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Short term outcomes of patients with decompensated cirrhosis on follow up at Tikur Anbessa Specialized Hospital: a 1-year retrospective cohort study

Principal Investigator: Dr. Edom Gebremedhin (MD, 3rd year internal medicine resident)

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Principal Investigator: Dr. Edom Gebremedhin (MD, 3rd year internal medicine resident) Email: edom.geberemedhin@aau.edu.et, Mobile: +251913931297

Advisor: Dr. Amir Sultan (Consultant Internist, Gastroenterologist and Hepatologist, Assistant Professor of Medicine)

Signature _____ Date _____

Department head: Dr Abdurezak Ahmed (Consultant Internist and Endocrinologist, Associate Professor of Medicine)

Signature _____ Date _____

Declaration

I, Edom Gebremedhin, declare that this thesis is my original work and has not been submitted elsewhere. I also declare that a complete list of references is provided indicating all the sources of information quoted or cited.

Signature _____ Date _____

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List of abbreviations

ACLF	Acute-on-chronic liver failure
ALD	Alcohol related liver diseases
CLD	Chronic Liver Diseases
COVID-19	Corona Virus Disease 19
CRP	C-reactive protein
CSPH	Clinically Significant Portal Hypertension
DAA	Direct acting antivirals
ED	Emergency department
ESLD	End Stage Liver Disease
GBD	Global Burden of Diseases
GI	Gastroenterology Unit
HBV	Hepatitis B Virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HMIS	Health Management Information System
HVPG	Hepatic Venous Pressure Gradient
ICU	Intensive Care Unit
MELD	Model for End Stage Liver Disease
MELD-Na	Model for End-Stage Liver Disease-Sodium
MRN	Medical Record Number

NASH	Non-alcoholic steatohepatitis
SBP	Spontaneous Bacterial Peritonitis
SIRS	Systemic Inflammatory Syndrome
TASH	Tikur Anbessa Specialized Hospital

Abstract

Background: Cirrhosis is the leading cause of liver-related death globally with the highest age standardized death rates recorded in low income countries in the Sub-Saharan Africa region. Studies that assess the short and long term outcomes of patients with chronic liver diseases in general and decompensated cirrhosis, in particular, are limited in Ethiopia.

Objectives: This study was conducted to assess the short term outcomes of patients with decompensated cirrhosis at Tikur Anbessa Specialized Hospital (TASH) within 06 months of their index hospital visit/ admission, and to explore the prevalence and factors associated with poor outcome among these patient groups. It also assessed the demographic and clinical characteristics as well as the commonest etiologic causes of cirrhosis among the study participants.

Methods: A single center, 1year retrospective cohort study was conducted including data from medical records of patients with decompensated cirrhosis who were admitted at the emergency department (ED), intensive care unit (ICU), or medical wards, or were seen as an outpatient at the Gastroenterology (GI) clinic at TASH from March 2020 to March 2021. Chi-square statistics and binary logistic regression were used to examine the presence and strength of association between categorical variables, and the Cox proportional hazard model was used to test the probability of occurrence of poor outcome among the study participants. The statistical significance was set at $P< 0.05$.

Results: Among 110 participants in this study 82(74.5%) were male. The mean age (± SD) of the participants was 40.35 (± 13.5) years and the median duration of known chronic liver disease was 20.5months (IQR 33). Chronic hepatitis B infection (46.36%) was the commonest identified etiology of cirrhosis followed by alcohol related cirrhosis and cryptogenic cirrhosis in 24.55% 20.9% participants respectively. Sixty one hospital admissions were documented during the study period, with 49(44.5%) participants having been admitted at index hospital visit. Upper GI bleeding, hepatic encephalopathy, and hepatocellular carcinoma were the most common reasons for hospitalization at all time points in the study. A total of 16(14.54%) participants died in the hospital during the study period. Chronic HBV infection was found to contribute significantly to overall poor outcomes [AOR=4.4; 95%CI: 1.15-16.93]. A statistically significant association was found between age above 40years and the development of upper GI bleeding after adjustment for other variables, but not with other complications of portal hypertension [AOR=2.8; 95%CI: 0.76-5.44]. However, sex, other etiologies of cirrhosis, Child Pugh score at index hospital visit/ admission and renal function were not found to be associated with poor outcome measures during the study period, ($p>0.05$).

Conclusion: Chronic HBV infection was the commonest etiology and a strong predictor of overall poor outcome, whereas age above 40 years was a significant contributor to the development of upper GI bleeding. Hepatic encephalopathy and upper GI bleeding were predictors of hospitalization.

Key words: Decompensated cirrhosis, End stage liver failure, Chronic liver disease

Introduction

Background

Chronic hepatitis represents a group of liver disorders of varying causes and severity in which hepatic inflammation and necrosis continue for at least 6 months leading to fibrosis of the liver parenchyma. (1) Cirrhosis, a final pathway for all chronic liver diseases (CLD) irrespective of etiology, is a pathologic entity that represents a late stage of progressive hepatic fibrosis leading to the replacement of the normal liver architecture by regenerative nodules. (1,2) Chronic hepatitis B virus (HBV), hepatitis C virus (HCV), alcohol related liver disease, and non-alcoholic steatohepatitis (NASH) are the most common causes of cirrhosis related morbidity and mortality worldwide. (3) Chronic liver disease caused by autoimmune hepatitis, drug induced hepatitis and cryptogenic hepatitis are less common causes of cirrhosis globally. (1,2)

Clinical features of cirrhosis are the result of pathologic changes and mirror the severity of liver disease. (1) At the early stages, patients with cirrhosis may have preservation of the synthetic and excretory functions of the liver thus might not be symptomatic. This clinical stage is referred to as 'compensated' cirrhosis and patients might remain in this stage for a prolonged period of time with median survival times of >12 years. (4,5) However, with progressive hepatic architectural distortion patients will present with various complications of portal hypertension and/or liver dysfunction and are said to have decompensated cirrhosis. (1,2,5) Decompensated cirrhosis is defined by the presence (or past history) of ascites, variceal bleeding, encephalopathy, and/or jaundice. (4,6,7)

Variable pathophysiologic mechanisms such as increasing portal venous pressure; bacterial translocation; inflammation, and hyperdynamic circulation are proposed to be the likely causes of decompensation in patients with cirrhosis. (8)

The transition from a compensated clinical state into decompensated cirrhosis is accompanied by a reduction in the quality of life and a significant decline in the rate of survival among patients with cirrhosis to approximately 2 years.(4,5,9) Death occurs after transition into a decompensated state in the majority of patients with cirrhosis. (10) Liver failure, bleeding, hepatocellular carcinoma (HCC), infections, hepatorenal syndrome, and acute-on-chronic liver failure (ACLF) are the most frequent causes of death in patients with cirrhosis. (4)

According to the Global Burden of Disease (GBD) Study, in 2017 there were 10·6 million prevalent cases of decompensated cirrhosis and 112 million prevalent cases of compensated cirrhosis globally. In the same year, cirrhosis caused more than 1·32 million deaths which accounted for 2·4% of total deaths globally. Sub-Saharan Africa had the highest age-standardized death rate among GBD super-regions for all years of the study period (32·2 [25·8–38·6] deaths per 100,000 population in 2017). (3)

The gold standard for the diagnosis of cirrhosis is liver biopsy, however, the presence of various findings on clinical, laboratory, and imaging assessment can be used in the diagnosis and prognostic stratification of patients with cirrhosis due to different etiologies. (2,5,11) These include the presence of peripheral stigmata of chronic liver disease such as jaundice, ascites, splenomegaly, hepatic encephalopathy, dilated abdominal veins, spider angiomata, and gynecomastia on physical examination; thrombocytopenia, elevated bilirubin, decreased serum albumin, deranged coagulation parameters and creatinine on laboratory workup; and evidence of liver fibrosis and/or complications of portal hypertension on imaging studies such as ultrasound, transient elastography, and magnetic resonance elastography. (1,2,12,13)

Among the variable clinical and laboratory parameters proposed to affect the prognosis of patients with cirrhosis, the presence of ascites; hepatic encephalopathy; coagulation abnormalities, as well as derangement in the values of serum albumin; bilirubin, creatinine, and serum sodium, lead to a disproportionately increased risk of death. (2,4,5,14) These clinical and laboratory parameters are included in prognostic scoring models such as the Child-Pugh score, Model for End-Stage Liver Disease (MELD) score, and Model for End-Stage Liver Disease-Sodium (MELD-Na), which are currently used to assess the eligibility of patients for liver transplantation. (7,11,15,16) Each of these scoring systems has a unique set of advantages and limitations for use in clinical settings.

Statement of the problem and significance of the study

Cirrhosis is the leading cause of liver-related death globally causing more than 1·32 million deaths in 2017 followed by hepatocellular carcinoma. (17) In the same year, cirrhosis and other chronic liver diseases caused by hepatitis B and hepatitis C virus infections accounted for 29% and 25.8% of liver-related deaths respectively followed by alcoholic liver disease and NASH.(17)

In the report of the Global Burden of Disease (GBD) Study, in 2017 low income countries in the Sub-Saharan Africa region had higher age standardized death rates caused by cirrhosis as

compared to other GBD super-regions. (3) This might be attributable to the low accessibility of standard medical care, decreased health seeking behavior, and scarcity of advanced diagnostic services and therapeutic interventions for decompensated cirrhosis in these countries. (18)

Studies that assess the short and long term outcomes of patients with chronic liver diseases in general and decompensated cirrhosis, in particular, are limited in Ethiopia. In a study conducted 30 years ago among 334 hospitalized patients with CLD in Ethiopia by E.Tsega and colleagues, 208 participants (62%) were documented to have cirrhosis by clinical and histologic diagnostic criteria. The most common first time clinical presentations among these participants with cirrhosis were ascites, splenomegaly, hematemesis, and/or melena from esophageal varices, and mental changes due to hepatic encephalopathy, most of which are events that characterize decompensation in cirrhosis. Infection with hepatitis B virus was the most commonly diagnosed cause of chronic liver disease in this study. (19) These results are comparable to studies assessing the survival and prognosis of patients with compensated and decompensated cirrhosis conducted in Italy and England. (6,20) However, the outcomes and specific causes of decompensation were not reported in this study.

