Clinical outcomes of patients with chronic liver disease admitted to selected tertiary care hospitals, Ethiopia: Prospective cohort study

By: Behailu Terefe (B. Pharm.)

A thesis submitted to Department of clinical Pharmacy, Institute of health, Jimma University; in partial fulfillment of the requirements for degree of Master of Science (MSc) in clinical pharmacy

December 2018

Jimma, Ethiopia

Clinical outcomes of patients with chronic liver disease admitted to selected tertiary care hospitals, Ethiopia: Prospective cohort study

By: Behailu Terefe (B. Pharm.)

Advisors: Teshale Ayele (B. Pharm, MSc)

Dr. Esayas Gudina (MD, chief clinical director)

December 2018

Jimma, Ethiopia

Abstract

***Background**: Chronic liver disease (CLD) is a series of liver derangement persisting for at least 6 months. The cause of CLD can be viral and/or non-viral. In Ethiopia, despite the high burden report; data on different aspects of CLD is limited.*

***Objective**: To assess clinical outcomes and associated factors among chronic liver disease patients admitted to medical wards of selected hospitals.*

***Methods:** A prospective cohort study was conducted on 109 adult CLD patients recruited using purposive sampling technique from April 1, 2018 –October 5, 2018. Data was collected using tool comprised of pertinent parameters, entered into Epi-Data 4.2.0.0 for cleaning and analyzed using STATA 13.0. Result of descriptive analysis was presented using text, tables and figures. Kaplan-Maier and cox-regression analysis was used to compare the survival experience and to determine explanatory variables, respectively. Hazard ratios with a p-value <0.05 was considered to declare statistical significance.*

***Result**: A total of 109 CLD patients (77.98% male) were included. Mean (±SD) age of the participants was 39.03 ± 13.80. From the total of 109 CLD patients, 52 (47.71%) were with viral etiology. The overall median length of hospital stay was 7 (4 -11) days. Seventeen (15.60%) patients developed major acute in-hospital complications of CLD; 9(8.26%) were from viral group. The incidence rate (IR) of in-hospital acute complications of CLD in the viral group was insignificantly lower (crude IRR=0.911 [95% CI, 0.311-2.714, p= 0.424]). Duration since diagnosis (AHR=1.029 [95%CI, 1.004-1.054, p=**0.025**]) and aspartate amino transaminase (AST) level (AHR=1.007 [95%CI, 1.003 -1.010, p<**0.001**]) were the identified predictors for in-hospital acute complication of CLD. The cumulative mortality from admission to 30 days of hospital discharge was 38 (34.86%); 18 (16.51%) were from patients with viral etiology. Of these, 31 (28.4%) deaths were in-hospital; 13 (11.93%) were from viral group. IR of in-hospital mortality was insignificantly lower in the viral group (crude IRR= 0.635 [95% CI, 0.286 - 1.372, p=0.108]). Furthermore, a higher median survival time [29 days (13-29 days)] was identified for the viral group (log rank, **p=0.04**). Mean corpuscular volume (MCV) was the independent predictor of in-hospital mortality (AHR=1.004 [95%CI, 1.001 - 1.007, p=**0.013**]).*

***Conclusion:** HBV was the commonest etiology identified in this study. Incidence of acute in-hospital complications of CLD and death were insignificantly lower among patients with viral etiology. Approximately, one death was observed for four admissions with CLD and the median survival time was significantly higher for the viral group. Prolonged duration since diagnosis and the increment in AST level were found to increase the rate for incidence of acute in-hospital complications of CLD. Since these factors are associated with progression of CLD, availing immunoprophylaxis and targeted treatments might benefit CLD patients. Furthermore, increment in MCV level at admission was identified to increase the risk of in-hospital mortality. As a result, attention is required in the early detection and correction of hematologic abnormalities. Finally, because of the small and unequal sample size used, the difference in clinical outcomes among patients with or without viral etiology cannot be concluded confidently; a further study with adequate sample size is recommended.*

***Key words**: chronic liver disease, Clinical Outcomes, Ethiopia*

Acknowledgments

First, I would like to acknowledge Jimma University for providing me the opportunity and fund to conduct this study.

Next, I would like to pass my deepest gratitude to my advisor Mr. Teshale Ayele for his countless endeavors in guidance of this work through correcting, editing and showing the way how to realize this research. I also pass my gratitude to my second advisor, Dr. Esayas Gudina, for his guidance in some of the clinical aspects in this study. I would also pass my gratitude to participants in this study for their kind cooperation during the follow-up period.

Finally, I would like to say thank you for data collectors and the entire staff members of Medical wards of the selected hospitals for their nice and attractive cooperation during the time of data collection.

Table of contents

Contents

List of Tables

List of Figures

List of Acronyms

ALD	Alcoholic Liver Disease
CDC	Centers for Disease Control and Prevention
CLD	Chronic Liver Disease
DALYs	Disability-Adjusted Life Years
EFMOH	Ethiopian Federal Ministry of Health
GBD	Global Burden of Disease Study
HBsAg	Hepatitis B Surface Antigen
HBV	Hepatitis B Virus
HCC	Hepatocellular Carcinoma
HCV	Hepatitis C Virus
HE	Hepatic Encephalopathy
HFSUH	Hiwot Fana Specialzed University Hospital
HIV/AIDS	Human immunodeficiency virus/Acquired immunodeficiency syndrome
HVPG	Hepatic Venous Pressure Gradient
IRB	Institutional Review Board
JUMC	Jimma University Medical Center
LAMA	Left Against Medical Advice
LOS	Length of Hospital Stay
NAFLD	Non-alcoholic Fatty Liver Disease
NSBB	Non-selective beta blocker
PH	Portal Hypertension
PMN	Polymorphonuclear
PPI	Proton pump inhibitor
QOL	Quality of Life
SBP	Spontaneous Bacterial Peritonitis
SPHMMC	St. Paul's Hospital Millennium Medical College
STATA	South Texas Art Therapy Association
VH	Variceal Hemorrhage
WHO	World Health Organization

1. Introduction

1.1 Background

Chronic liver disease (CLD) is a series of liver derangement in which hepatic inflammation and subsequent necrosis persists for at least 6 months. It could assume milder (non-progressive or progress only insidiously) or severe forms (which may result in cirrhosis) (1). Cirrhosis is the end spectrum of all CLD characterized by advanced fibrosis, scarring, and formation of regenerative nodules leading to hepatic architectural distortion(2). It is characterized by the longest asymptomatic phase termed as compensated cirrhosis, followed by the occurrence of complications, termed decompensated cirrhosis. The rate of transition is estimated to be 5%-7% per year and this period of transition is critical step, which end up in hepatic decompensation unless controlled(3,4).

By far, CLD has a significant public health and economic burden(5,6). According to Global Burden of Disease study (GBD), CLD was responsible for an estimated 2.3% of the total mortality and 38,856,731.05 Disability-Adjusted Life Years (DALYs) in the years between 1990-2016(7). In United States(US), data analyzed from 1993–2012 showed that, cirrhosis and its complications accounted for 160,280 hospitalizations, with a mean length of stay(LOS) of 5.8 days(8). In 2015, Centers for Disease Control and Prevention (CDC) reported that CLD was responsible for an estimated mortality of 40,326 i.e. 1.5 % of total deaths, making it to rank 12th among the 15 leading causes of death (9).

In Sub-Saharan Africa, GBD reported an estimated figure of 131,535.22 death due to CLD from 1990-2016. The predominant causes of CLD related mortality were hepatitis B virus (HBV), hepatitis C virus (HCV) and alcohol; accounting for 0.65%, 0.33% and 0.44% of the total mortality, respectively. In Ethiopia, an estimated 18,007.92 deaths were attributable to CLD in the year 2016. HBV, HCV and Alcohol accounted for 0.94%, 0.63% and 0.66% of total deaths, respectively(7,10).

There are several causes of CLD, among which viral causes are recognized as a major public health challenge that requires an urgent response(11,12). According to the 2017 Global Hepatitis Report of World health Organization (WHO), viral hepatitis has caused 1.34 million deaths in 2015. Hepatitis B and C were responsible for 96% of the total mortality. Most of these deaths were due to CLD, particularly cirrhosis and hepatocellular carcinoma (HCC) accounted for 720, 000 and 470, 000 deaths respectively(13).

The stage of CLD is important in determining survival, symptoms and patients` quality of life (QOL). Those patients with compensated cirrhosis have a significantly longer median survival (>9-12 years vs. 1.8 years), usually free of symptoms with a better QOL than decompensated cirrhosis (14–17). Decompensated cirrhosis is associated with most of the complications, of which, portal hypertension (PH) is the most common. In these patients, the risk of developing varices, overt clinical decompensation[ascites, variceal hemorrhage (VH), and encephalopathy (HE)] and HCC increases when hepatic venous pressure gradient (HVPG) is ≥ 10 mm Hg(18,19).

Clinically, the predominant decompensation event is ascites occurring in about 50% of patients with compensated cirrhosis within 10 years. It is also the most common reason for CLD related hospital admission, accounting for approximately 15% of death in one year and 44% in five year after its occurrence (20–22). In these patients, infections are the leading cause of death, among which ascitic infection (12%) is the commonest at admission ridding the mortality rate as high as 19%(23,24). Some drugs, like proton pump inhibitors have been identified to increase the incidence rate of these infections(25).

The second clinical decompensation is hepatic encephalopathy; which occurs in an estimated 30%-45% of cirrhotic patients resulting in judgmental impairment, poor QOL and increased risk of accident(26). Several factors can precipitate hepatic encephalopathy (HE) in cirrhotic patients including; infections, GI bleeding, electrolyte disorder,constipations and diuretics(27,28). About 50% of cirrhotic patients experience gastro-esophageal varices, which results in the most lethal complication termed VH; for which non-selective beta blockers (NSBBs) are used as primary and secondary prophylaxis. The existence of varices is related with the severity of liver disease and carries a mortality rate of 20% at 6 week (29–35).

Recently, improvement or even reverse in the progression of cirrhosis have been shown with treatments targeting the underlying cause. Nevertheless, managing patients with cirrhosis is still a challenge requiring an organized and systematic approach(2). Several factors affecting clinical outcomes of these patients were reported, and poor outcome was reported in resource limited countries. As a result, assessing clinical outcomes and associated factors was by far important(36). Therefore, this study was intended to assess the clinical outcomes of hospitalized CLD patients.

1.2 Statement of the problem

Globally, CLD accounts for a significant public health and economic burden. It is associated with increased morbidity, mortality and health care costs. Most of this burden occur among patients with advanced disease(6,18). The epidemic of obesity, hazardous alcohol consumption and viral hepatitis (HBV and HCV) are partly contributing to the current rise of CLD burden (37).

Global report showed that, CLD had caused an estimated 2.3% of the total mortality in the year 1990-2016 (7,10). In Ethiopia, the prevalence and burden of CLD is estimated to be high(10,38). Notwithstanding this, CLD has not been given the attention it deserves as can be witnessed by the lack of nationwide representative data. This posed difficulty to present: incidence, prevalence, and mortality rates accurately. Some community and institutional based studies were conducted in different parts of the country. In one community-based longitudinal study, CLD was attributed to 2% of the overall deaths(39). In other similar study, CLD was among the top 10 cause of death in the age group 15–49 years (13.7%)(40). Furthermore, in other study 2.3% medical admissions and 41% in-hospital mortality were ascribed to CLD(41). A Study from Harar also reported 6% in-hospital mortality due to CLD(42).

