30,31). A Study from Japan reported median OS, 1- and 2year OS of 8months, 34.6% and 12.4% respectively(19). Only one patient in our study survived 44 months, and the five-year survival rate was zero, indicating poor overall survival. This was lower than studies from Korea and Iceland, where reported five-year overall survival rates were 15% for males and 24% for females respectively (6,15)

## 7. CONCLUSION

In this study, the survival outcomes of BTCs patients treated at TASH is very poor and the 5-year survival is significantly less than reported in most countries. The median OS is 6 months and the 1, 2, 3, 5 years survival were 28.6%, 11.4%, 2.9% and 0% respectively. Among treatment patterns, giving doublet chemotherapy is the commonest practice and surgery, which is the only curative method for BTCs is rarely done. Completing or receiving 6 cycles of doublet systemic chemotherapy and having hypertension as a comorbidity were associated with improved survival.

### **Strength and Limitation**

First and foremost; it was the only study that explored median and long-term survival at this center on such a rare malignancy that gave information on the actual outcome

Since this study was done at a single institution, it has several additional advantages. It serves as preliminary information and helps in generating new hypotheses that can inform the design of future, more robust prospective studies. For such a rare cancer type, a single institution may be the only practical way to gather a full cohort of patients for study when a multicenter trial is not feasible. Data were collected from routine clinical practice which can provide insights into outcomes in a broader context.

Our study has several limitations. It was a retrospective single institutional study with a homogenous population and limited sample size and therefore generalizability was not possible. Due to the nature of the study (chart review) we could not adequately investigate the causality, important tumor markers and laboratory reports and treatment response statuses. Information on molecular profile was not available. The sample size of the study was too small to analyze predictors of survival with multivariate cox regression including socio-demography, clinical presentation and treatment pattern. In addition, only a limited number of patients had radical surgery which significantly affected the survival; because surgery is the only curative treatment in surgically candidate patients. The lack of local adjuvant or neoadjuvant therapy in this study also affected the survival. Final limitation of the study was short study period in such a rare cancer

### **Recommendation For Health care provider**

- ✓ Implement timely and appropriate patient referrals for biopsy, imaging, and advanced treatment.
- ✓ Enhance multidisciplinary team coordination for effective treatment planning and follow-up care management.
- ✓ Maintain standardized documentation and patient record-keeping for better continuity of care delivery.

**Recommendation to TASH:**

- ✓ Raising awareness about BTCs, improving diagnostic and treatment protocols and multidisciplinary team care

**Recommendations to Policymakers/Ministry of Health (MOH)**

- ✓ Establish and implement community-based health education programs to raise public awareness about BTC and encourage early diagnosis.

**Recommendations to Researchers and Academic Institutions**

- ✓ Initiate additional studies to explore the role of comorbidities in influencing BTC outcomes.
- ✓ Prioritize longitudinal research to track survival patterns in low-resource settings.
- ✓ Establish evidence-based guidelines to inform clinical practice and policy-making.

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## **ANNEX : DATA COLLECTION TOOLS**

Title: Patterns of Presentation, Treatment Approach, and Outcomes of Biliary Tract Cancer Patients in Tikur Anbessa Specialized Hospital, Ethiopia

Hello. My name is ..... I am 4<sup>th</sup> year clinical oncology resident. I am doing my research on how biliary tract cancer patient present, what treatment was offered and their outcome. I will collect information from your medical records and I may ask you some questions about your illness and treatment. No extra medical tests or procedures will be done and you may not directly benefit, but your participation will help improve treatment and care for other patients in the future. You are invited to participate in research. Your personal details will not be shared.

Do you agree to provide information? Yes    No

**I-CARE:** \_\_\_\_\_

Date: \_\_\_\_\_

**Investigator's Name:** \_\_\_\_\_

**Signature:** \_\_\_\_\_

**I. Sociodemograph and medical history**

1. I - CARE number \_\_\_\_\_
2. Age \_\_\_\_\_
3. Sex
  - A. Male
  - B. Female
4. Region
  - a) Addis Abeba
  - b) Amhara
  - c) Oromia
  - d) SNNP
  - e) Gambella
  - f) Benishangul
  - g) Afar
  - h) Tigray
  - i) Harar
  - j) other \_\_\_\_\_
5. Residency
  - A. Rural
  - B. Urban
6. Level of Education Completed:
  - a) No Education
  - b) Less than high school
  - c) High school diploma
  - d) Degree and above
7. Underlying Medical Conditions (Co-morbidity)
  - A. Yes
  - B. No
8. If yes, what medical condition did the patient have?
  - A. Hypertension
  - B. Diabetes mellitus
  - C. Chronic kidney disease
  - D. Cardial disease
  - E. Chronic liver disease
  - F. Others.....