In a couple of recent studies conducted among hospital admitted CLD patients in our country, inpatient mortality rates were found to be 28.5% - 41%.(21,22) This might reflect a sampling bias since the participants of the study were selected among CLD patients admitted to the hospital representing patients with advanced liver disease with high predicted mortality rates. Despite the high inpatient mortality rates reported from these studies, data regarding the specific causes of decompensation as well as predictors of mortality and complications are not adequately available.

This study assessed the short term outcomes of patients with decompensated cirrhosis at Tikur Anbessa Specialized Hospital (TASH), the largest tertiary hospital in the country, within 06 months of their index hospital visit/ admission. The sociodemographic, clinical, and laboratory parameters of the participants were stratified and used to identify the predictors of mortality, hospital admission, and complications of portal hypertension among these patient cohorts. Therefore, the findings of this study can be used as a baseline for further studies that assess the predictors of poor outcome and design pathways to provide better clinical care to patients with chronic liver disease.

Literature review

Transition from a compensated to a decompensated stage of cirrhosis occurs at a rate of 5–7% per year with ascites being the most frequent first decompensating event in patients with cirrhosis followed by bleeding, encephalopathy, and jaundice. (4,5) The defining events of decompensation in cirrhosis result from the complications of portal hypertension and/or impairment in hepatic synthetic/ excretory functions.(2,4,5,23)

The annual rate of decompensation varies with the etiology of liver disease; it was found to be 4% for patients with HCV-related cirrhosis, 6% to 10% in those with alcohol-associated cirrhosis (and even higher if they continue to drink actively), and 10% in those with HBV-related cirrhosis among a cohort of patients listed for liver transplantation. (24)

In cirrhosis, the increased hepatic resistance to blood flow results from both mechanical obstacles due to the architectural distortion and vasoconstriction which gradually leads to portal hypertension. (4) Progressive increase in portal pressure up to the clinically significant portal hypertension (CSPH) threshold of ≥10 mmHg is the earliest consequence of cirrhosis above which decompensation and esophageal varices commonly occur. (4,25)

The mortality and morbidity resulting from cirrhosis markedly increase once patients develop decompensation, and the 1-year case-fatality rate can be as high as 80% depending on the cause of decompensation. (4,5,9) Survival rates and predictors of death are different between patients with compensated and decompensated cirrhosis. (23) In an inception cohort study of 494 patients in Italy, conducted to assess the competing risks and prognostic stages of cirrhosis over 25 years, decompensation occurred before death in nearly 60% of patients with compensated cirrhosis. (10)

Two prognostic sub stages within compensated cirrhosis (stage 1 and 2) and decompensated cirrhosis (stages 3 and 4) have been proposed in a systematic review by D' Amico and colleagues, which are defined by the presence of a constellation of variable complications of portal hypertension in patients with cirrhosis. (5) One year mortality rate increases significantly as patients are classified in higher clinical stages with the highest mortality of 20% and 57% observed in patients with stage 3 [patients with ascites (with or without varices) but without variceal hemorrhage] and stage 4 [patients presenting with variceal hemorrhage (with or without ascites] cirrhosis respectively. (5,23)

The Child– Pugh and MELD scores are the most commonly used prognostic models in patients with cirrhosis currently. In studies comparing the two models, MELD was found to be more reproducible than the Child– Pugh score because it does not include subjective variables such as ascites and encephalopathy. However, obtaining the score requires computing and it is, therefore, much less practical than the Child–Pugh score for individual estimates at the bedside. Moreover, the MELD score has not been proven to be superior to the Child–Pugh score in terms of predictive accuracy. (5,26–28)

In a nested cohort study conducted by Ripoll and colleagues as part of a randomized controlled trial evaluating the use of β-blockers in preventing varices in patients with compensated cirrhosis, a baseline hepatic venous pressure gradient (HVPG) of <10mmHg was associated with 90% negative predictive value of clinical decompensation over a median follow up period of 4 years. In a multivariate model derived to predict the risk of clinical decompensation from the results of this study, the quantitative degree of portal hypertension was relevant in addition to the baseline MELD and albumin levels. The HVPG had a hazard ratio of 1.11, implying that for each 1 mm Hg increase in HVPG there is an 11% higher risk of clinical decompensation. (25) However, HVPG was not an independent predictor of death in decompensated cirrhosis since liver insufficiency and hemodynamic factors leading to renal dysfunction rather than portal pressure determine patient survival in advanced stages of cirrhosis. (23)

Hemodynamic studies have demonstrated that the development of hyper dynamic circulation in cirrhosis due to various pathophysiologic mechanisms maintains and aggravates portal hypertension. This is more evident in cirrhotic patients who have CSPH and especially those with varices.(29,30)

Systemic inflammatory activation resulting from translocation of bacterial or pathogen-associated molecules from the intestinal lumen to the systemic circulation has been proposed to be associated with the hyper dynamic circulatory state of advanced experimental and human cirrhosis through increased production of proinflammatory cytokines. (8,30) This has been shown to contribute to worsening of portal hypertension and poor prognosis in patients with compensated and decompensated cirrhosis.

In a single center, prospective cohort of 238 patients with cirrhosis undergoing per protocol hepatic and right-heart catheterization and C-reactive protein (CRP) measurement to assess hepatic/ systemic hemodynamics and inflammation (by CRP) among the different sub-stages of cirrhosis and to investigate their interrelationship and prognostic relevance, hyperdynamic/ hypodynamic circulatory state and CRP were independent predictors of the risk of decompensation and death/ liver transplant in patients with compensated and decompensated cirrhosis respectively. (30)

Infections were associated with a greater risk of death independent of the severity of the underlying liver disease in a single center retrospective cohort study of 501 patients with cirrhosis. The incidence of proven bacterial infection in this study was 25.6% (of which 60% were community acquired). Survival rates at 3, 6, 12 and 30 months were 83%, 77%, 71%, and 62% in patients without diagnosis of infection, versus 50%, 46%, 41% and 34% in patients with diagnosis of infection. Bacterial infection was an independent predictor of survival even when patients who died within the first 30 days were excluded from the analysis in Cox regression (HR 2.013) and competing risk Cox models in all patients (HR 1.46) and propensity risk score matched infected and non-infected patients (HR 1.67). (31)

In another multicenter cohort study of patients listed for liver transplantation with an infection at index hospitalization, the risk of being delisted/death within 6 months was much higher in infected patients with cirrhosis (42%) than in uninfected waitlisted patients. In these patient cohorts infections that resulted in multiorgan failure (failure of >2 organ systems) and higher MELD score were associated with an increased probability of delisting/ death within 06 months of the index hospitalization. Except for SBP which was more common in listed patients, there wasn't a significant difference in the focus of infections diagnosed at admission in the study participants. Listed patients in this study were likely to be on treatment with lactulose, rifaximin, and prophylactic antibiotics for SBP as compared to the patients that delisted/died.(24)

In the EPA-SCO study, a nationwide prospective inception cohort study conducted by Bruno and colleagues including 490 consecutive cirrhotic patients in Italy to evaluate the disease course of cirrhosis since the onset time of the first complication, ascites were identified in 76.6 % of patients, followed by gastroesophageal variceal bleeding, ACLF and hepatic encephalopathy in descending proportions. Among these, the cumulative incidence of failure defined by death or orthotopic liver

transplantation was found to be highest throughout the study period in patients with ACLF and overt ascites respectively increasing annually until the end of the study period. (32)

In a systematic review of 118 studies conducted by D'Amico and colleagues, the most consistent predictor of death in cirrhosis was found to be the Child–Pugh score and/or its components (albumin, bilirubin, ascites, encephalopathy, and prothrombin time) as well as the age of the patient. The value of Child–Pugh score in prognostication is more prominent in patients with decompensated cirrhosis. (5) In addition to the Child–Pugh score, the presence of factors such as bleeding, HCC, and renal failure were found to be strong predictors of death in patients with decompensated cirrhosis in different studies and systematic reviews.