The existing studies specific to CLD in Ethiopia are very few and some of them were conducted many years ago. The institutional-based studies were also single center and retrospective. Additionally, these studies also lack comprehensiveness with regard to clinical spectrum. Hence, there was a need for further prospective study with inclusion of different aspects of CLD. Therefore, this study was aimed to assess clinical outcomes of CLD patients admitted to internal medicine wards of Jimma University Medical center (JUMC), Saint Paul's Hospital Millennium Medical College (SPHMMC) and Hiwot Fana University Hospital (HFSUH).

1.3 Significance of the study

Prevention and control of diseases is one of the strategic initiatives setted by Ethiopian government in order to achieve the desire to have the highest possible level of health and quality of life for all its citizens in the country. With this, one of the most important strategies to prevent CLD is the identification and management of potentially avoidable or manageable factors. Thus, this study attempted to identify factors, like etiology of CLD, which will help as a target in the prevention and control of this disease. This study had also assessed the outcome of admitted CLD patients associated with considerable mortality which should alarm health institutions and policy makers to reconsider their measures.

Results generated from this study will also be used as input for further studies on this and related topics. Furthermore, it will benefit JUMC, SPHMMC, HFSUH and other health institutions in setting targets of intervention for improving their patients care.

2. Literature Review

Various studies have been conducted in different parts of the world regarding different aspects of CLD such as etiologies, outcomes and so on.

2.1 Etiology of CLD

Etiology of CLD shows a marked geographic difference worldwide between countries (43,44). In one retrospective cohort study conducted on cirrhotic patients in Australia; alcohol (43.9%) was identified as the most common cause of cirrhosis, followed by viral hepatitis (34.1%)(5). In other retrospective cohort study conducted in New Zealand on 746 cirrhotic patients; chronic HBV(37.3%), alcoholic liver disease (ALD) (24.1%), chronic HCV (22.3%) and NAFLD (16.4%) were identified as the primary causes of cirrhosis(45).

Moreover, in a retrospective cohort study done on 522 cirrhotic patients in Greece, HCV (41%) was identified as the commonest cause of cirrhosis followed by alcohol (31%)(3). Similarly, in a study conducted on 1080 subjects in the same country; Chronic HBV, Chronic HCV and co-infection together accounted for 86.1% of CLD causes. While, Chronic HCV alone, NAFLD and ALD accounted for 44.9%, 9.2%, and 4.8% as a cause for CLD(46).

In a cross-sectional study conducted among 13,014 CLD patients in India; the commonest reported cause of CLD was HBV (47). Similarly, in a cross-sectional study conducted on 334 hospitalized adult patients with CLD in Ethiopia; chronic HBV was identified in 86% of patients(38). In other retrospective cohort study done on 117 CLD patients admitted to intensive care unit (ICU) or internal medicine wards, in Ethiopia; HBV(44.4%), HCV(18%), ALD(2%) and mixed infection(3 individual cases) were reported as etiologies of CLD(41). Furthermore, in a cross-sectional study conducted on 212 patients with CLD in two public hospitals in Harar; cause of CLD was not identified in 55.3% of the patients; but, Chronic HBV (36.7%), hepatic schistosomiasis(2.7%), alcohol misuse(2.0%), Chronic HCV(1.3%), autoimmune hepatitis (AIH) (1.3%) and visceral leishmaniasis (0.7%) were CLD causes identified in others(42).

2.2 Chronic liver disease Outcomes

CLD is a major public health problem accounting for significant morbidity and mortality(44). Various studies have been conducted in different parts of the world to determine the morbidity and mortality associated with CLD, and variable outcomes were reported.

2.2.1 Incidence of acute in-hospital chronic liver disease complications

In one retrospective cohort study conducted among 746 cirrhotic patients; a lower incidence of acute complications of CLD were reported among patients with viral etiology as compared to their non-viral counterpart (45).

On the other hand, a prospective cohort study undertaken in France among 64 Cirrhotic patients admitted with gastrointestinal bleeding; 18(43%) new cases of bacterial infections were documented within 7 days of admission. Four(6.35%) late SBP incidences were reported(48). In other prospective cohort study conducted in tertiary centers on 1,560 hospitalized cirrhotic patients with best standard of care; 117(22.67%) patients developed new cases of HE during hospitalization. Of these, 41(35.5%) had grade 3 to 4 HE(49).

2.2.2 Incidence of mortality

In one prospective cohort study conducted among cirrhotic patients admitted to general critical care unit in United Kingdom; 52.9% in-hospital mortality was reported(50). On the other hand, in a cross-sectional study undertaken in Argentina on 180 adult alcoholic cirrhosis patients; 10.56% in-hospital mortality was recorded(51). On the other hand, a prospective cohort study conducted in Colombia among adult patients with cirrhosis, documented a 23.5% in-hospital mortality(52). Other prospective cohort study done including 402 patients with compensated HCV-related cirrhosis in Cuba; 10% deaths was reported (53).

Furthermore, in a cross-sectional study conducted on 1080 hospitalized cirrhotic patients in Morocco; 8.7% in-hospital mortality was quantified(54). In other cross-sectional study on CLD patients in Ethiopia; a 41% in-hospital death and about 17% discharge without improvement in disease condition was documented(41).

2.3 Predictors of Clinical Outcomes

Parameters helpful in the prediction of acute complications of CLD and mortality were reported in different studies. A prospective cohort study conducted in tertiary centers on 1,560 hospitalized cirrhotic patients showed an increased risk of complications with severity of HE. Furthermore, an increased risk of in-hospital as well as 30-day mortality was documented with increased severity of HE(49). In other prospective cohort study conducted among CLD patients in Europe, recent diuretic use was reported as independent predictors of

HE. In this study, a significant increase in the hazard of mortality was reported with increment in age, creatinine, bilirubin, INR, and severity of HE(28).

Various literatures had shown increased risk of acute complications of CLD in conditions like: GI bleeding, infections, diuretic use, renal derangements, alcohol use, and proton pump inhibitors (PPI)use(25,27,43,55).

A cross-sectional study conducted in Argentina on 180 adult alcoholic cirrhosis patients identified serum urea, creatinine and prothrombin time, as predictors of in-hospital mortality(51). Furthermore, a retrospective cohort study reported a significantly highest all-cause and non-HCC mortality rate among patients with ALD and NAFLD cirrhosis as compared with viral hepatitis cirrhosis(45). In other retrospective cohort study, patients who experienced variceal bleeding survived better as compared to other mode of decompensation. Moreover, simultaneous multiple complications resulted in high mortality rate(3).

Furthermore, in a retrospective cohort study conducted in Korea; a significant increase in the risk of liver related mortality was reported with elevation in MCV level (56). In other retrospective cohort study conducted in Morocco; hepatic encephalopathy, infection, renal failure (serum creatinine $\geq$ 15 mg/l) and hyponatremia were revealed as independent predictors of in-hospital mortality(54).

On the other hand, a cross-sectional study conducted among CLD patients; late presentation, unavailability of specific therapies and advanced hepatology centers were reported as a reasonable factors for increased mortality of CLD patients(41).

2.3 Conceptual framework

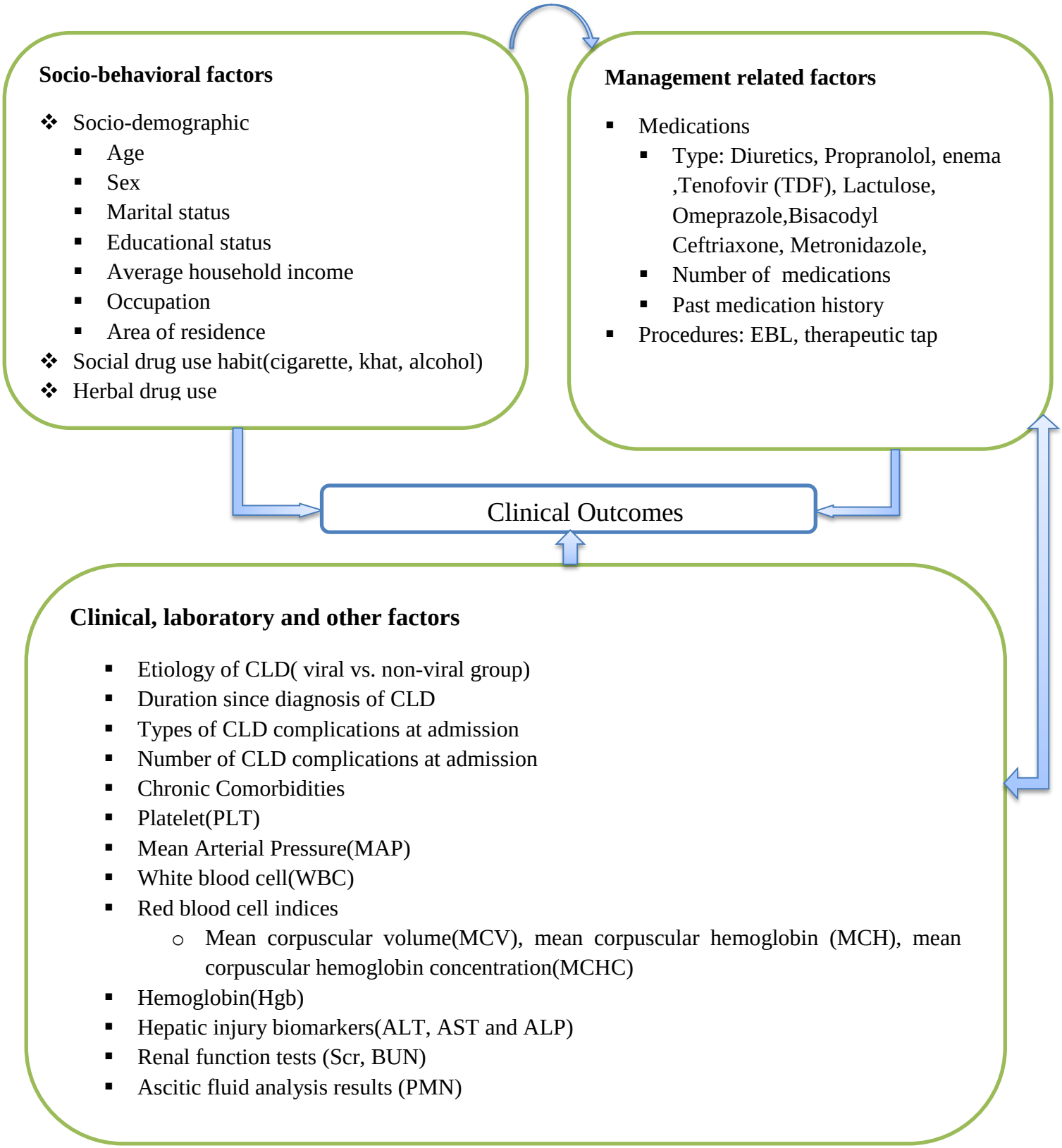


Figure 1: Conceptual framework for factors associated with CLD Clinical Outcomes

3 Objectives

3.1 General objective

To assess clinical outcomes and associated factors among chronic liver disease patients admitted to medical wards of selected hospitals.