**II. Clinical presentation**

9. Did the patient notice any symptoms?
  - A. Yes
  - B. No
10. What was the initial symptom?
  - A. Right upper quadrant pain/discomfort
  - B. Dyspepsia
  - C. Jaundice
  - D. Urine color change
  - E. Abdominal bloating
  - F. Abdominal swelling

G. Pruritus

H. Other

11. Duration of above symptom (days)---

A. <30days

B. 30-90days

C. >90days

### III. Diagnosis

12. When did you visited health care provider(dd/mm/yy)-----

13. What initial test done?

A. CT scan

B. MRI

C. Endoscopy

D. Ultrasound

E. Biopsy

F. Fine needle aspiration

G. Other \_\_\_\_\_

14. When was cancer diagnosis made?

➤ Date the most precise (Calendar) : \_\_\_\_\_ (dd/mm/yyyy)

➤ Estimation of the date: \_\_\_\_\_

15. Where was the diagnosis made?

A. Hospital other than TASH

B. TASH

C. Abroad

D. Private Clinic

16. On what basis the diagnosis of BTC made?

A. CT scan

B. MRI

C. Ultrasound

D. Biopsy

E. Fine needle aspiration

F. ERCP

G. CEA

H. CA19-9

I. AFP

J. During/after surgery done for other benign condition

K. Other \_\_\_\_\_

17. Primary cancer site

A. Gallbladder

B. ICCA

C. eCCA

18. Histologic type of primary tumor

A. Cholangiocarcinoma

B. Undifferentiated carcinoma

C. Sarcoma

D. Lymphoma

E. Adenocarcinoma

- F. SCC
- G. Other \_\_\_\_\_

19. If metastatic, site

- A. Liver
- B. Lung
- C. Bone
- D. Peritoneum
- E. Brain
- F. Other

20. T/N/M stage--

- A. T---
- B. N ----
- C. M ----

21. ECOG Performance status during diagnosis

- A. 0
- B. 1
- C. 2
- D. 3
- E. 4

22. CA19-9 Level during diagnosis/base line----

23. CEA level base line \_\_\_\_\_

24. AFP level baseline \_\_\_\_\_

#### IV. Treatment Information

25. When was the first-line treatment started?

- Date the most precise (Calendar) : \_\_\_\_\_ (dd/mm/yyyy)
- Estimation of the date: \_\_\_\_\_

26. What was the first-line treatment?

- A. Surgery
- B. Chemotherapy
- C. Radiotherapy
- D. Targeted therapy
- E. Immunotherapy
- F. Best supportive care
- G. Other \_\_\_\_\_

27. If surgery was performed, what was the intention

- A. Palliative
- B. Curative
- C. Unknown

28. If curative/radical surgery, what was the outcome

- A. R0
- B. R1
- C. R2
- D. Unknown
- E. Other \_\_\_\_\_

29. If chemotherapy was included in the first course of cancer treatment, what was the intent
- Adjuvant
  - Palliative
  - Neoadjuvant
  - Other \_\_\_\_\_
30. What chemotherapy and cycle did you receive/are you receiving
- Chemotherapy type---
  - Total cycle received----
31. Did you complete the total cycle of first course of chemotherapy
- Yes
  - No
32. If no what was the reason
- Still receiving the chemotherapy
  - Discontinued
  - Poor PS
  - Patients wish
  - Unknown
33. If the patient was discontinued his /her first line chemotherapy, what was the reason
- Due to toxicity
  - Poor PS
  - Patients wish
  - Disease progression
  - Disease recurrence
  - Unknown
  - Other \_\_\_\_\_
34. Did you receive Radiotherapy
- Yes
  - No
35. What was the intent of RT?
- Palliative
  - Adjuvant
  - Neoadjuvant
  - Radical
36. What dose and fraction of radiotherapy give if palliative RT? \_\_\_\_\_
37. To which anatomic site RT given?
38. If the patient received palliative radiotherapy what was the indication?---
- Bone metastasis and pain
  - Brain met
  - Other \_\_\_\_\_

#### **V. Response assessment tools**

39. What modality was used to assess tumor response
- Imaging
  - Tumor marker
  - Unknown
  - Imaging and tumor marker \_\_\_\_\_
40. If Imaging was done, which \_\_\_\_\_

- A. MRI
  - B. CT
  - C. X-ray
  - D. US
  - E. Other \_\_\_\_\_
41. CA 19.9 level
42. What was the tumor response outcome for first-line/ course treatment?
- A. Partial response
  - B. Complete response
  - C. Stable disease
  - D. Progressive disease
  - E. Recurrence
  - F. Unknown
43. Where was the site of disease progression?
- A. Loco regional
  - B. Lung
  - C. Peritoneum
  - D. Liver
  - E. Bone
  - F. Brain
  - G. Other \_\_\_\_\_
44. How was disease progression detected
- A. Mid cycle imaging assessment
  - B. Mid cycle tumor marker rise
  - C. End cycle imaging
  - D. End cycle tumor marker
  - E. Patient develop symptom/sign of disease progression/recurrence
  - F. Follow up imaging
  - G. Follow up tumor marker
45. Is second line treatment started?
- A. Yes
  - B. No
46. If no, why secondly is not started?
- A. Poor PS
  - B. Patients wish
  - C. Death
  - D. unknown
47. If yes; what kind of treatment the patient started for the progressive disease after the first course of treatment?
- A. Chemotherapy
  - B. RT
  - C. Best supportive care
  - D. Biliary draining
48. If chemotherapy please
- A. Type of chemotherapy-----

- B. Total Cycle-----
49. Did the patient completed second line therapy
- A. Yes
  - B. No
50. If no why not completed?
- A. Poor PS
  - B. Death
  - C. Patients wish
  - D. Unknown
51. What was the tumor response for second course cancer treatment
- A. Partial response
  - B. Complete response
  - C. Stable disease
  - D. Progressive disease
  - E. Unknown
52. If progressive for second time tumor progression what treatment was provided?
- A. chemotherapy
  - B. RT
  - C. BSC
  - D. Unknown
- VI. Survival status
53. Is the patient alive?
- A. Yes
  - B. No
  - C. Unknown
54. If no, when was the death (dd/mm/yyyy)-----
55. If alive last date of follow up (dd/mm/yyyy)