Renal dysfunction in patients with cirrhosis is common especially in individuals with end stage liver disease (ESLD). The causes of renal dysfunction in the setting of cirrhosis are multifactorial with variable contributions of circulatory dysfunction and arterial underfilling, systemic inflammation, and infections such as spontaneous bacterial peritonitis (SBP), drugs as well as the presence of other comorbidities. (33,34)

Renal dysfunction is a key determinant of outcomes in cirrhosis, in that it is associated with increased in hospital mortality as well as shortened survival after hospital discharge. (33,34) In a retrospective analysis of 22,680 non-status 1 adults on the waitlist for liver transplantation for >90 days, competing risk analysis showed that even after adjusting for confounders including the final MELD-Na score, the pattern of renal dysfunction is associated with mortality in patients with cirrhosis. (14)

In a retrospective cohort study conducted in Côte d'Ivoire by Mahassadi and colleagues to assess the use of systemic inflammatory response syndrome (SIRS) and MELD score to predict in-hospital mortality among black African patients with decompensated cirrhosis at initial hospitalization, both SIRS and MELD score >16 were found to be independent predictors of mortality in these group of patients. However, only MELD score of >16 was useful in predicting complications such as hepatorenal syndrome and encephalopathy. (35)

In a retrospective cohort study conducted by Chirapongsathorn et al., at the Mayo Clinic Hospital to assess risks for first hospitalization and the rate, risk factors, costs, and 1-year outcome of 30-day readmission among 2048 patients admitted for complications of cirrhosis, the incidence of

hospitalization for complications of cirrhosis was 100/ 100,000 population, with increasing age and male sex being the strongest risks for hospitalization. The overall 30-day readmission rate for the study participants was 32% mainly for complications of portal hypertension (52%) and infections (30%). Annual post index hospitalization costs for those with 30-day readmission were substantially higher than those readmitted beyond 30 days or those not readmitted. 50.4% total mortality was documented up to 1 year of follow up among the patients who were readmitted within 30 days of the index hospitalization. (36)

Early outpatient follow-up after discharge i.e., within 7 days of discharge was associated with a small increase in readmissions but lower overall mortality in patients with cirrhosis in a large retrospective cohort study conducted to evaluate the relationship between early outpatient follow-up and short-term readmission and mortality in patients with cirrhosis. (37)

Although data on the outcome of cirrhotic patients in Ethiopia is limited, high mortality rates were reported among hospital admitted patients diagnosed with chronic liver diseases. In a study conducted at St Paul's Hospital to assess the magnitude, clinical profile and outcome of CLD among 117 medical admissions, ascites and jaundice were the commonest presenting symptoms followed by upper gastrointestinal bleeding, and inpatient mortality was found to be 41%. Causes of death and predictors of mortality were not specifically assessed in this study. (21)

In another study conducted in three selected teaching hospitals in Ethiopia to assess the short term clinical outcomes of 109 admitted patients with CLD, 30day mortality was documented to be 34.9%. Among these deaths, 81.6% occurred before hospital discharge. In this study, hepatic encephalopathy at admission; unidentified etiologies of CLD, and total bilirubin level were independent predictors of in-hospital mortality. (22)

Objectives

General Objective:

- To assess the short term outcomes of patients with decompensated cirrhosis on follow up at Tikur Anbessa Specialized Hospital (TASH)

Specific objectives:

- To assess the demographic and clinical characteristics of patients with decompensated cirrhosis on follow up at TASH
- To assess the etiologic causes of cirrhosis among the study participants
- To assess the outcomes of patients with decompensated cirrhosis within 6 months of index hospital admission/ visit
- To explore the prevalence of poor outcome in patients with decompensated cirrhosis, and
- To assess the predictors of poor outcome in patients with decompensated cirrhosis

Methods

Study area and period

The study was conducted in Tikur Anbessa (Black Lion) Specialized Hospital, the largest tertiary hospital in the country, which was established in 1964 in Addis Ababa, Ethiopia. It provides specialized clinical services to patients from all parts of the country through its various departments and subspecialty units. In addition, it is the main teaching center for the College of Health Sciences, Addis Ababa University where both undergraduate and postgraduate clinical training is provided in various disciplines. The Gastroenterology unit in the Department of Internal Medicine provides both inpatient and outpatient clinical services, as well as diagnostic and therapeutic endoscopic procedures. Consultants, fellows and internal medicine residents in training actively participate in the provision of care.

The study was conducted from August 2021 – October 2021 G.C.

Study design

The study was a single center, 1year retrospective cohort study.

Study population

Among patients with chronic liver disease, all patients diagnosed with decompensated cirrhosis based on clinical and laboratory data who were admitted at the emergency department (ED), medical wards or intensive care unit (ICU), and outpatients on follow up seen at the Gastroenterology (GI) clinic at TASH from March 2020 to March 2021 were included in the study.

Inclusion and exclusion criteria

Inclusion criteria

- Age > 18yrs
- Diagnosed with decompensated cirrhosis based on the operational definition of this study
- Admitted at ED, medical wards or ICU at TASH at least 06 months prior to the study period, or
- On follow up at GI clinic at TASH

Exclusion criteria

- Patients with decompensated cirrhosis with incomplete medical records or clinical assessment.
- Patients with portal hypertension resulting from disorders other than cirrhosis

Sampling procedure

Sample size calculation

The minimum sample size for this study was calculated according to the following assumptions:

- The probability of having poor outcomes in patients with decompensated cirrhosis is taken to be 50%.
- 95% confidence level (α = 0.05)
- The degree of precision to be 5%.
- 10% non-response rate will be added.

The following single proportion population formula was used to obtain the desired sample size (n):

$$n = \frac{(Z_{\propto/2})^2 P(1-P)}{d^2}$$

Where,

n = the required sample size

Z= level of confidence of 95% which is equal to 1.96

d= margin of error at a level of confidence of 95% which is equal to 0.05

p= expected proportion of the population with the event of outcome (prevalence). It is assumed to be 50% for this study.
q =1-p: the probability of non-occurrence of the event of interest

By using the single population formula, the least sample size for the study was calculated to be 384. The following finite population correction formula was used to calculate the final sample size of the study:

$$n_{new} = \frac{n_o}{\left(1 + \frac{n_0}{N}\right)}$$

Where,

n_{new} = the corrected sample size

n_0 = the initial sample size

N= total number of patients with cirrhosis and complications on monthly follow up at GI clinic and admitted patients to medical wards which are approximately 140 (data taken from monthly clinical audit reports).

After finite population correction, the new sample size of the study was calculated to be 103, and adding a 10% non-response rate it was calculated to be 113.

Sampling technique

Among adult patients with CLD, all patients that fulfilled the inclusion criteria of the study were recruited consecutively into the study by using a convenient sampling technique.

Study variables

The independent variables in this study were:

- Age
- Sex
- Etiology of cirrhosis
- Child-Pugh score
- Renal function
- Presence of comorbidities

The dependent variables in this study were:

- Mortality at 01, 03, and 06 months of enrollment into the study
- Hospital admission
- Rate of occurrence of complications such as variceal bleeding, spontaneous bacterial peritonitis, hepatic encephalopathy, and hepatorenal syndrome

Operational definitions

Compensated cirrhosis: Clinical stage of cirrhosis where liver fibrosis is documented but complications of portal hypertension that define decompensation are absent.

Decompensated cirrhosis: Clinical stage of cirrhosis defined by the presence (or past history) of ascites, variceal bleeding, encephalopathy, and/or jaundice.

Poor outcome: defined by readmission to the hospital, development of variceal bleeding, hepatic encephalopathy, and/or spontaneous bacterial peritonitis within 1, 3, and 6 months of enrollment into the study.

Data collection procedures

Patients admitted to the ED, medical wards, or ICU or seen as outpatients at the GI clinic at TASH with a diagnosis of decompensated cirrhosis from March 2020 to March 2021 were identified from the admission and outpatient Health Management Information Systems (HMIS) registers and enrolled into the study. Medical records numbers (MRN) were used to retrieve the medical records of patients both from the electronic medical record system and paper based charts.

A structured questionnaire was prepared in the open data kit (ODK) format and pretested before data collection was started. Data regarding the demographic characteristics; clinical information including etiology of cirrhosis, results of laboratory and imaging tests, management decisions, and outcome which were documented on the patients' medical records were reviewed and entered into the ODK by the primary investigator.

Eligible patients whose medical records were lost or incomplete i.e., did not include any documentation of clinical information, laboratory or radiographic investigations, and therapeutic interventions performed during the study period were excluded from the final analysis.

Data quality assurance

The completeness and consistency of the data were checked by the primary investigator. The data were cleaned and edited before the ODK questionnaires were exported for analysis using SPSS (statistical package for the social sciences) version 26 software.

Data analysis

Data from a total of 110 patients were used for the final analysis using the SPSS version 26.0 statistical package. Descriptive statistics for the demographic and clinical data were presented using mean with standard deviation (SD) and median with interquartile range (IQR) for continuous data; and frequency and percentage tables for categorical data.

Chi-square statistics and binary logistic regression were used to examine the presence and strength of association between categorical variables, and the Cox proportional hazard model was used to test the probability of occurrence of poor outcome among the study participants. The statistical significance was set at $P< 0.05$.

Ethical Considerations

To respect patients' rights and the regulation of the hospital where the study was conducted, permission to undertake the study was obtained from the Ethical Review Committee of the Department of Internal medicine to access the medical records of the patients. All personal data of participants were de-identified.

Plans of disseminating the findings of the study

Results of the study will be submitted to the Department of Internal Medicine, School of Medicine College of Health Sciences at Addis Ababa University as part of the dissertation requirement for the postgraduate certificate program in Internal Medicine and will be presented in a seminar prepared by the research committee for all staff and residents in the department. It will also be submitted to peer reviewed medical journals for possible publication.