3.2 Specific objectives

- To describe chronic liver disease etiologies identified in chronic liver disease patients admitted to medical wards of selected hospitals
- To assess incidence of acute in-hospital complications of chronic liver disease in chronic liver disease patients admitted to medical wards of selected hospitals
- To assess mortality in chronic liver disease patients admitted to medical wards of selected hospitals
- To determine predictors for in-hospital incidence of acute complications of chronic liver disease in chronic liver disease patients admitted to medical wards of selected hospitals
- To determine predictors for in-hospital mortality of chronic liver disease patients admitted to medical wards of selected hospitals

4 Methods and Materials

4.1 Study settings and period

General setting: Ethiopia is a landlocked country in the Horn of Africa splitted by valley of the East African Rift (also known as Gregory Rift)(57). Based on the most recent United Nations projections, this country is a home for an estimated population of 107.53 million. This makes it to be the second most populous country in Africa next to Nigeria, and the 14th most populous country in the world. The capital city is Addis Ababa(58). Despite its wealth in culture, the economic wealth of its citizens is poor with a Gross Domestic product (GDP) per capita of US$ 861 in 2017(59). Infectious and communicable diseases account for about 60-80 % of the health problems in the country; likewise, non-communicable diseases are thought to be rapidly increasing in this country(60)**.**

Study sites: The study was conducted in three tertiary teaching hospitals in Ethiopia: JUMC, SPHMMC and HFSUH medical wards. JUMC is located in Jimma town; Jimma Zone, Oromia Region, Southwest Ethiopia and is about 346 km away from Addis Ababa. This hospital serves for a Catchment's population of 15,000,000. This hospital has 632 beds and internal medicine is one of the service provided by this hospital(61).. SPHMMC is a tertiary hospital delivering medical services to patients referred from all over the country. This hospital has an inpatient capacity of more than 700 beds and sees an average of 1200 clients daily. It was the first hospital offering chronic HBV treatment in the country. It also provides services like, EBL and has subspeciality/fellowship in gastroenterology program(62). HFSUH is a specialized hospital located in East Hararge, Ethiopia. The study was conducted at medical ward, Harar, Ethiopia. The medical ward has female and male wing. The study was conducted in the period from April 1– October 5, 2018 G.C**.**

4.2 Study design

Hospital based prospective cohort study was employed.

4.3 Population

4.5.1 Source population

All adult patients admitted to internal medicine wards of the three selected hospitals during the study period.

4.5.2 Study population

All adult CLD patients admitted to internal medicine wards of the three selected hospitals during the study period fulfilling eligibility criteria.

4.5.3 Eligibility criteria

Inclusion criteria

- Consenting adult CLD patients (age≥18years old)
- Both newly diagnosed and previously diagnosed CLD patients

Exclusion criteria

- Readmitted CLD patients
- CLD patients admitted for other than CLD related problems(s)
- Pregnant CLD patients

4.6 Sample size determination and sampling technique

The sample size was calculated using Fisher`s single population proportion formula as follows:

$$n=\frac{(Za/2)2P(1-P)}{d2}=372$$ Where,

n= minimum sample size required for the study

Z= standard normal distribution (Z=1.96) with a confidence interval of 95% and $\propto$=0.05

P= in-hospital mortality due to CLD=41% (from study conducted in SPHMMC).

d= level of precision or tolerable margin of error=5%

Reviewing admissions in selected hospitals in the past 6 months before starting this study, the total number of admitted CLD patients were 134, which was <10,000. So, using correction formula, $n_f = \frac{n*N}{n+N}\approx 99$. Adding 5% contingency the total sample size became 105. So, the minimum sample size required for this study was 105 CLD patients. The flow chart for sampling takes the following form:

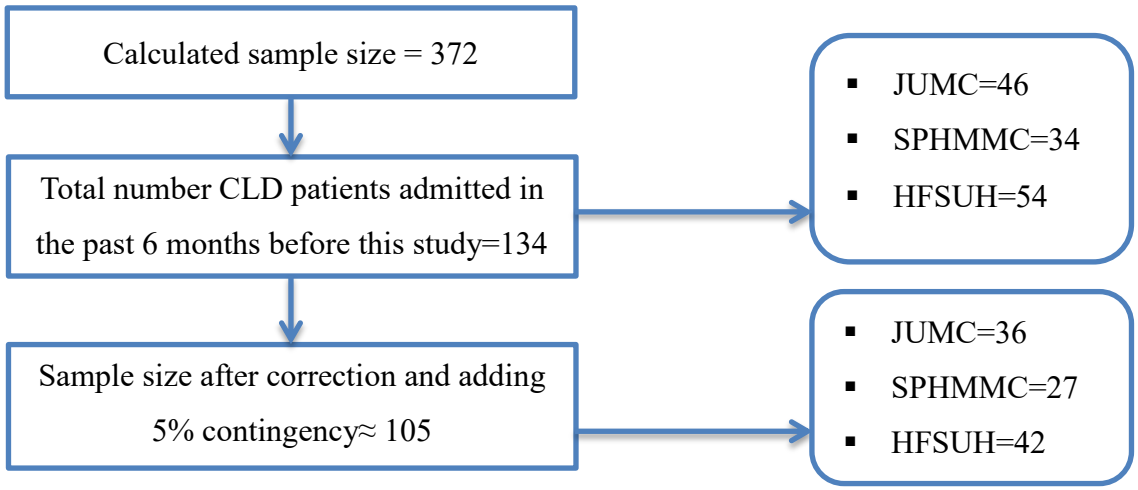


Figure 2: Flow chart shows sampling procedure planned at the conception of this study

In actual scenario, all CLD patients admitted to medical wards of selected hospitals during the study period and who fulfilled the inclusion criteria (N=109) were included. Purposive sampling technique was used for recruiting participants.

4.7 Study variables

4.7.1 Dependent variables

- Primary outcome variables
  - Clinical outcomes
- Secondary outcome variables
  - Length of hospital stay

4.7.2 Independent variables

- **Patient related factors**
  - Age
  - Sex
  - Marital status
  - Educational status
  - Average monthly household income(ETB)
  - Occupation
  - Herbal drug use
  - History of Social drug use
    - Cigarette, khat, alcohol
  - Residence(Rural, Urban)
- **Management related factors**
  - Medications
    - Past medication history
    - Types: Diuretics, Propranolol, enema Tenofovir (TDF), Lactulose, Bisacodyl, Ceftriaxone, Metronidazole
    - Number of medications
  - Procedures: EBL, therapeutic tap
- **Clinical, biochemical factors and other**
  - Etiology of CLD (viral vs. non-viral group)
  - Duration since diagnosis of CLD
  - Types of CLD complications at admission
  - Number of CLD complications at admission
  - Chronic Comorbidities
  - Platelet(PLT)
  - Mean Arterial Pressure(MAP)
  - White blood cell(WBC)
  - Red blood cell indices
    - Mean corpuscular volume(MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC)
  - Hemoglobin(Hgb)
  - Hepatic injury biomarkers (ALT, AST and ALP)
  - Renal function tests (Scr, BUN)
  - Ascitic fluid analysis results (PMN)

4.8 Data collection tool and Procedure

For this study, data collection tool designed after reviewing relevant literatures and active patient follow-up charts was used. The tool consists of relevant components for collecting socio-behavioral and clinical data. Then, data was collected prospectively from active patient`s medical chart, patients and/or caregivers**.** Data on socio-behavioral and baseline clinical characteristics [including, baseline laboratory findings; etiology; chief complaints; CLD complications and management(s) at admission, chronic comorbid illnesses)] were recorded at admission. The presence/absence of any CLD complications at admission or the new development of acute complications of CLD after admission was ascertained from physician`s diagnosis with/without laboratory test results. Besides, only the first incident acute in-hospital complication was considered throughout the analysis process. Patients were followed from admission till 30 days of hospital discharge, and in-hospital acute complications of CLD, and mortality were recorded upon occurrence. Patients were censored at their last day of contact. Data on 30 days post discharge status was collected after making telephone interview with patient`s caretakers or close friends report via telephone interview

4.9 Outcome measures and validating methods

Patients were followed from admission till 30 days of hospital discharge. During hospital stay, patients were followed for incidence of acute complications of CLD as well as mortality. In-hospital incidence of SBP was diagnosed when ascitic fluid absolute neutrophil count was >250/μL (in patients deemed free of SBP at admission). Physician`s clinical judgment and diagnosis was used for incident HE with further request for ascertainment. Then, HE was graded using West Haven Criteria (I, II,III and IV). Incident acute or overt gastrointestinal bleeding was diagnosed clinically by physician`s with/without endoscopic evaluation. Furthermore, due to resource limitation for identification of bleeding types (variceal or non-variceal), with support from epidemiology evidences, all acute gastrointestinal bleeding was considered CLD complication. Gastrointestinal bleeding was assessed clinically by the presence of hematemesis, melena, or hematochezia. In-hospital death was ascertained from physician`s and discharge summary note. Post discharge 30-day status was ascertained from patient`s caretakers or close friends report via telephone interview.

4.10 Data Quality Assurance

A carefully designed data collection tool comprising variables to collect important data required to meet the setted objectives was used. Four data collectors (two Pharmacists with Bachelor pharmacy degree and two clinical nurses with Bachelor of Science degree) and four supervisors (Medical interns) were hired and two days training on the data collection tool and general procedures was given by the principal investigator (PI). The supervisors were mandated to supervise data collectors and facilitate the daily activities. Filled formats were reviewed for completeness and consistency on daily basis by supervisors and PI. Prior to actual data collection, pre-test was conducted and the tool was amended accordingly.

4.11 Data processing and analysis

Data was entered into Epi-Data 4.2.0.0 for cleaning and exported to STATA 13 (STATA Corporation, Texas, USA) for analysis. In this study there were missing data for laboratory variables ranging from 1(0.92%) to 3(2.75%). These missing data were imputed for the purpose of increasing power of prognostic variables and to fit all regression models. Subsequently, patients were categorized into with or without viral etiology because of the consideration that in-hospital incidence of acute complications of CLD and prognosis of CLD patients may differ according to etiology. For continuous data, normality test was conducted using Shapiro-Wilk's W test. For this purpose, level of significance of 0.05 was used. Parametric data were reported with mean and standard deviation and compared using student's t-test. Non-parametric data were reported with median and interquartile (IQ) range and compared using the two-sample Wilcoxon rank-sum (Mann-Whitney) test. Proportions were compared using chi-squared test or Fisher's exact test, as appropriate. All *p* values calculated were two-sided, and the statistical significance threshold was <0.05. Then, results of analysis were presented by text, tables and charts. For this study, time of hospital admission was time of origin (t) and the time from first admission to acute complication of CLD and/or mortality was the random outcome variable (T)**.** The time scale of T was days. After setting these, survival experience of patients with or without viral etiology was checked using Kaplan-Meier curve and their survival difference was compared using log-rank test. Median time to clinical outcomes and incidence rate ratio (IRR) were calculated. Chi-square test was done to check adequacy of cells before running regression. Cox regression model assumption of proportional hazards was checked by testing an interaction of covariates with time. Binary Cox regression was performed to identify variables candidate for multivariable Cox regressions. Variables with p-value < 0.25 in bivariate cox-regression were considered as candidates for multivariate cox-regression. After doing so, the interaction between

independent variables was checked for collinearity before running multivariate Cox regression. Finally, multivariate Cox regression was performed. Hazard ratio was used as a measure of strength of association and p-value < 0.05 was considered to declare statistical significance.

4.12 Ethical consideration

Prior to data collection, the study was ethically approved by an Institutional Review Board (IRB) of JUMC. After informing the overall concerns of the study and confidentiality of personal information, only consented patients were included in this study. For those patients with HE, consent was requested from caregivers.