Results

Demographic characteristics of the study participants

A total of 110 participants were included in the final analysis of this study with a response rate of 97.3%. Eighty two (74.5%) participants were male and 28(25.5%) were female. The median age of the participants was 40 years (IQR 18) with mean age (± SD) of 40.35(± 13.5) years. (Table 1) (Fig 1)

Table 1. Demographic characteristics of patients with decompensated cirrhosis at TASH

Variable (n = 110)		Number (percentage)
Sex	Male	82 (74.5%)
	Female	28 (25.5%)
Age category	<35 years	39 (35.5%)
	35 – 44 years	26 (23.6%)
	45 – 54 years	27 (24.5%)
	55 – 65 years	11 (10%)
	>65 years	7 (6.04%)

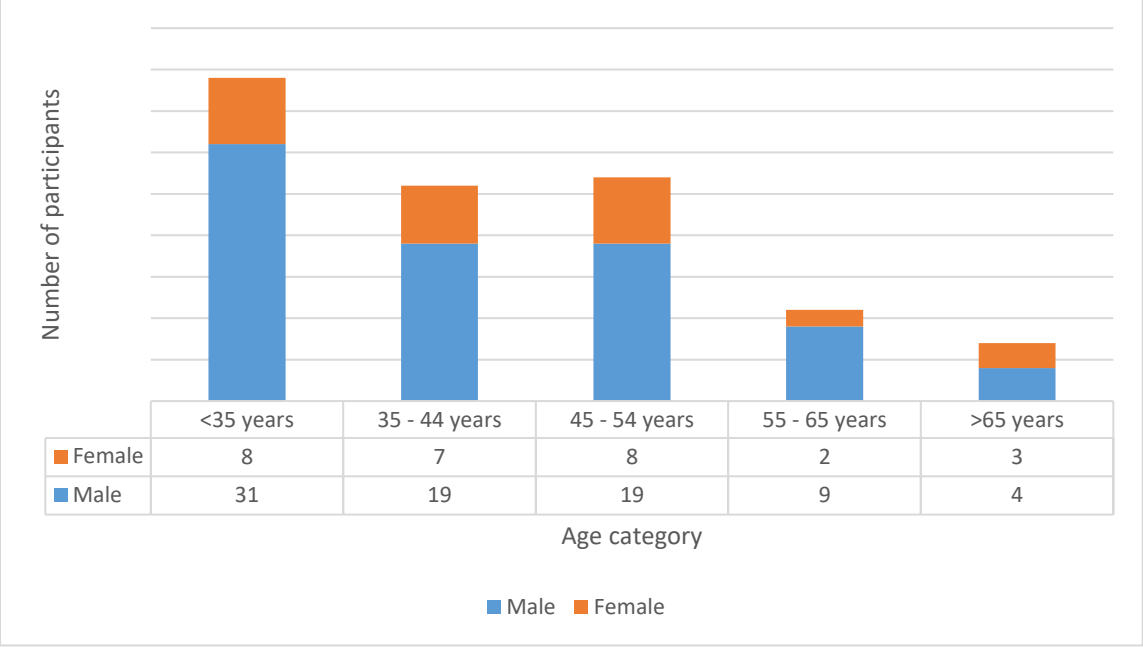


Figure 1. Distribution of patients with decompensated cirrhosis at TASH by sex and age category

Clinical characteristics of the study participants

Clinical profile of study participants

In this study chronic Hepatitis B virus infection was the commonest identified etiology of cirrhosis affecting 51(46.36%) of the participants followed by alcohol related cirrhosis and cirrhosis of unknown cause in 27(24.55%) and 23(20.9%) participants respectively. Chronic Hepatitis C virus related cirrhosis and autoimmune hepatitis were documented in 11(10%) and 3(2.73%) participants respectively. Alcohol related liver disease was incriminated as a concomitant etiology of cirrhosis in 3 and 1 participants with chronic HBV and HCV related cirrhosis respectively. Possible Hepatitis B – Hepatitis C virus co-infection was documented in a single participant.

The median duration of known chronic liver disease in this study was 20.5months (IQR 33) with the mean duration (±SD) being 24.8 (±28.75) months. Twenty three (20.9%) participants were newly diagnosed with decompensated cirrhosis during the study period. The longest duration of CLD documented in this study was 14 years in 1 participant with cryptogenic cirrhosis.

Thirty four (30.9%) participants in this study had a documented chronic medical illness other than chronic liver disease with HIV being the commonest comorbidity in 8 followed by diabetes mellitus, hypertension, and chronic kidney disease in 6, 4, and 3 participants respectively. Table 2 summarizes the clinical characteristics of patients with decompensated cirrhosis at TASH.

Table 2. Clinical profile among patients with decompensated cirrhosis at TASH

Variable		Number (percentage)
Etiology of cirrhosis (n=110)		
	Chronic HBV related cirrhosis	51 (46.36%)
	Chronic HCV related cirrhosis	11 (10%)
	Alcohol related cirrhosis	27 (24.55%)
	Autoimmune hepatitis	3 (2.72%)
	Cirrhosis of unknown cause	23 (20.9%)
Duration of known CLD (n=110)		
	Newly diagnosed	23 (20.9%)
	<12 months	22 (22%)
	13 – 24 months	25 (22.7%)

	25 – 36 months	16 (14.5%)
	37 – 48 months	12 (10.9%)
	49 – 60 months	4 (3.6%)
	>60 months	8 (7.3%)
Comorbidities (n=34)		
	HIV	8 (7.27%)
	Diabetes Mellitus	6 (5.45%)
	Hypertension	4 (3.63%)
	Chronic kidney disease	3 (2.72%)
	Structural heart disease	2 (1.81%)
	Others	15 (13.63%)

Among 31(28.18%) participants for whom there was a documented positive history of alcohol intake, daily alcohol consumption was quantified in terms of standard drinks for 25 participants only. Nine and 8 participants consumed 3-4 and 5-6 standard drinks per day respectively. Twenty two (20%) participants had no history of alcohol consumption. Only 7(6.36% participants had a documented cigarette smoking history, all of whom had 5 or more pack years of smoking.

History of traditional/ herbal medicine use was documented for 5(4.55%) participants of the study, and family history of chronic liver disease was present in only 1 participant.

Clinical presentation of participants

In this study, the common presenting complaints among participants at enrollment include abdominal distension in 44(40%), tarry stools in 40(36.4%), bloody vomiting, and abdominal pain in 35(31.8%) participants each, fatigue in 32(29.1%) and yellowish discoloration of the eyes/ skin in 29(26.4%) participants. Sleep pattern disturbance and altered mental status were documented in 11(10%) and 4(3.6%) participants only.

Among 95 study participants for whom physical examination findings were documented at index hospitalization/ clinic visit, the commonest finding was ascites found in 61(64.2%) participants, followed by splenomegaly in 41(37.3%), and pallor in 36(32.9%) participants. Jaundice and pleural effusions were seen in 33(30%) and 24(25.3%) participants respectively.

Hepatic encephalopathy was documented in 20(18.18%) participants at index hospital admission/ clinic visit, among which 9(8.18%) and 8(7.27%) had grade I and II hepatic encephalopathy respectively. At 1, 3, and 6 months of the study hepatic encephalopathy was documented in 4, 2, and 3 participants respectively with the majority having grade I hepatic encephalopathy. Among the 61 participants with ascites at enrollment, 35(31.8%) and 15(13.64%) had moderate and severe ascites respectively. The relative frequency of subjective complaints and physical examination findings among the study participants is comparable at 01 month, 03 months, and 06 months after enrollment into the study. The details are shown in Table 3.

Table 3. Comparison of clinical presentation among patients with decompensated CLD over 06 months at TASH

	At index hospital visit Number (%)	At 01month Number (%)	At 03months Number (%)	At 06months Number (%)
History	(n=110)	(n=92)	(n=83)	(n=77)
Abdominal distension	44 (40%)	12 (11.8%)	11 (13.25%)	11 (14.29%)
Bloody vomiting	35 (31.8%)	4 (4.3%)	4 (4.8%)	8 (10.4%)
Tarry stools	40 (36.4%)	2 (2.1%)	4 (4.8%)	8 (10.4%)
Yellowish discoloration of eyes	29 (26.4%)	4 (4.3%)	3 (3.6%)	2 (2.6%)
Abdominal pain	35 (31/8%)	7 (7.6%)	2 (2.4%)	1 (1.3%)
Fatigue	32 (29.1%)	9 (9.7%)	4 (4.8%)	2 (2.6%)
Sleep pattern disturbance	11 (10%)	4 (4.3%)	2 (2.4%)	2 (2.6%)
Altered mental status	4 (3.6%)	1 (1.0%)	1 (1.2%)	1 (1.3%)
Other	34 (24.5%)	40 (43.4%)	55 (66.2%)	43 (55.8%)
Physical examination				
Ascites	61 (64.2%)	18 (19.5%)	18 (21.7%)	15 (19.5%)
Splenomegaly	41 (37.3%)	25 (27.1%)	25 (30.1%)	30 (38.9%)

Pallor	36 (32.9%)	11 (11.9%)	7 (8.4%)	8 (10.4%)
Jaundice	33 (30%)	11 (11.9%)	6 (7.2%)	4 (5.2%)
Peripheral edema	33 (30%)	8(8.7%)	6(6.5%)	5(5.4%)
Pleural effusion	24 (25.3%)	5 (5.4%)	1 (1.2%)	1 (1.3%)
Abdominal tenderness	13 (13.7%)	3 (3.2%)	1 (1.2%)	3 (3.9%)

Results of laboratory and imaging investigations

Moderate anemia and thrombocytopenia were the most common findings on complete blood counts determination at all time points of the study, with mild leukopenia documented in a few participants. The results of renal function tests and serum electrolytes at index hospitalization/ clinic visit were with in normal range for the majority of the participants.

The performance and documentation of liver function tests and enzymes were found to be variable during the study period. Moderate hypoalbuminemia, hyperbilirubinemia, and modest transaminase elevations (1.5-2.5ULN of the laboratory reference range) were documented for the majority of the participants. (Table 4) (Fig 2)

Table 4. Laboratory profiles of patients with decompensated cirrhosis at TASH

	At index hospital visit Median (IQR)	**At 01 month** Median (IQR)	**At 03 months** Median (IQR)	**At 06 months** Median (IQR)
WBC (10^3/µL)	6.0 (5.58)	4.27 (3.55)	4.0 (2.55)	3.3 (2.6)
Hemoglobin (g/dL)	11.65 (4.12)	11.98 (3.55)	13.3 (3.68)	13 (4.3)
Platelet (10^3/µL)	109 (95.5)	90 (88)	79 (54)	71 (49)
Serum creatinine (mg/dL)	0.82 (0.71)	0.7 (0.39)	0.7 (0.12)	0.6 (0.3)
Total bilirubin (mg/dL)	2.7 (3.16)	1.7 (1.65)	1.24 (1.25)	1.15 (0.98)
Albumin (g/dL)	2.45 (0.98)	3.1 (1.13)	3.6 (1.46)	3.5 (1.1)
PT (sec)	21.55 (6.68)	25.6 (19.9)	16.2	20.8 (3.1)
INR	1.9 (0.74)	1.89 (0.49)	1.39 (1.24)	1.85 (0.43)

Serum sodium (mmol/L)	130.8 (10.4)	132.5 (6)	136.7 (6.9)	136.8 (4)
Serum potassium (mmol/L)	3.99 (1.02)	4.5 (1.02)	4.68 (0.84)	4.25 (0.56)

Child Pugh scores were calculated for 47(42.7%) participants at enrollment with a median value of 11. Twenty eight (25.4%) participants had Child scores of >10 (Child class C) whereas 12(10.9%) participants' scores were 7-9 (Child class B). At 1, 3, and 6 months of the study, Child scores were documented for 6, 2, and 6 participants respectively.

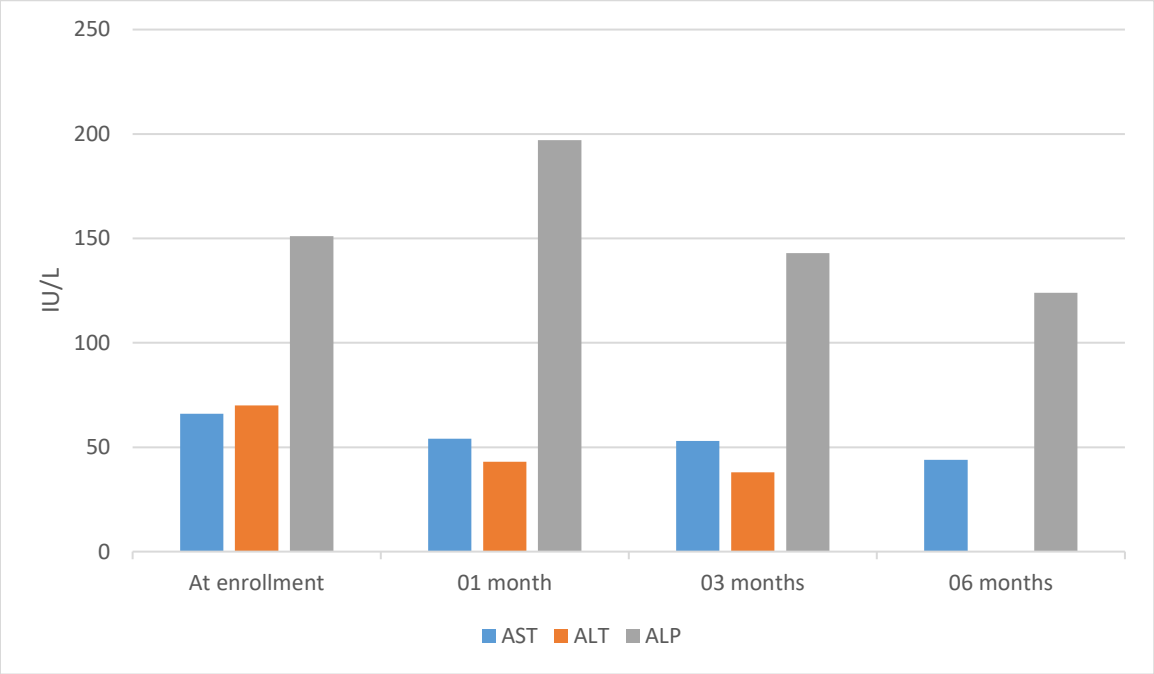


Figure 2. Median liver enzyme values of patients with decompensated cirrhosis at TASH

Among 27(24.5%) participants for whom ascitic fluid analysis was done at index hospital visit, median total white cell count was 700 cells/µL (IQR 1471.8). However, a differential count was performed for only 19(17.27%) participants with 8 samples having absolute neutrophil counts of >250 cells/µL. Among 16(14.5%) peritoneal fluid samples for which ascitic fluid albumin was documented, 15 had SAAG of >1.1g/dL. In 11 participants Gram stain of peritoneal fluid showed no organism and no growth was documented for 2 participants for whom culture was done as part of their work up. Ascitic fluid analysis was done for 2 and 1 participants only at 1 and 3 months

of the study, for both samples only total white cell count and glucose were documented with no objective evidence of spontaneous bacterial peritonitis.

Among 51 participants with chronic HBV infection, quantitative HBV DNA levels were determined for 17 participants with a median viral load of 6670 IU/ml. Six participants had HCV RNA results documented among whom 3 had documented viral clearance after therapy with DAAs.

Features of cirrhotic liver, ascites, and splenomegaly were the commonest findings on different modalities of abdominal imaging performed for the study participants. Portal vein thrombosis was documented for 13 participants majority of which were tumor thrombi. Variable sized liver masses were reported on triphasic abdominal CT for 18(16.3%) patients. (Fig 3)

Transient elastography was done for 4 participants in this study for whom the documented liver stiffness measurement in kPa ranges from 12-14.9. However, the fat attenuation measurement was documented for a single participant only (270UAP).

Liver biopsy was documented for a single participant only with the reported finding of cirrhosis (details of other pathologic findings were not documented).

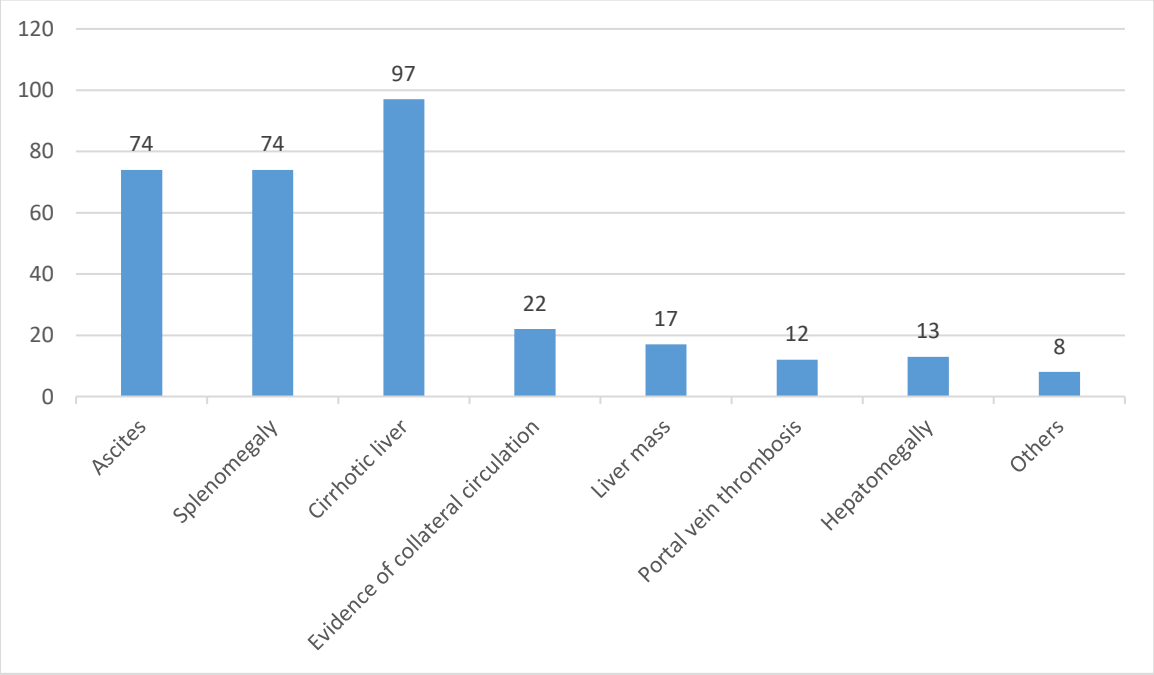


Figure 3. Common ultrasound findings among patients with decompensated cirrhosis at TASH

Results of upper GI endoscopy were documented for 68(61.8%) participants with the commonest findings being variable degrees of portal hypertensive gastropathy, followed by grade 3 and 2 esophageal varices in 37(33.6%), 34(30.9%), and 19(17.3%) participants respectively. Three additional participants had screening endoscopy but the specific findings were not documented in their medical records. Nine participants had duodenitis and duodenal ulcers were reported in 4 participants. Stigmata of recent bleeding were documented in 22(20%) participants with varices and endoscopic variceal ligation was done for 17(15.45%) participants.

Outcome of the participants over 06 months of index hospital admission/ OPD visit

Forty nine (44.5%) participants were admitted to the hospital at enrollment with a mean (±SD) duration of hospital stay of 9.5(±7) days. On subsequent follow up 5, 3, and 4 participants were admitted to the hospital at 1, 3, and 6 months of the study period respectively with mean lengths of hospital stay of 3.75, 27.3, and 5.25 days.

The most common reasons for admission among the study participants at all time points in the study period were upper GI bleeding, hepatic encephalopathy, hepatocellular carcinoma, and spontaneous bacterial peritonitis. Hepatorenal syndrome was documented to occur during hospital stay in 5 participants. Alcoholic hepatitis, aspiration pneumonia, and acute kidney injury of variable causes were documented in a few participants. See Figure 4 for details.