4.13 Dissemination plan

Upon approval, results of this study will be disseminated to different stakeholders such as JUMC, SPHMMC, and HFSUH. An attempt will also be made to publish this study on reputable journal to make it accessible to the scientific communities.

4.14 Operational definition of terms

Active alcohol user: refers to patients who used to drink alcohol in the past 3 months before the current hospital admission(28)

Acute or overt gastro-intestinal bleeding: implies gastrointestinal bleeding visible in the form of hematemesis, melena, or hematochezia (63).

Adult is a person 18 years of age or above(64)

CLD complications: implies major complications and includes ascites, SBP, hepatic encephalopathy, variceal bleeding, and hepatorenal syndrome(65) and HCC.

Clinical outcome/outcome: acute in-hospital CLD complications, in-hospital and cumulative mortality of 30-day of hospital discharge.

Comorbidities: implies diseases listed as comorbidity in Charlson comorbidity index after removing liver disease(66).

Decompensation: defined by the development of clinically evident complications of portal hypertension (ascites, variceal hemorrhage, hepatic encephalopathy) or liver insufficiency (jaundice)(4).

Past medication history: denotes history of taking medications in the past three months before hospital admission

Non-viral group/ without viral etiology: represents CLD patients with serologic test confirmed negative result for chronic viral hepatitis.

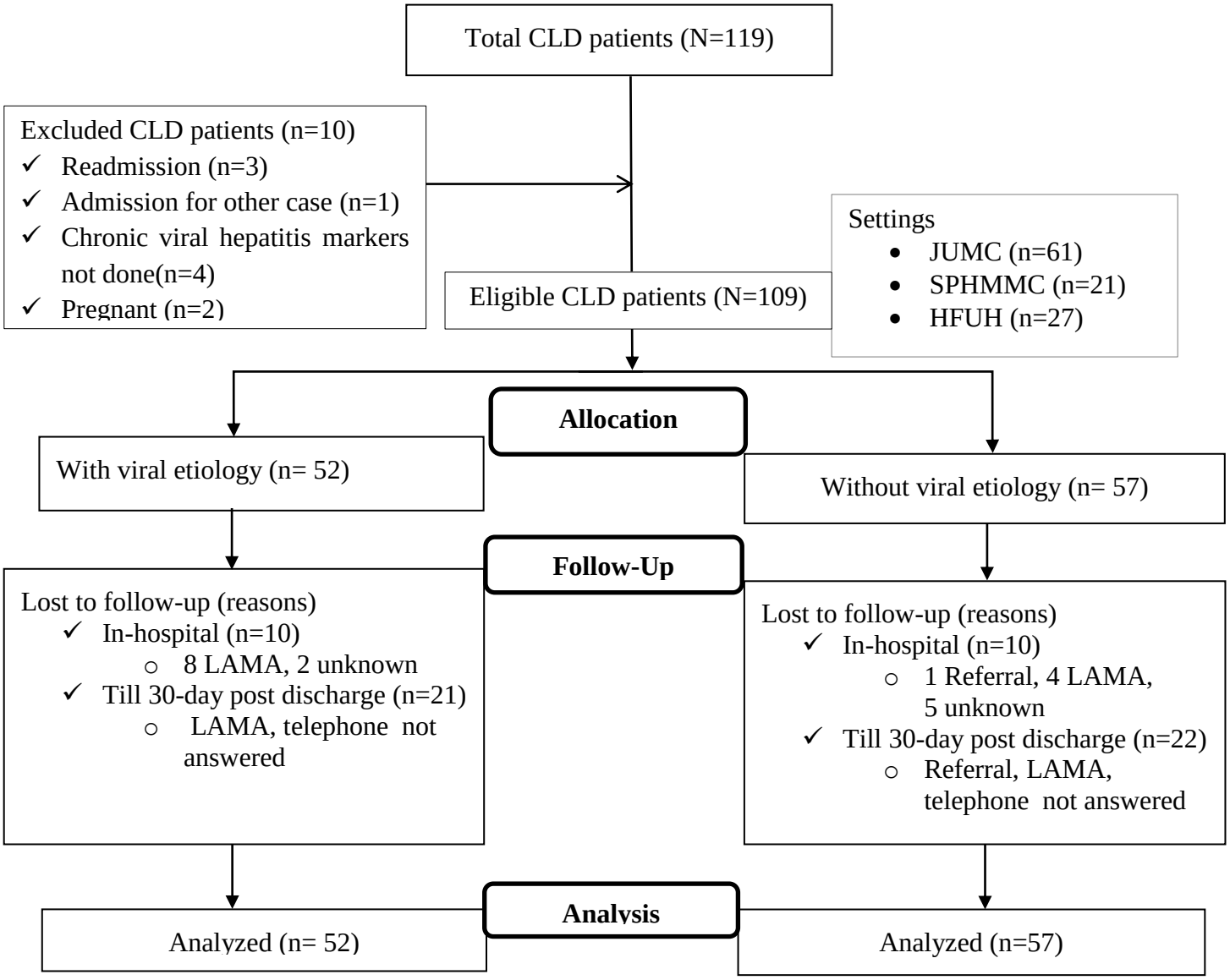
Undetermined etiology: Patients with negative chronic viral serologic test and no etiology was traced.

Viral group/viral etiology/viral cause: represents CLD patients with serologic test confirmed positive result for chronic hepatitis virus.

5 Result

5.1 Overview of the study

Over the study period, a total of 119 CLD patients were admitted to internal medicine wards of the selected hospitals; of these 109 fulfilled inclusion criteria **figure2.**



JUMC-Jimma university medical center, HFSUH-Hiwot fana university hospital, SPHMMC-Saint Paul hospital millennium medical college, LAMA-Left against medical advice

Figure 3: Flow chart of the overview of the study conducted among CLD patients with or without viral etiology from April 1 - October 5, 2018.

5.1.1 Socio-demographic and behavioral characteristics of Patients

From the total of 109 patients, 52 (47.71%) of them had viral etiology (HBV and/or HCV). The mean (± SD) age of participants included in this study was 39.03 ± 13.80 years. Eighty five (77.98%) of the participants were male. Eighty two (75.23%) patients were either formerly or currently married. Higher numbers of patients (53.21%) were from rural areas. Religiously, the majority of the patients were Islam followers (64.22%). A higher proportion of patients (52.29%) had no formal education, and the majority of patients (71.56%) had no job. In 72 (66.06%) patients, average household income was less than 500 ETB. Herbal medication use history was identified in 32 (29.36%) patients. Regarding history of social drug use habit, 47.71%, 35.78% and 14.68% of the participants reported khat chewing, alcohol consumption and cigarette smoking history, respectively. Patients with or without viral etiology did not differ significantly in all socio-behavioral characteristics. (**Table1)**

Table 1: Socio-demographic and behavioral characteristics among CLD patients with or without viral etiology admitted to the selected hospitals from April 1- October 5, 2018.

Characteristics		**Total(N=109)**	**CLD etiology**		
			Viral (n=52)	**Non-viral (n=57)**	**p-value**
Settings	JUMC	61(61.0%)	26(29.10%)	35(31.90%)	0.354
	HFSUH	27(27.0%)	16(12.90%)	11(14.10%)	
	SPHMMC	21(21.0%)	10(10.0%)	11(11.0%)	
Age, years, mean ±SD		39.03 ± 13.80	38.19 ± 11.94	39.79 ± 15.37	0.549
Gender	Male	85(77.98%)	40(36.70%)	45(41.28 %)	0.799
	Females	24(22.02%)	12(11.01%)	12(11.01%)	
Marital status					0.346
Never married		27(24.77%)	15(13.76%)	12(11.01%)	
Currently/formerly married		82(75.23%)	37(33.94%)	45(41.28%)	
Residence	Urban	51(46.79%)	23(21.10%)	28(25.69%)	0.609
	Rural	58(53.21%)	29(26.61%)	29(26.61%)	
Religion	Christianity	36(33.03%)	15(13.76%)	21(19.27%)	0.559
	Islam	70(64.22%)	36(33.03%)	34(31.19%)	
	Other(s)	3(2.75%)	1(0.92%)	2(1.83%)	
Educational status					
	Formal education	52(47.71%)	22(20.18%)	30(27.52%)	0.281
	No formal Education	57(52.29%)	30(27.52%)	27(24.77%)	
Occupation	Employed	31(28.44%)	11(10.09%)	20(18.35%)	0.107
	Unemployed	78(71.56%)	41(37.61%)	37(33.94%)	
Average household income(ETB)					
<500		72(66.06%)	35(32.11%)	37(33.94%)	0.792
≥500		37(33.94%)	17(15.60%)	20(18.35%)	
Herbal medication use history		32(29.36%)	17(15.60%)	15(13.76%)	0.465
Khat chewing history		52(47.71%)	28(25.69%)	24(22.02%)	0.220
History of Cigarette smoking		16(14.68%)	9(8.26 %)	7(6.42%)	0.459
Alcohol consumption history		39(35.78%)	17(15.60%)	22(20.18%)	0.521

***** Parametric variables were described by mean (±SD) and compared using t-test. Non-parametric variables were described using median (IQ) and compared using two-sample Wilcoxon rank-sum (Mann-Whitney) test. Categorical variables were described using numbers and proportion, n (%) and compared Chi-square test or Fisher's exact test, as appropriate. In all tests, <0.05 was used as cut-off p-value.

5.1.2 Baseline clinical and laboratory characteristics of Patients

Abdominal ultrasound was done in 105 (96.33%) patients and the commonest finding on the liver was increased echogenicity (20%). Among identified etiologies of CLD, chronic HBV (35.78%) was the predominant. (**Table 2)**

Table 2: Etiological spectrums and ultrasound findings of chronic liver disease patients admitted to selected hospitals from April 1- October 5, 2018.

Etiology of CLD	Total, n%	**Ultrasound findings**	Total, n%
HBV	39(35.78%)	Increased echogenicity	21(20.00%
Alcohol	15(13.76%)	Nodular liver surface	19(18.10%)
HCV	12(11.01%)	Heterogeneous echotexture	19 (18.10%)
Hepatic schistosomiasis	7(6.42%)	Coarse echotexture	16(15.24%)
Fatty liver	2(183%)	Smooth liver surface	10(9.52%)
HBV and HCV	1(0.92)	Periportal fibrosis	7(6.67%)
Others*	5(4.59%)	Mild uneven liver surface	3(2.86%)
Undetermined	28(25.69%)	Others	10(9.52%)

Others*: Autoimmune hepatitis, Wilson`s disease, cryptogenic, biliary cirrhosis

At presentation, highest number of patients complained abdominal swelling (43%), succeeded by generalized body swelling (18%). **(Figure4)**.