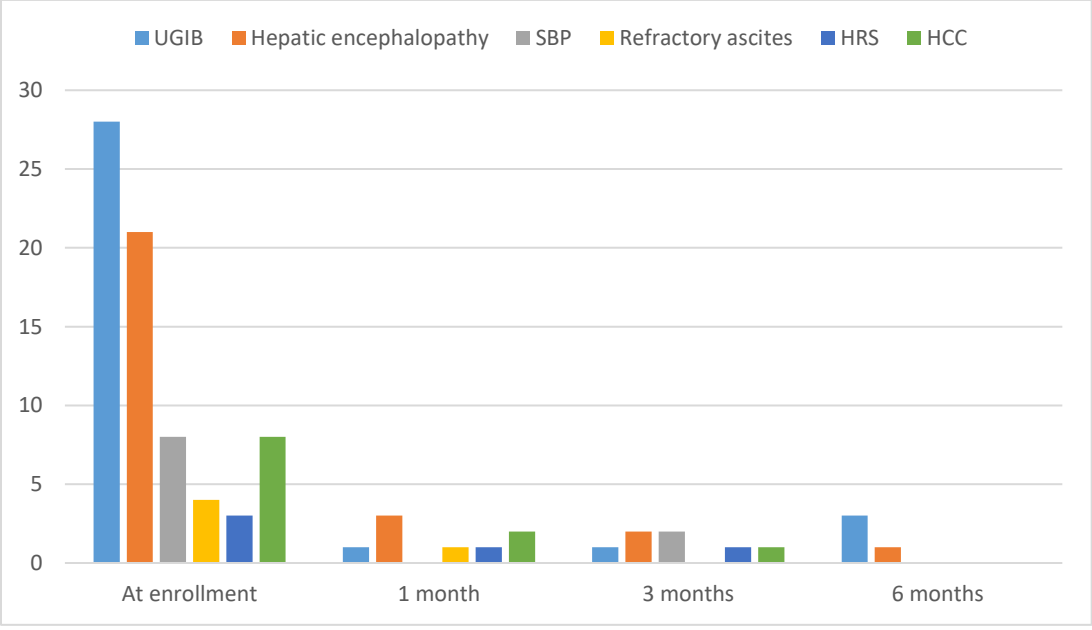


Figure 4. Reasons of hospital admission among patients with decompensated cirrhosis at TASH

Majority of the participants received treatment with non-selective β-blockers (mostly Propranolol to a maximum dose of 60mg PO TID), diuretics as indicated (maximum dose of Spironolactone 200mg PO daily and Furosemide 80mg PO/IV BID), proton pump inhibitors, and antibiotics (mostly 3rd generation cephalosporins), with treatment escalation based on indication.

In hospital death occurred in 12 participants during their index admission and 6 participants left against medical advice. The median from hospital admission to death was 9days (IQR 8). Additional 4 deaths occurred during the rest of the study period and 4 participants left against medical advice. 20(18.18%) participants were lost to follow up and 6(5.45%) participants were transferred to other hospitals to continue their follow up. (Table 5)

Among the total 16(14.54%) participants who died in the hospital during the study period, the most common immediate causes of death were sepsis/ septic shock in 6(5.45%) participants, and multiorgan failure related to advanced liver failure in 5(4.54%). Massive upper GI bleeding with shock and raised intracranial pressure related to presumed intracranial hemorrhage were documented for 1 participant each.

Table 5. Outcomes of patients with decompensated cirrhosis over 06 months of follow up at TASH

	At Index hospital visit Number (%)	**1 month Number (%)**	**3 months Number (%)**	**6 months Number (%)**
Documented hospitalization during the study period	49(44.54%)	5(5.4%)	3(3.6%)	4(5.1%)
Documented complications of portal hypertension during the study period:				
Upper gastrointestinal bleeding	40(36.36%)	4(4.3%)	4(4.8%)	8(10.4%)
Hepatic encephalopathy	22(20%)	5(5.4%)	2(2.4%)	3(3.9%)

Spontaneous bacterial peritonitis (SBP)	8(7.2%)	-	2(2.4%)	-
Hepatorenal syndrome (HRS)	3(2.72%)	1(1.0%)	1(1.2%)	-
Documented outcomes during the study period:				
Death	12(10.9%)	1(1.0%)	1(1.2%)	2(2.6%)
Left against medical advice	6(5.4%)	3(3.2%)	-	1(1.3%)
Lost to follow up	-	4(4.3%)	5(6.0%)	10(12.9%)
Transferred to another health facility	-	1(1.0%)	-	5(6.5%)
Discharged alive and/or on follow up at TASH	92(83.6%)	83(90.2%)	77(92.7%)	59(76.6%)

Predictors of poor outcome among patients with decompensated cirrhosis

Poor outcome was defined in this study by the presence of any readmission to the hospital, development of variceal bleeding, hepatic encephalopathy, and/or spontaneous bacterial peritonitis within 1, 3, and 6 months of enrollment into the study.

On binary logistic regression analysis, there was a statistically significant association between the presence of comorbidities and upper GI bleeding documented over the study period [COR=2.51; 95%CI: 0.97-6.50] (p=0.057). However, this association was not seen for individual comorbidities. The association between age above 40years and upper GI bleeding was also found to be statistically significant when adjusted for comorbidity, [AOR=2.8; 95%CI: 0.76-5.44] (p=0.017).

A statistically significant association was found between chronic HBV infection and overall mortality during the study period, [COR=4.52; 95%CI: 1.2-16.9] (p=0.025). The association was present even when the risk was adjusted for upper GI bleeding, [AOR=4.4; 95%CI: 1.1-16.9] (p=0.030).

Cryptogenic cirrhosis was found to have a negative association with overall poor outcome during the study period which was statistically significant [COR=0.26; 95%CI: 0.08-0.82] (p=0.022).

Upper GI bleeding and hepatic encephalopathy were found to have a statistically significant association with hospital readmission at 1, 3, and 6 months of the study with adjusted OR (95%CI) of 10.59 (95%CI: 3.76-29.3) [p<0.000] and 93.35 (95%CI: 11.13-782.8) [p<0.000] respectively. However, documented upper GI bleeding during the study period was found to have a negative but weak association with overall mortality during the study period [AOR=0.11; 95%CI: 0.014-0.88] (p=0.038).

The association between age, sex, other etiologies of cirrhosis, Child Pugh score at enrollment and renal function with poor outcome measures during the study period was not found to be statistically significant. (Table 6)

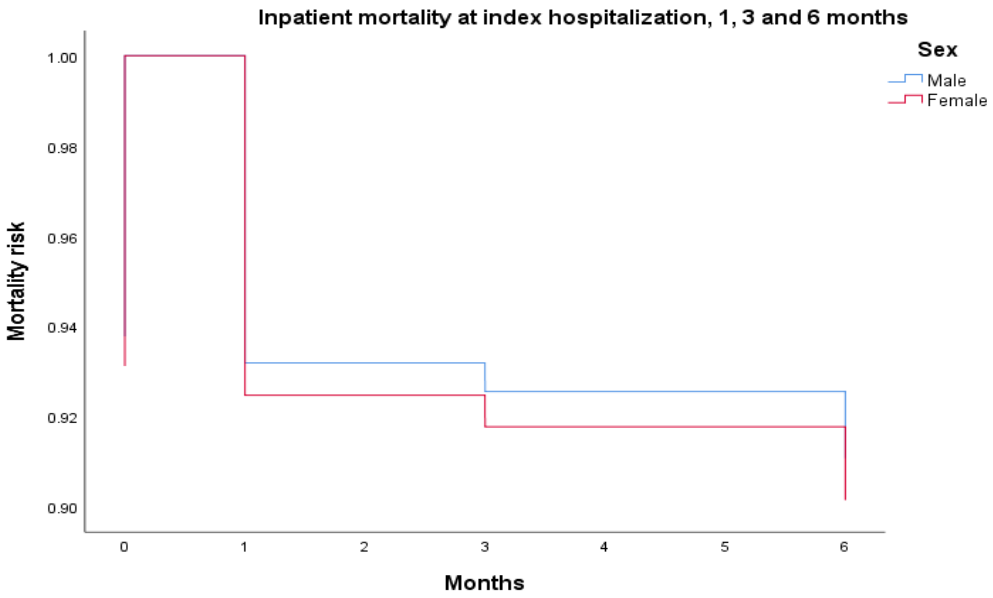
Table 6. Results of Pearson's Chi-square test of factors associated with poor outcome in patients with decompensated cirrhosis at TASH

	Poor outcome at any time during the study period		
	Value	df	Asymptotic significance (2-sided)
Sex	1.87	1	0.171
Age	4.49	1	0.343
Presence of comorbidities	0.09	1	0.764
Etiology of cirrhosis	7.54	4	0.110
Renal function test	21.76	27	0.749
Child Pugh score	4.85	2	0.088