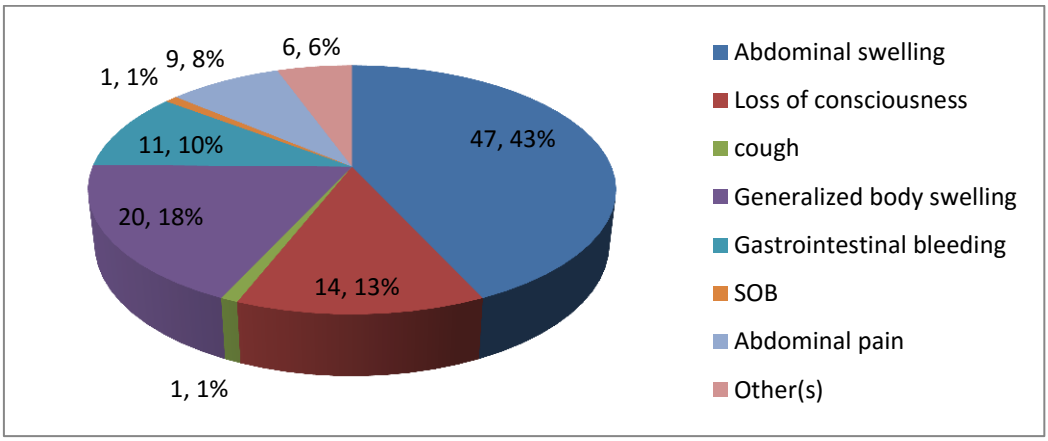


Figure 4: Pie chart shows chief complaints' identified at presentation from chronic liver disease patients admitted to selected hospitals from April 1- October 5, 2018.

The number of CLD complications identified per individual at admission ranges from one to five with an overall average figure of 1.87 ± 0.93. Ultrasound impression of splenomegaly was identified in 37 (33.94%) patients. Ascites (92.66%) was the most common complication identified at admission and observed in 101 (92.66%) patients. HE (38.53%) was the second most common complication identified at admission next to ascites. In terms of the West Haven criteria of grading HE; highest number of patients (47.62%) were diagnosed with grade I HE. Gastrointestinal bleeding (25.69%) was the third common CLD complication

diagnosed on admission. HRS was identified in 22 (20.18%) patients, while 23(21.1%) patients were diagnosed with SBP at presentation. Of the 23 patients with SBP at admission, SBP was confirmed by ascitic fluid analysis in 21 (91.3%), and clinical diagnosis was made in 2 (8.70%) patients. Furthermore, a positive ultrasound impression of HCC was identified in 19(17.43%) patients.

Chronic comorbidities were identified in 12 (11.01%) patients. The identified comorbidities were: diabetes (6.42%), chronic kidney disease (2.75%), congestive heart failure (2.75%), and HIV/AIDS and peripheral vascular disease (each 0.92%).

Furthermore, patients with or without viral etiology did not differ significantly in terms of mean arterial pressure (MAP) and laboratory parameters: white blood cell (WBC) count, red blood cell (RBC) indices [mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC)], hemoglobin, platelet (PLT), liver parameters [alanine aminotransferase (ALT), aspartate aminotransferase (AST), and serum creatinine (Scr). Blood urea nitrogen (BUN) was slightly, but significantly low among patients with viral etiology (p=**0.018**).

Overall, clinical and laboratory parameters difference between patients with or without viral etiology were insignificant except for HRS (p=**0.032**), BUN (p=**0.018)** and HCC (P=**0.013). (Table 3**)

Table 3: Baseline clinical characteristics and laboratory findings of CLD patients with or without viral etiology admitted to the selected hospitals from April 1- October 5, 2018.

Variables		**Total (N=109)**	**CLD etiology**		***P*-value**
			Viral (n=52)	**Non-viral (n=57)**	
Past medication history	Yes	64(58.72%)	29(26.61%)	35(32.11%)	0.614
	No	45(41.28%)	23(21.10%)	22(20.18%)	0.344
Number of medications before acute in-hospital CLD complication(s)		3(2- 5)	3(2-5)	3(2 - 4)	0.1546
Previously diagnosed CLD patients		34(31.19%)	14 (12.84%)	20(18.35%)	0.358
Duration since diagnosis, Months		7.85(0 - 120)	6.35 (0 – 96.0)	9.21 (0 – 120.0)	0.262
Decompensated patients		108(99.08%)	52 (47.71%)	56(51.38%)	1.000
Number of CLD complications		1.84 ± 0.95	1.87 ± 0.93	1.82 ± 0.98	0.071
CLD complications at admission					
Ascites		101(92.66%)	48 (44.04%)	53(48.62%)	1.000
SBP		23 (21.10%)	10 (9.17%)	13(11.93%)	0.648
Gastrointestinal bleeding		28 (25.69%)	13 (11.93%)	15(13.76%)	0.875
Hepatic encephalopathy		42 (38.53%)	23 (21.10%)	19(17.43%)	0.243
Grades of HE	I	20(47.62%)	12(28.57%)	8(19.05%)	0.313
	II	15(35.71%)	6(14.29%)	9(21.43%)	

	III	7(16.67%)	5(11.90%)	2(4.76%)	
	Hepatorenal syndrome	22 (20.18%)	6 (5.50%)	16(14.68%)	**0.032**
	Hepatocellular carcinoma	19 (17.43%)	14 (12.84%)	5(4.59%)	**0.013**
	Porto pulmonary HTN	1 (0.92%)	1 (0.92%)	0	0.477
	Splenomegaly	37(33.94%)	17(15.60%)	20(18.54%)	0.792
Laboratory and other parameters					
MAP, mmHg		82.33 ± 13.10	83.51 ± 12.52	81.26 ± 13.62	0.372
WBC,*10^9/L		7.2 (4.5 - 11.4)	8.34 (4.65-13.25)	7.11(4.43-10.50)	0.338
Hgb, g/dl		11(7.6-12.6)	11.15(7.60-12.95)	10.4(8.20-12.60)	0.409
MCV, fl		86.5 (80 - 90.6)	84.95(78.60-90.0)	86.5(80.5- 91.8)	0.281
MCH, pg		29.15 (27 - 31)	28.85(27.5 - 30.95)	29.15(27.0-31.1)	0.894
MCHC, g/dl		33.6 (32.2-35.1)	33.6(32.15 - 35.75)	33.6(32.2- 34.7)	0.686
PLT*10^3		169 (95 - 248)	169.0 (85.0- 252)	169.0(107-230.0)	0.794
ALT, u/l		45.5(29.3-72)	47.45(33.25-72.1)	45.5(23.60-69.10)	0.171
AST, u/l		67 (42.0-143.5)	78 (55.6-167.80)	49(34.0-123.18)	0.171
ALP, u/l		256.5(169.1- 348)	256.5(172.1-342.1)	256.5(169.1-348)	0.913
Scr, mg/dl		0.87(0.70-1.33)	0.81(0.68-1.06)	0.90(0.70-1.59)	0.099
BUN		25.5 (20.0-39.72)	24.1 (18.3-30.0)	29.79(21.1-72.30)	**0.018**
Chronic comorbidity	Yes	12 (11.01%)	6 (5.50%)	6(5.50%)	0.866
	No	97(88.99%)	46 (42.20%)	51(46.79%)	

***** Parametric variables were described by mean (±SD) and compared using t-test. Non-parametric variables were described using median (IQ) and compared using two-sample Wilcoxon rank-sum (Mann-Whitney) test. Categorical variables were described using number and proportion, n (%) and compared using Chi-square test or Fisher's exact test, as appropriate. In all tests, <0.05 was used as cut-off p-value to reject the hypothesis.

5.1.3 Pharmacological and non-pharmacological managements

There is no significant difference between the two groups in terms of managements given for CLD complications at presentation. Except two patients who were receiving antiviral medication (daily dose of TDF 300mg), all were receiving supportive managements for CLD complication(s). Combinations of pharmacologic and non-pharmacologic therapies were used in 78(93.97%) ascitic patients for its management. In 40(48.19%) of these patients: a combination of therapeutic tap, diuretics and dietary salt restriction was used. SBP prophylaxis was initiated in 27(24.77%) patients, and history of bleeding (59.26%) was the most common risk identified. Ceftriaxone was used for both prophylaxis and management of SBP. Management was initiated in 97.62% of patients with HE; lactulose and metronidazole were used in majority (65.85%) of these patients. Primary prophylaxis for variceal hemorrhage primary prophylaxis was initiated in 9(8.26%) patients. With regard to gastrointestinal bleeding; endoscopic evaluation and band ligation after stabilization was

done only in 8(7.34%) patients. In 10 (37.03%) patients, propranolol was initiated as secondary prophylaxis. (**Table 4)**

Table 4: Managements provided for CLD patients with or without viral etiology admitted to the selected hospitals from April 1- October 5, 2018.

CLD Complications and pharmacological/non-pharmacological managements/ prophylaxis	**Total, n%**	**CLD Etiology**		***P*-value**
		Viral	**Non-viral**	
Ascites				
Therapeutic tap, diuretics and dietary salt restriction	40 (48.19%)	2(2.41%)	3(3.61%)	0.727
Dietary salt restriction and diuretics	38 (45.78%)	18(21.69%)	20(24.10%)	
Therapeutic tap and dietary salt restriction	5(6.02%)	22(26.51%)	18(21.69%)	
SBP management				
Ceftriaxone				
Yes	23(21.1%)	10(9.17%)	13(11.93%)	0.648
No	86(78.90%)	42(41.0%)	44(45.0 %)	
SBP prophylaxis				
Ceftriaxone				
Yes	27(24.77%)	12(11.01%)	15(13.76%)	0.696
No	82(75.23%)	40(38.53%)	42(36.70%)	
Propranolol primary prophylaxis				
Yes	9(8.26%)	3(2.75%)	6(5.50%)	0.367
No	100(91.74%)	49(44.95%)	51(46.79%)	
Medications for secondary prophylaxis of variceal hemorrhage and related problems				
Propranolol	6(22.22%)	5(18.52%)	1(3.70%)	0.071
Propranolol and omeprazole	4(14.81%)	2(7.41%)	2(7.41%)	
Omeprazole	17(62.96%)	5(18.52%)	12(44.44)	
Endoscopic band ligation	8 (7.34%)	2 (1.83%)	6 (5.50%)	0.182
Hepatic encephalopathy				
Lactulose and metronidazole	27(65.85%)	16 (26.83 %)	11 (39.02%)	0.419
Lactulose, metronidazole and Bisacodyl	6(14.63%)	4(9.76%)	2(4.88%)	
Metronidazole and Bisacodyl	4(9.76%)	1(7.32 %)	3(2.44)	
Lactulose only	4(9.76%)	1(2.44 %)	3(7.32%)	
Enema	1(2.56%)	1(2.56%)	0	

5.2 Outcomes

In-patient improvement and discharge, discharge without improvement, leave against medical advice (LAMA), lost on follow-up, and referral were observed in 51 (46.79%), 7(6.42%), 12(11.01%), 7(6.42%) and 1(0.92%), patients, respectively. Accordingly, in-hospital retention rate was 81.65%. In-hospital median follow-up period was 4(2.5-7) days for patients lost from the study over hospital stay, and 7(5-11) days for those followed up until

in-patient death or census date, respectively (*p*=**0.001**). The proportion of lost patients were equal (9.17%) in patients with or without viral etiology (*P*=0.82).