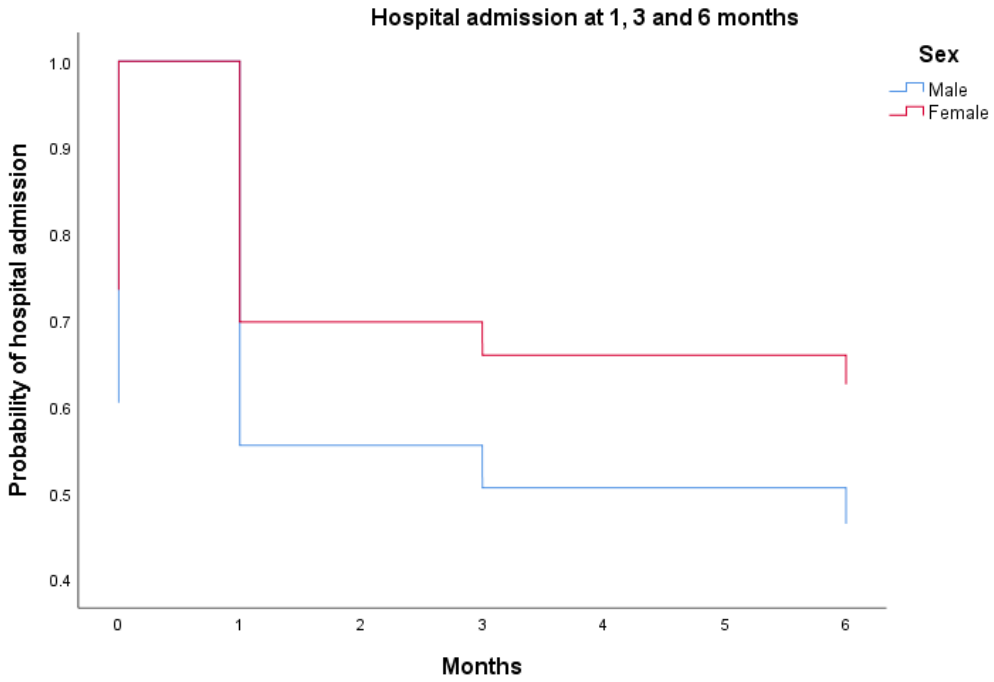
In this study multivariate analysis to estimate the probability of inpatient mortality, hospital admission, and development of new decompensating events (hepatic encephalopathy, upper GI bleeding, SBP, and hepatorenal syndrome) among patients with decompensated cirrhosis was performed using the Cox proportional hazard model. Age was to have a statistically significant association with a higher probability of developing upper GI bleeding, HR 0.97 (95% CI 0.94 - 0.99) but not other poor outcome measures. There was no statistically significant difference with sex, comorbidity, and etiology of cirrhosis in terms of the risk of developing poor outcomes in patients with decompensated cirrhosis at TASH. (Table 7) (Fig 5)

Table 7. Probability of in patient mortality, hospitalization, hepatic encephalopathy, and upper GI bleeding at 1, 3, and 6 months in patients with decompensated cirrhosis at TASH

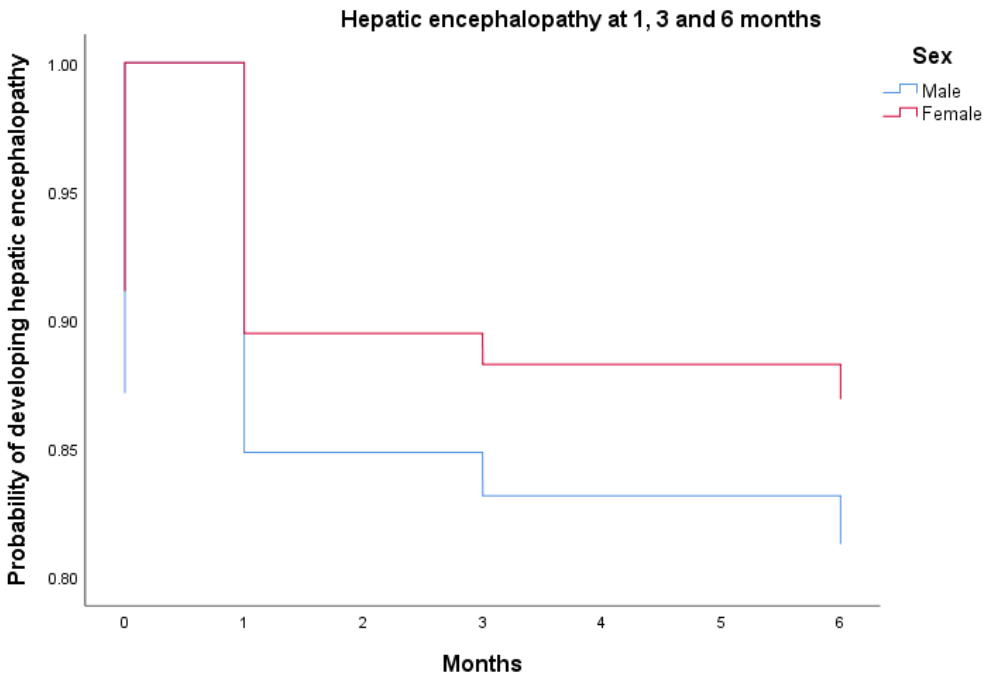
Variables	Inpatient mortality	Hospitalization	Upper GI Bleeding	Hepatic encephalopathy
Age	HR 1.00 (95% CI 0.96-1.05), p=0.847	HR 0.99 (95% CI 0.97-1.01), p=0.539	HR 0.97 (95% CI 0.94-0.99), p=0.03	HR 1.02 (95% CI 0.99-1.06), p=0.07
Sex	HR 0.61 (95% CI 0.19-1.93), p=0.847	HR 1.50 (95% CI 0.76-2.98), p=0.240	HR 1.62 (95% CI 0.66-3.98), p=0.288	HR 1.37 (95% CI 0.50-3.73), p=0.541
Comorbidity	HR 0.74 (95% CI 0.22-2.45), p=0.404	HR 0.78 (95% CI 0.42-1.45), p=0.435	HR 1.42 (95% CI 0.59-3.41), p=0.429	HR 1.26 (95% CI 0.48-3.35), p=0.637
Etiology of cirrhosis	HR 1.12 (95% CI 0.81-1.55), p=0.470	HR 1.09 (95% CI 0.92-1.29), p=0.303	HR 1.03 (95% CI 0.84-1.26), p=0.77	HR 1.09 (95% CI 0.83-1.43), p=0.511


Inpatient mortality at index hospitalization, 1, 3 and 6 months
Sex
Male
Female
Mortality risk
1.00
0.98
0.96
0.94
0.92
0.90
0
1
2
3
4
5
6
Months

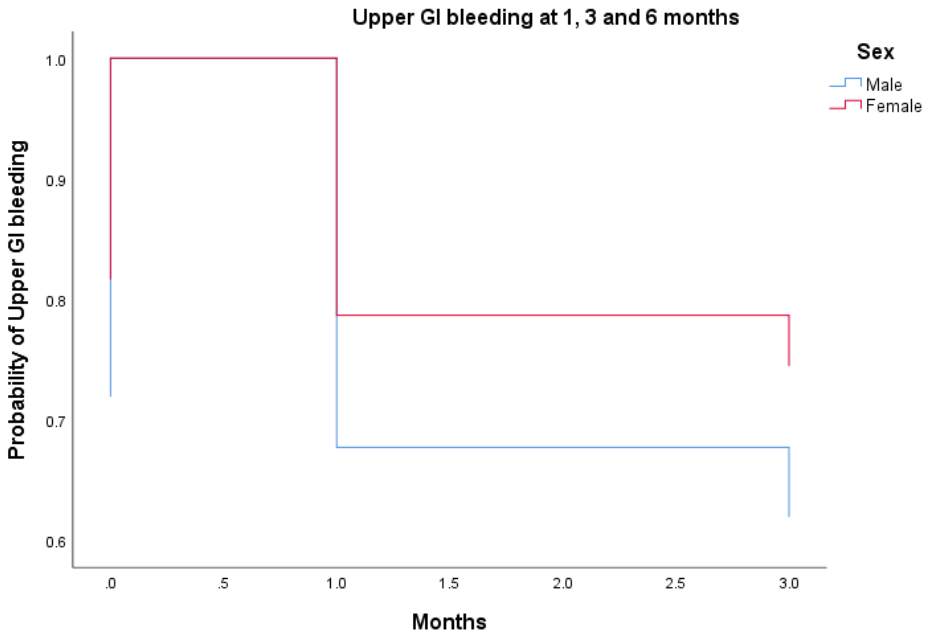
A.


Hospital admission at 1, 3 and 6 months
Sex
Male
Female
Probability of hospital admission
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0
1
2
3
4
5
6
Months

B.



C.



D.

Figure 5. Probability of inpatient mortality (A), hospital readmission (B), hepatic encephalopathy (C), and upper GI bleeding (D) over 06 months in patients with decompensated cirrhosis at TASH

Discussion

A total of 110 patients with decompensated cirrhosis admitted at medical wards, ED and ICU, or seen as an outpatient at GI clinic at TASH from March 2020 – March 2021 were included in this study. Majority of the participants 82(74.5%) were male and the median age of the participants was 40(IQR 18) years. This is comparable to a study by Terefe Tesfaye et al. including 109 admitted patients with CLD in three selected teaching hospitals, where 85(78%) participants were male with the median age of participants being 38(IQR, 30–48) years. (22)

Chronic hepatitis B virus infection was the most common identified etiology of cirrhosis affecting 51(46.36%) of the participants in this study followed by alcohol related cirrhosis in 27(24.55%). Other hospital based studies from Ethiopia also show an equivalent prevalence of HBV infection as a cause of CLD.(19,21,22,38) In a study conducted among 117 admitted patients at St Paul's Hospital Millennium Medical College, hepatitis B virus was diagnosed in 44.4 % and 18% of the causes were due to Hepatitis C Virus. (21)

The most common presenting complaints among participants at index hospital admission/ visit into this study were abdominal distension in 44(40%), tarry stools in 40(36.4%), and bloody vomiting in 35(31.8%), with yellowish discoloration of the eyes/ skin present in 29(26.4%) participants. This finding is also comparable to other studies assessing the clinical profiles and outcomes of admitted CLD patients in Ethiopia. (19,21)

Thirty four (30.9%) participants in this study had a documented comorbidity, mostly HIV and diabetes mellitus. Although the presence of these particular comorbidities concurrently with cirrhosis has been found to significantly reduce survival and confer poor prognosis to patients with decompensated cirrhosis independent of other factors in other studies from France and Spain, the presence of comorbidities was not found to have a statistically significant association with the overall prevalence of poor outcome in this study [COR=0.88: 95%CI: 0.38-2.01] (p=0.7640). (39–41)

In this study, chronic HBV infection was found to have a moderate association with overall mortality during the study period [AOR=4.4; 95%CI: 1.1-16.9], whereas cryptogenic cirrhosis was found to have a statistically significant but negative association with overall poor outcome during the study period [COR=0.26; 95%CI: 0.08-0.82].

In this study, the association between age, sex, etiologies of cirrhosis other than HBV and cryptogenic cirrhosis, and renal function with poor outcome measures during the study period was not found to be statistically significant. This is in contrast to findings from a retrospective cohort study conducted by Kim et al. to determine the mean survival period and cumulative survival rate by classifying patients into high-risk and low-risk groups based on MELD-Na, and to investigate the mortality prognostic factors where age and sex were found to be significant variables in the mortality high group. (16)

Complications of cirrhosis were found to have a significant association with poor outcome in this study. Documented upper GI bleeding during the study period was found to have a moderate association with overall mortality and hospital readmission at 1, 3, and 6 months of the study [AOR=0.11; 95%CI: 0.014-0.88] and [AOR=10.59; 95%CI: 3.76-29.3] respectively. Hepatic encephalopathy had a relatively strong association with hospital readmission during the study period [AOR=93.35; 95%CI: 11.13-782.8].

In comparison, in a study from India conducted to explore the predictors of hospital readmission in patients with decompensated cirrhosis, MELD score at discharge and serum sodium independently predicted 1- month and MELD score, serum sodium, and male gender independently predicted 3-months readmissions. However, neither etiology nor complications of cirrhosis emerged as risk factors. (42)

The presence of renal failure in patients with decompensated cirrhosis is an important predictor of mortality, with the most common incriminated causes being hypovolemia, bacterial infections, and hepatorenal syndrome.(14,33,43) In contrast to the findings from previous studies, renal function was not found to increase the risk of death significantly in this study HR 1.26 (95%CI 0.98-1.61).

Although the accuracy of various prognostic models in predicting in hospital mortality was found to be high in other studies,(11) the association between baseline Child Pugh scores and overall poor outcome was statistically insignificant in this study.

Strengths and limitations of the study

This study has tried to assess the prevalence of poor outcome in patients with decompensated cirrhosis and assess the predictors of poor outcome in the study participants over a follow up period which is longer than previous studies conducted in the country.

However, due to the retrospective design of the study, various confounders that can contribute to the development of poor outcomes could not be adequately explored. The utilization and documentation of laboratory and imaging investigations were very erratic as seen during data collection. This might limit the use of these parameters by incorporation into risk prediction models for the specific patient population.

Finally, since the study period overlaps with the peak of the COVID-19 pandemic in our country, utilization of virtual clinic services (where physical examination and laboratory parameters were not usually documented in the electronic medical record system) and longer appointment times might affect the estimation of overall survival and the rates of loss to follow up.

Conclusion

Chronic hepatitis B infection was the most common etiologic cause of cirrhosis among the participants and a strong predictor of death during the study period. Age above 40 years was found to contribute significantly to the development of upper GI bleeding. Hepatic encephalopathy and upper GI bleeding were predictors of hospitalization among the study participants. Sex, other etiologies of cirrhosis, Child Pugh score at enrollment and renal function were not found to be associated with poor outcome measures during the study period.

Recommendations

A prospective multicenter study designed to assess short and long term outcomes of patients with cirrhosis in the context of specific etiologies and available therapeutic options in the country is needed to fully explore the predictors of poor outcome among this patient population.

Since chronic HBV infection was found to be the commonest etiology and strong predictor of poor outcomes among patients with decompensated cirrhosis, improving the availability of vaccine and treatment for HBV might improve the overall outcome of these patient groups.

Documentation of clinical data in electronic as well as paper based medical recording systems should be standardized to include disease specific parameters so that future data collection and analysis can be thorough.

Availability of routine laboratory and imaging tests without frequent interruption, and their appropriate utilization at recommended intervals is necessary for the follow up and risk stratification of patients with decompensated cirrhosis.

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Annex

Structured Questionnaire

Participant Identification Number: _____

1. Age: _____
2. Sex: ☐ Male ☐ Female
3. Duration of chronic liver disease: _____
4. Etiology of cirrhosis

☐ HBV
☐ HCV
☐ Alcoholic liver disease
☐ NASH
☐ Autoimmune hepatitis
☐ Cryptogenic cirrhosis
☐ Others: Specify _____

5. Presence of comorbidities

☐ Diabetes mellitus
☐ Hypertension
☐ HIV
☐ Chronic kidney diseases
☐ Heart failure
☐ Others: Specify _____

6. Current list of medications: Please tick on all that apply to the participant

Medication	Yes	No	Regimen	Dose
Diuretics				
Furosemide				
Spironolactone				
Others: Specify _____				
Non-selective β-blocker				
Propranolol				
Carvedilol				
Others: Specify _____				
Antiviral therapy				
DAAs				

TDF/TAF				
3TC/FTC				
Others:				
Antibiotics: Specify				
Anti TB: Specify				
Anti-retroviral therapy: Specify				
Anti-hypertensive: Specify				
Hypoglycemic agents: Specify				
Others: Specify				

7. Clinical information: Please tick on all that apply to the participant

	At presentation	01 month	03 months	06 months
History at presentation				
Fatigue				
Yellowish discoloration of the eyes/skin				
Abdominal distension				
Generalized body swelling				
Bloody vomiting/ tarry stools				
Altered behavior/ mental status				
Others: Specify _____				
Physical examination findings				
Fever				
Jaundice				
Conjunctival/ palmar pallor				
Splenomegaly				
Hepatomegaly				
Intraabdominal mass				
Abdominal tenderness				
Ascites				

Peripheral edema				
Mental status (GCS)				
<7				
7-12				
13-15				
Asterixis				
Others: Specify _____				

8. Assessment of alcohol intake:
    a. Does the patient consume alcohol currently? ☐ Yes ☐ No
    b. If the answer to the above question is yes, is the quantity of alcohol intake documented?
        ☐ Yes ☐ No
    c. Quantification of alcohol intake per week ☐ <2 drinks ☐2-5drinks ☐ >5drinks
9. Laboratory parameters: Please tick on all that apply to the participant

	At presentation	01 month	03 months	06 months
Complete Blood Count				
WBC count/uL				
Hemoglobin/Hematocrit (g/dL)				
Platelet counts/uL				
Renal function test				
Creatinine (mg/dL)				
Liver function tests				
Albumin (g/dL)				
Bilirubin Total (mg/dL)				
Coagulation profiles PT (Sec) INR				
Liver enzymes				
AST (IU/L)				

ALT (IU/L)				
ALP (IU/L)				
Serum electrolytes				
Sodium (mmol/L)				
Potassium (mmol/L)				
Peritoneal fluid analysis				
WBC count/uL				
Absolute neutrophil count/uL				
SAAG (g/dL)				
Gram stain /Culture				
Others analysis parameters: Specify _____				
Miscellaneous				
HBV viral load				
HCV genotype/ viral load				
Others: Specify _____				

10. Imaging studies (finings): Please tick on all that apply to the participant

	At presentation	01 month	03 months	06 months
Abdominal ultrasound				
Ascites	☐ Absent ☐ Mild ☐ Moderate ☐ Massive	☐ Absent ☐ Mild ☐ Moderate ☐ Massive	☐ Absent ☐ Mild ☐ Moderate ☐ Massive	☐ Absent ☐ Mild ☐ Moderate ☐ Massive

Splenomegaly				
Evidence of collateral circulation				
Small sized nodular liver				
Liver mass				
Portal vein thrombosis				
Others: Specify _____				
Triphasic abdominal CT				
Ascites				
Splenomegaly				
Evidence of collateral circulation				
Liver mass				
Portal vein thrombosis				
Non malignant				
Malignant				
Others: Specify _____				

11. Other tests

	At presentation	01 month	03 months	06 months
Endoscopy				
Varices				
Esophageal	☐Small ☐Medium ☐Large	☐Small ☐Medium ☐Large	☐Small ☐Medium ☐Large	☐Small ☐Medium ☐Large
Gastric	☐Small ☐Medium ☐Large	☐Small ☐Medium ☐Large	☐Small ☐Medium ☐Large	☐Small ☐Medium ☐Large

Portal hypertensive gastropathy				
Evidence of recent bleeding				
Sclerotherpay				
Band ligation				
Others: Specify _____				
Transient elastography (Fibroscan®) Liver stiffness (kPa)				
Liver biopsy				

12. Child-Pugh score: _____

	At presentation	01 month	03 months	06 months
Class A				
Class B				
Class C				

13. Number of admissions during the study period: _____

14. Reason for most recent/ current admission:

☐ Massive/ refractory ascites

☐ SBP

☐ Upper GI bleeding

☐ Hepatic encephalopathy

☐ Hepatorenal syndrome

☐ Hepatocellular carcinoma

☐ Others: Specify _____

15. Total duration of hospital stay: _____

16. Therapeutic interventions (specific to cirrhosis and its complications):

	At presentation	01 month	03 months	06 months
Supportive				
Antibiotics				
Diuretics				
Therapeutic peritoneal tap				
Albumin infusion				
Endoscopic band ligation				
TIPS				
Others: Specify _____				
Definitive				
Antiviral treatment Specify _____				
Liver transplantation				
Others: Specify _____				

17. Outcome

	At 01 month	03 months	06 months
Alive and well			
Admitted to hospital			
Died			
Lost to follow up			
Others			

Specify cause of death (if it is known) _____

18. Interval between hospital admission/discharge and death _____