5.2.1 Incidence of acute complication of chronic liver disease

Seventeen (15.60%) patients developed in-hospital acute complications of CLD. More than one acute complications of CLD were identified in two patients. Nine (8.26%) of the complications were in the viral group. The overall analysis time at risk was 838 days (463 days for the viral group and 375 days for non-viral group) (*p*=0.39); resulting in an overall acute complication of the CLD crude incidence rate of (IR) of 2.03%. The crude incidence rate ratio (IRR) of in-hospital acute complication of CLD among the viral to non-viral group was 0.911 [95% CI, 0.312 - 2.714, *p*= 0.424]. There was no statistically significant difference in median time of first in-hospital acute complication of CLD in viral and non-viral group, 6 (4-11) and 6 (4-8) days, respectively (*p*=0.697). The identified in-hospital acute complications of CLD were; acute gastrointestinal bleeding, HE and SBP; revealed in 7 (8.64%), 6 (8.96%) and 4 (4.65%) patients, respectively. HE was grade II in three of the six patients and grade I in the rest, except in one of the patient in whom HE was not graded. Acute gastrointestinal bleeding was observed in five of the patients with viral etiology and in two of the non-viral group (*p*=0.20). Endoscopic evaluation was done in only 1 of the 7 patients. Likewise, slightly higher number of SBP was identified in the viral group (n=3 vs. n=1) (*p*=0.27). On the other hand, HE was found higher in non-viral group (n=4 vs. n=2) (*p*=0.50). Overall, the difference in cumulative incidence of in-hospital acute CLD complication among the group was statistically insignificant (log rank, *p*=0.80). (**Figure5)**

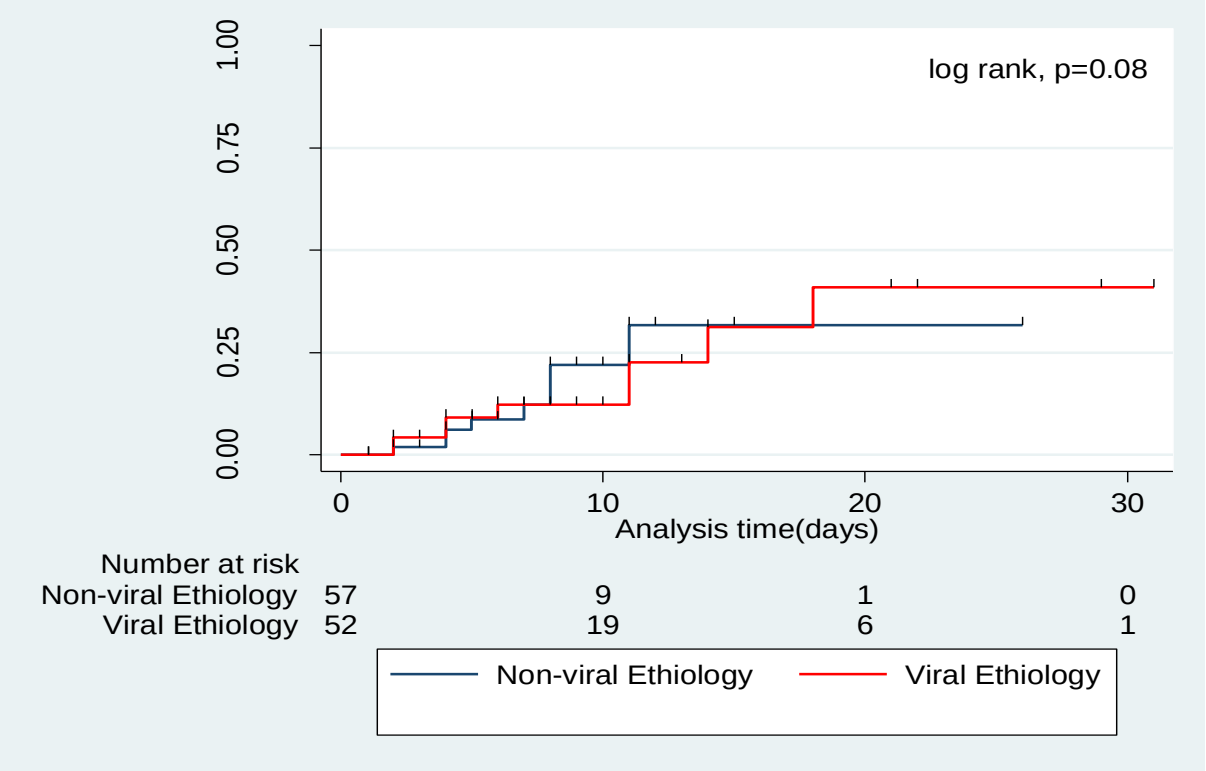


Figure 5: Kaplan-Meier estimates of cumulative incidence of in-hospital acute complication of CLD from April 1- October 5, 2018.

5.2.2 Mortality

The cumulative mortality from admission to 30 days of hospital discharge was 38(34.86%); 18(16.51%) deaths were in the viral group. The overall analysis time at risk was 1806 days (927days in the viral group and 879 days in the non-viral group). The incidence of in-hospital mortality was insignificantly lower among viral group, crude IRR 0.853 [0.426-1.699, *p*=0.314]. The difference in cumulative survival probability was insignificant (log rank, *p*= 0.569). In-hospital deaths were 31 (28.4%); 13 (11.93%) in the viral and 18(16.51%) in the non-viral group. In-hospital overall analysis time at risk was 906 days; 482 days for the viral and 424 days for the non-viral group (*p*= 0.43). Accordingly, the crude mortality IRR among viral to non-viral group was 0.635 [95% CI, 0.286-1.371, *p=0.108*]. The overall median survival time was 15 (9-29) days; 29 days (13-29 days) for the viral group and 12 days for the non-viral group (log rank, *p*=0.040) (**Figure6**).

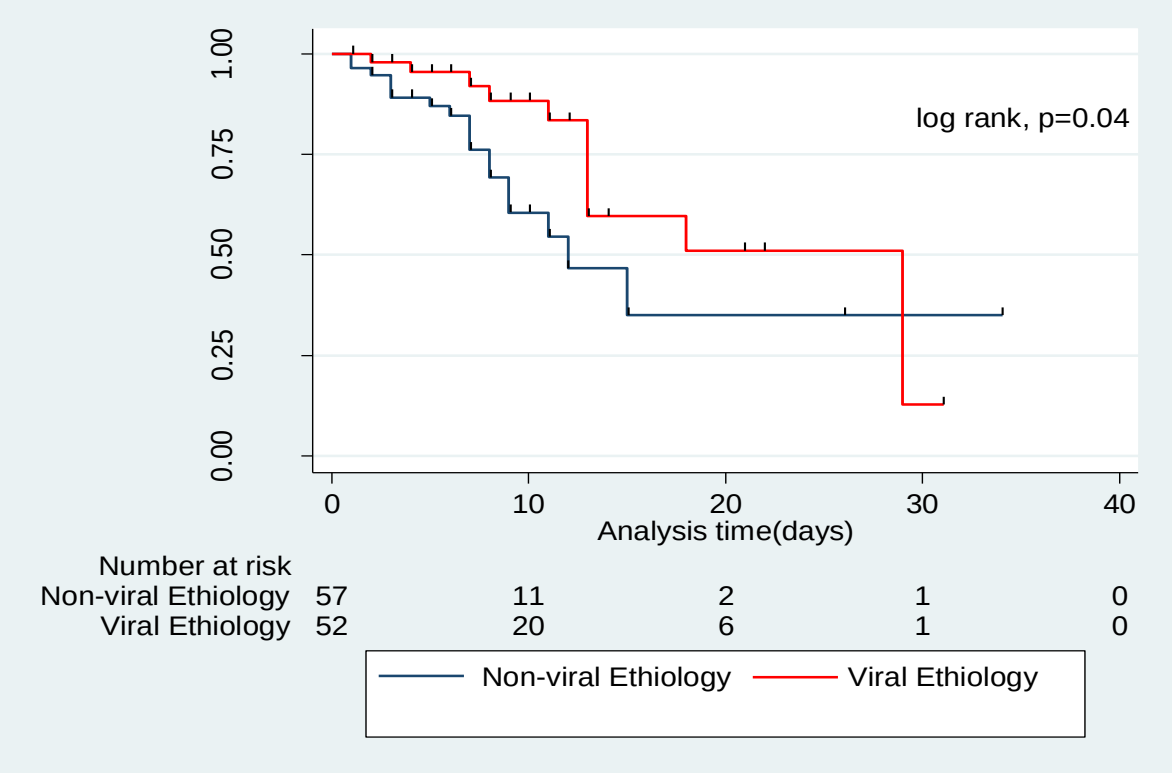


Figure 6: Kaplan-Meier in-hospital survival estimates of CLD patients admitted to selected hospitals from April 1- October 5, 2018.

Table 5: Tabular summary of core outcomes of CLD patients admitted to selected hospitals from April 1- October 5, 2018.

Outcomes			CLD etiology		Total, n%
			Viral	Non-viral	
Incident acute complications of CLD during hospital stay					
Acute gastrointestinal hemorrhage			5	2	7(8.64%)
Hepatic encephalopathy	Grade I II III	 2 3 Not graded	2	4	6(8.96%)
SBP			3	1	4(4.65%)
Mortality					
In-hospital mortality			13(11.93%)	18(16.51%)	31(28.4%)
Cumulative mortality			18(16.51%)	20(18.35%)	38(34.86%)

5.3 Predictors of outcomes

5.3.1 Predictors of In-hospital acute complication of chronic liver disease

In binary cox regression, residence (p=**0.020),** Cigarette smoking history (p<**0.001**), duration since diagnosis (p<**0.001**), age, previous diagnosis of CLD, MCV, and AST were identified as candidates for multivariate Cox regression Then, multivariate Cox regression was

conducted by including etiology into the regression. Finally, duration since diagnosis (***p*=0.025**) and AST (***p*=<0.001**) were identified as the independent predictors for the incidence of in-hospital acute complication(s) of CLD. Accordingly, a one month increase in duration after diagnosis of CLD was resulted in a 2.9% increase in the risk of in-hospital acute complication(s) of CLD (AHR= 1.029 [1.004-1.054, *p*=**0.025**]). Besides, the hazard of in-hospital acute complication of CLD was increased by 0.7 % for a one u/l increment in AST level (AHR=1.007 [95%CI, 1.003-1.010, *p*=<**0.001**]). Despite lack of statistical significance, a 7% decrease in risk of in-hospital acute complication of CLD was identified in patients with viral etiology (AHR= 0.931 [95% CI, 0.254 - 3.406, *p*= 0.914]) (**Table 6**).

Table 6: Regression for identifying predictors of acute in-hospital CLD complications among CLD patients admitted to the selected hospitals from April 1- October 5, 2018

Factors		Incidence of acute in-hospital CLD complication		CHR[95% CI]	*P*-value	AHR[95%CI]	*P*-value
		Yes(n=17)	No(n=92)				
Age, years		43.71 ± 14.68	38.16 ± 13.54	1.025[0.996 -1.054]	**0.089**	1.011[0.970-1.053]	0.607
Gender	Male	12(11.01%)	73(66.97%)	0.953[0.333 - 2.723]	0.928		
	Female	5(4.59%)	19(17.43%)	1			
Marriage							
	Never married	3(2.75%)	24(22.02%)	1.713[0.523 - 5.613]	0.374		
	Formerly/currently married	14(12.84%)	68(62.39%)	1			
Residence							
Urban		14(12.84%)	37(33.94%)	4.303[1.254-14.760]	**0.020**	4.514[0.932-21.85]	0.061
Rural		3(2.75%)	55(50.46%)	1			
Educational status							
Formal education		10(9.17%)	42(38.53%)	1			
No formal education		7(6.42%)	50(45.87%)	0.810[0.325 - 2.080]	0.662		
Occupation							
Employed		4(3.67%)	27(24.77%)	1			
Unemployed		13(11.93%)	65(59.63%)	1.473[0.470 - 4.628]	0.506		
Average household income (ETB)							
	<500	12(11.01%)	60(55.05%)	1.503[0.562 - 4.029]	0.416		
	≥500	5(4.59 %)	32(29.36%)	1			
Herbal medication use							
	Yes	6(5.50%)	33(30.28%)	0.825[0.285 - 2.387]	0.723		
	No	11(10.09%)	59(54.13%)	1			
khat chewing history							
	Yes	6(5.50%)	46(42.20%)	0.679[0.260 - 1.773]	0.429		
	No	11(10.09%)	46(42.20%)	1			
Alcohol consumption history							
	Yes	6(6.1 %)	33(32.9%)	1.233[0.454 - 3.349]	0.635		
	No	11(10.9 %)	59(59.1%)	1			
Cigarette smoking history							
	Yes	0	16(14.68%)	$6.730e^{-20}$ [$3.170e^{-20}$ - $1.430e^{-19}$]	**<0.001**	$8.980e^{-22}$[$8.390e^{-53}$- $9.620e^{09}$]	0.184
	No	17(15.60%)	76(69.72%)				

Past medication history						
Yes	9(8.26%)	25(22.94%)	1.077 [0.405- 2.864]	0.882		
No	8(7.34%)	67(61.47%)	1			
Total number of medication (s)	3(2-4)	3(2 – 5)	1.059[0.796 - 1.409]	0.695		
Known CLD patients						
Yes	10(9.17%)	65(59.63%)	2.063[0.793 - 5.361]	**0.137**	1.125[0.306-4.134]	0.860
No	7(6.42%)	27(24.77%)	1			
Duration since diagnosis, Months	15.59 (0-120)	6.42 (0-96)	1.017 [1.09 - 1.026]	<**0.001**	1.029[1.004-1.054]	**0.025**
Number of CLD Complications	1.76 ± 0.97	1.86 ± 0.96	0.910[0.595 - 1.393]	0.664		
CLD complications						
Ascites						
Yes	17(15.60%)	84(77.06%)	$4.650e^{18}$			
No	0	8(7.34%)	1			
SBP						
Yes	2(1.83%)	21(19.27%)	0.453[0.099 - 2.079]	0.308		
No	15(13.76%)	71(65.14%)	1			
Gastrointestinal bleeding						
Yes	5(4.59%)	23(21.10%)	1.226[0.442 - 3.403]	0.696		
No	12(11.01%)	69(63.30%)	1			
Hepatic encephalopathy						
Yes	7(6.42%)	35(32.11%)	1.199[0.477 - 3.013]	0.700		
No	10(9.17%)	57(52.29%)	1			
Hepatorenal syndrome						
Yes	5(4.59%)	17(15.60%)	0.413[0.139 - 1.231]	**0.113**	0.598[0.165-2.169]	0.434
No	12(11.01%)	75(68.81%)	1		1	
Hepatocellular carcinoma				0.539		
Yes	3(2.75%)	16(14.68%)	1.493[0.416 -5.361]			
No	14(12.84%)	76(69.72 %)	1			
Diuretics at admission				0.846		
Yes	13(15.48%)	64(76.19%)	0.862[0.194 - 3.837]			
No	2(2.38%)	5(5.95%)	1			
Chronic Comorbidity						
Yes	2(1.83%)	10(9.17%)	0.792[0.177 - 3.533]	0.759		
No	15(13.76%)	82(75.23%)	1			
MAP, mmHg	78.76 ± 12.47	82.99 ± 13.17	0.975[0.931 - 1.021]	0.284		
WBC,*10^9/L	7.2(5.43- 9.8)	7.20(4.50-11.54)	0.969[0.898 - 1.046]	0.421		
Hgb, g/dl	11(10.2-12.4)	11.10(7.60-12.60)	1.006[0.884 - 1.144]	0.929		
MCV, FL	90(86.5-94)	85.85(79.15-90.05)	0.998[0.998 - 1.001]	**0.139**	1.058[0.948-1.174]	0.327
MCH, pg	30(29.15- 33.1)	28.8 (26.7-30.85)	1.026[0.978 - 1.077]	0.298		
MCHC, g/dl	33.6(32.2-36.5)	33.6(32.15-35.05)	1.094[0.782 - 1.531]	0.600		
Plt1*10^3/µl	18(17- 27)	164.5(83.5-230.5)	1.001 [0.998- 1.003]	0.773		
ALT, u/l	61(45.5-78.0)	45.5(29.15-69.05)	1.002[0.996 - 1.009]	0.391		
AST, u/l	78(45.8-203.0)	67(41.1-134.4)	1.003[0.999 - 1.007]	**0.144**	1.007[1.003-1.010]	<**0.001**
ALP, u/l	223(122.7- 348)	256.5(180-346.6)	1.000[0.998 - 1.003]	0.542		
Scr, mg/dl	0.90(0.70-1.70)	0.87(0.68 - 1.31)	1.112[0.882 - 1.401]	0.370		
BUN, mg/dl	26.3(22.4 - 45)	25.5(18.85-34.95)	1.002[0.994 - 1.011]	0.596		

*Parametric variables (Age, number of CLD complications, MAP, total number of in-hospital medications) were described by mean (±SD). The rest were non-parametric variables and described using median (IQ), All Categorical variables were described using numbers and proportion, n (%).

5.3.2 Predictor of In-hospital Mortality

In bivariate cox regression; HE at admission (*p*=**0.011**), MCV (*p*=**<0.001**), Scr (*p*=**0.034**), and BUN (*p*=**0.046**), khat chewing history (*p*=**0.055)**, Cigarette Smoking history (*p*=**0.117**), HRS at admission (*p*=**0.063**), MAP (*p*=**0.117**), WBC (*p*=**0.161**), MCV (*p*<**0.001**), MCH (*p*=**0.167**), MCHC (*p*=**0.148**), ALT (*p*=**0.240**), Scr (*p*=**0.034**), BUN (*p*=**0.046**), presence of chronic comorbidity (*p*=**0.188**), and in-hospital incidence of CLD complication (*p*=**0.221**) were identified as candidates for multivariate Cox regression. Running multivariate Cox regression after including etiology yielded MCV (*p*=**0.013**) as the sole independent predictor of in-hospital mortality. As a result, the hazard of in-hospital mortality was found to increase by 40% for every 100-fl increment in MCV (1.004 [95% CI, 1.001 - 1.007, *p*=**0.013**]). Being with viral etiology was found protective, but this protection failed to achieve statistical significance (AHR=0.431 [95% CI, 0.171 - 1.087, *p*= 0.075]. **(Table 7)**

Table 7: Regression for identifying predictors of in-hospital mortality of CLD patients admitted to the selected hospitals from April 1- October 5, 2018

Factors	In-hospital mortality		CHR [95% CI]	*P*-value	AHR [95% CI]	*P*-value
	No (n=78)	**Yes (n=31)**				
Age, years	43.71 ± 14.68	38.16 ± 13.54	1.007[0.983-1.032]	0.552		
Gender						
Male	64(58.72%)	21(19.27%)	1.572[0.647 -3.815]	0.318		
Female	14(12.84%)	10(9.17%)	1			
Residence						
Urban	33(30.28%)	37(33.94%)	1.224 [0.585 - 2.561]	0.591		
Rural	45(41.28%)	12(11.93%)	1			
Educational status						
Formal education	33(30.28%)	19(17.43%)	1			
No formal education	45(41.28%)	12(11.01%)	0.864[0.414 - 1.803]	0.696		
Occupation						
Employed	18(16.51%)	13(11.93%)	1			
Unemployed	60(55.05%)	18(16.51%)	0.725 [0.342 - 1.537]	0.402		
Average household Income (ETB)						
<500	53(48.62%)	19(17.43%)	1.239 [0.585 - 2.625]	0.575		
≥500	25(22.94%)	12(11.01%)	1			
Herbal medication use						
Yes	25(22.94%)	7(6.42%)	0.85 [0.36 - 2.01]	0.717		
No	53(48.62%)	24(22.02%)	1			
Khat chewing history						
Yes	43(39.45%)	9(8.26%)	0.466[0.214 - 1.015]	**0.055**	0.749[0.274- 2.051]	0.574
No	35(32.11%)	22(20.18%)	1		1	
Alcohol consumption history						
Yes	30(27.9%)	9(11.1%)	1.037[0.468- 2.230]	0.928		
No	48(50.1%)	22(19.9%)	1			
Cigarette smoking history						
Yes	9(8.26%)	7(6.42%)	1.985[0.842 - 4.677]	**0.117**	2.558[0.760 - 8.614]	0.129
No	69(63.30%)	24(22.02%)	1		1	
Past medication history						

Yes		43(39.45%)	21(19.27%)	0.872 [0.396 - 1.921]	0.735		
No		35(32.11%)	10(9.17%)	1			
Known CLD patients							
Yes		10(9.17%)	65(59.63%)	0.627 [0.254 - 1.550]	0.312		
No		7(6.42%)	27(24.77%)	1			
Duration since CLD diagnosis, Months		8.375(0 – 96)	7.846(0-120)	0.996 [0.975 - 1.018]	0.732		
Numbers of CLD complication at admission		2.06 ± 0.99	2.29 ± 0.97	0.985 [0.789 - 1.233]	0.899		
Type of CLD complications					.		
Ascites					0.818		
Yes		71(65.14%)	30(27.52%)	1.269[0.170 - 9.425]			
No		7(6.42%)	1(0.92%)	1			
SBP					0.339		
Yes		18(16.51%)	5(4.59%)	0.626 [0.240 - 1.636]			
No		60(55.05%)	26(23.85%)	1			
Gastrointestinal bleeding					0.507		
Yes		20(18.35%)	8(7.34%)	1.329 [0.574 - 3.080]			
No		58(53.21%)	23(21.10%)	1			
Hepatic encephalopathy					**0.011**		
Yes		27(24.77%)	15(13.76%)	2.708 [1.252 - 5.859]		2.189[0.792 - 6.048]	0.131
No		51(46.79%)	16(14.68%)	1		1	
Grade of HE	I	12(12.9%)	8(7.1%)	1			
	II	10(9.6%)	5(5.4%)	1.641[0.515 - 5.223]	0.402		
	III	5(4.5%)	2(2.5%)	2.203[0.437 - 11.101]	0.339		
Hepatorenal syndrome					**0.063**		
Yes		14(15.7%)	8(6.3%)	0.442 [0.187 - 1.044]		0.974[0.160 - 5.937]	0.977
No		64(62.3%)	23(24.7%)	1			
Hepatocellular carcinoma					0.558		
Yes		11(10.09 %)	8(7.34%)	1.302 [0.539 - 3.149]			
No		67(61.47%)	23(21.10%)	1			
Diuretics at admission							
Yes		57(55.1%)	20(21.9%)	0.576[0.192- 1.723]	0.324		
No		21(22.9%)	11(9.1%)	1			
Chronic Comorbidity							
Yes		40(36.70%)	18(16.51%)	0.379[0.089 - 1.608]	**0.188**	0.551[0.116 - 2.619]	0.454
No		38(34.86%)	13(11.93%)	1			
MAP, mmHg		83.85 ± 13.69	78.53±10.74	0.973 [0.940 - 1.007]	**0.117**	0.980[0.940 - 1.022]	0.346
WBC ,*10^9/L		6.25(4.20-11.4)	9.10(7.20-12.7)	1.036 [0.986 - 1.089]	**0.161**	1.019[0.946 - 1.099]	0.618
Hgb, g/dl		11.1(8.2-12.5)	10.3(7.6-13)	1.010 [0.897 - 1.137]	0.868		
MCV, fl		85.45(79– 90)	89.2(83.8-93.5)	1.005 [1.002 - 1.007]	**<0.001**	1.004[1.001 - 1.007]	**0.013**
MCH, pg		28.75(27.0-30.3)	30.1(27.9-32.4)	1.029 [0.988 - 1.073]	**0.167**	1.028[0.958 - 1.104]	0.435
MCHC, g/dl		33.55(32-34.8)	33.8(33-36)	1.115 [0.962 - 1.292]	**0.148**	1.065 [0.921 - 1.23]	0.394
PLT*10^3		162.5(83 -210)	178(154-392)	1.001 [0.999 - 1.004]	0.298		
ALT, u/l,		45.5(28.9-61.2)	47.2(32.4-78.0)	1.004 [0.998- 1.010]	**0.240**	1.004[0.997 - 1.011]	0.299
AST, u/l		67(35-126.2)	90(48.9- 167.8)	1.001[0.997- 1.005]	0.672		
ALP, u/l		256.5(165-318.7)	256.5(169.1-437)	1.001[0.999 - 1.002]	0.294		
Scr, mg/dl		0.88(0.71-1.30)	0.85(0.55-1.70)	1.233[1.016- 1.495]	**0.034**	1.181[0.753 - 1.854]	0.468
BUN, mg/dl		25.5(19.5-36.9)	25.5(21 - 48.9)	1.007[1.0001- 1.014]	**0.046**	0.999[0.987 - 1.011]	0.891
In-hospital acute Complication of CLD							
Yes		7(6.42%)	10(9.17%)	1.607[0.752 - 3.432]	**0.221**	1.633[0.658 - 4.049]	0.290
No		71(65.14%)	21(19.27%)	1			
Total number of In-hospital medications		4.74 ± 2.07	4.87 ± 2.53	0.984 [0.826 - 1.173]	0.858		

* Parametric variables (Age, number of CLD complications, MAP, total number of in-hospital medications) were described by mean (±SD). The rest were non-parametric variables and described using median (IQ), All Categorical variables were described using numbers and proportion, n (%).

6 Discussion

The aim of this study was to assess the clinical outcomes of admitted CLD patients. Accordingly, in this cohort of patients with short-term follow-up, we described the identified etiologies of CLD and categorized them into those with or without viral etiology for analysis. Patients with viral etiology were lower in the investigated cohort.

6.1 Etiology of Chronic liver disease

In this study, viral etiology was identified in almost half of the patients. Despite this, very limited specific treatments were provided. Moreover, no patient received immunoprphylaxis.

HBV is the main etiology of CLD in developing countries(67). Similarly, Chronic HBV (35.78%) infection was identified as the most common etiology of CLD in this study. This result was consistent with other studies conducted in Ethiopia, which revealed chronic HBV in majority of CLD patients(38,41,42). In their study, Hsiang et al.(45) and Mukherjee et al.(47) also reported chronic HBV as predominant etiology of CLD. Inconsistent to this finding, in a study conducted by Fagan et al. (5), alcohol was reported as the primay etiology of CLD. But, Samonakis et al.(3) and Giannousis et al.(46) reported HCV as the primary etiology of CLD. This inconsistency could be due to geographical difference in etiology of CLD(43,44).

6.2 In-hospital Clinical outcomes

6.2.1 Acute complications of chronic liver disease: occurrence and predictors

In this study, 15.60% of patients developed acute complication of CLD during their hospital stay; 4(3.67%) of the complications were SBP. However, Bernard et al.(48) reported a higher percentage of incidences of SBP. This could be due to the relatively lower number of SBP free patients at baseline. Furthermore, in this study HE was identified in 5.50% of the patients. Compared to this, Bajaj et al.(49) reported higher new cases of HE during hospital stay. This discrepancy could be partly justified by potential difference in diagnosis experience or difference in baseline characteristics of participants .

The incidence of acute complications of CLD was comparable among patients with or without viral etiology. Literatures have shown an increase in the risk of acute complications of CLD under circumstances such as; GI bleeding, infections, diuretic use, renal derangements, active alcohol use, and PPI use(25,27,28,43,55). These circumstances were

relatively lower in figure/proportion among patients with viral etiology [gastrointestinal bleeding (13 vs. 15), active alcohol use (7 vs. 12), SBP (10 vs. 13) and omeprazole use (5 vs. 13)] which do not justify the little higher finding incidences of acute complications of CLD observed in this study. In our study, lower incidence rate of in-hospital acute complication of CLD was observed among the viral group, but insignificant (crude IRR=0.911 [95% CI, 0.312 - 2.714, p= 0.424]). This is partially consistent with reports of study conducted by Hsiang et al., which showed a lower IR of acute complications of CLD among patients with viral etiology as compared to their non-viral counterpart(45). This inconsistency might be attributed to the unequal number of participants in the two groups included in our study. Besides, other factors mentioned above, such as gastrointestinal bleeding, active alcohol use, lower omeprazole prescription and others might have suppressed the effect of diuretics.

In this study, the difference in cumulative incidence of in-hospital acute complication of CLD among the group was found statistically insignificant. This finding was likely because of the small numbers of patients in the group which might have hindered the power to rule out a real difference and avoid a type two error.

On the other hand, etiology of CLD was failed to predict acute in-hospital complication of CLD; but lower risk was observed among patients with viral etiology (AHR= 0.930 [95% CI, 0.250 - 3.410]). However, an increase in duration since diagnosis of CLD was identified to increase the risk of in-hospital acute complication(s) of CLD (AHR= 1.029 [1.004 - 1.054, p=***0.025***]). This could be related to the progressive nature of CLD. Over time, progression increases the amount of fibrosis resulting in the development of regenerative nodules in the liver, which lead to portal hypertension. One of the most important complications of portal hypertension is gastrointestinal bleeding. Impaired hepatic degradation together with port-systemic shunting of vasodilators leads to reduced splanchnic vascular resistance. Consequently, vasoactive systems become activated which mediates vasoconstriction within the kidney with increased risk of development of HRS. Translocation of bacteria from the gut to lymph nodes leads to complicating infections in relation to variceal bleeding and infected ascitic fluid as SBP. Impaired phagocytic activity in cells belonging to the reticuloendothelial system seen over time may facilitate infections(68).

AST level at admission (p<**0.001)** was another independent predictor of in-hospital acute complication of CLD in this study. AST level increases with development of advanced liver disease like cirrhosis. Once a patient developed cirrhosis, he/she is at the doorstep of complications(69). Therefore, given that AST level increases with the development of

cirrhosis, which is the doorstep for CLD complications, the revealed independent prediction of AST for in-hospital acute complication of CLD in our study is not surprising. Accordingly, the risk of in-hospital acute complication of CLD was found to increase about 0.7% times with a unit increment in AST level (AHR=1.007[1.003 - 1.010, $p<$**0.001**]

6.2.2 Mortality: occurrence and predictors

The cumulative mortality from admission to 30 day of hospital discharge was 38(34.86%). Of these, 31(28.4%) deaths were in-hospital. Similar in-hospital mortality finding was reported from Colombia (52). But, Mulugeta et al., and Warren et al. revealed a higher percentage of in-hospital mortality (41,50). On the other hand, lower in-hospital mortality was documented from Argentinean and Moroccan studies (51,54).These discrepancy could be partly due to the difference in settings included in the studies. The current stiudy included patients admitted to medical wards only; while, the comparator studies were conducted among patients admitted to critical care unit or else included patients admitted to both ICU and internal medicine ward. Besides, potential difference in baseline characteristics could also exist between patients included in these studies. Furthermore, late presentation, unavailability of specific therapies and advanced hepatology centers in Ethiopia could also have contributed to the discrepancy seen.

In this study, despite lack of statistical significance, a lower IR of in-hospital mortality was observed among patients with viral etiology (IRR=0.635[95%CI, 0.286 - 1.37, p=0.108]). Significantly better cumulative survival was also seen among this group (p=0.04). Furthermore, MCV was identified as independent predictor of in-hospital mortality, and the hazard of mortality was found to increase with an elevation in MCV (1.004 [95% CI, 1.001 - 1.007, p=**0.013**]). Likewise, in a study conducted by Yoon HJ et al. (56), a significant increase in the risk of liver related mortality was identified with elevated MCV level. In fact, CLD is frequently associated with hematological abnormalities; among which, anemia is the most frequent (75%). Anemia is in turn associated with many complications such as increase in cardiovascular morbidity and mortality, cognition impairment, and decreased QOL, thereby imposing a significant and negative impact on patients(70).

Furthermore, lower risk of in-hospital mortality was identified among patients with viral etiology, but failed to predict (AHR=0.431 [95% CI, 0.171 - 1.087, p= 0.075]. This finding was consistent with study conducted by Bernard et al, in which etiology of CLD failed to be independent prognostic factor(71). In other study, viral origin of CLD was identified as

predictor of mortality increasing the risk of death(54).This discrepancy could be due to the potential baseline difference among the patients included.

Moreover impaired renal function occurs frequently in end-stage liver disease, and is associated with significant morbidity and mortality. In the absence of liver transplantation, short-term mortality associated with renal derangement in advanced liver disease is very high(72). Our study also revealed an increase in the risk of mortality with increment in Scr [AHR=1.181[95% CI, 0.753 - 1.854, *p*=0.468]. Likewise, different studies have also shown an increased risk of in-hospital mortality with increase in Scr level(51,73).

In our study, despite failed to predict; the hazard of in-hospital mortality was found to increase by two fold among patients with HE at presentation (AHR=2.189 [95%CI, 0.792 - 6.048, *p*=0.131]). In line with this, studies have shown an increase in the risk of mortality among patients with HE at presentation(28,54). HE is associated with poor outcomes with an overall decline in liver function, increased risk of in-hospital and short life expectancy(49,74). Besides, unlike in our study, simultaneous multiple complications of cirrhosis were shown to increase the risk of mortality(3). This might be ascribed to relatively small sample size employed in our study.

With these all, the observed significant survival difference among the two groups favoring those with viral etiology might be partly because of the difference in the following factors at presentation: 1) the lower median MCV in patients with viral etiology (84.95 vs. 86.50) (*p*=0.281). 2) The lower median Scr level among the viral group and significant baseline difference in HRS (*p*=0.032) and BUN (*p*=0.018) among the two groups 4) small and unequal sample size among the two groups.

Limitation of the study

Limitations of this study begins with the small and unequal sample size employed for comparator groups, which could have underpowered the intended results. Moreover, only the absence of significant distributional confounder in terms of viral and non-viral etiology was checked for the three settings in which this study was conducted. Even though all the three hospitals were tertiary; due to the difference in their experience in both aspects of achieving the correct diagnosis combined with treatment strategies could influence the findings. Merging all etiologies of CLD only into with or without viral etiology was also the other limitation. Not including very important variables, like INR, bilirubin, and albumin; and employment of imputation due to missing values was also a limitation of the study. The other limitation of this study was a failure of confirmation of the presence/absence of gastrointestinal bleeding which might result in under diagnosis of this event. The final limitation was the consideration chronic comorbidities only.

7 Conclusion

In summary, HBV was the commonest etiology identified in this study. Incidence of acute in-hospital complications of CLD and death were insignificantly lower among patients with viral etiology. Approximately, one death was observed for four admissions with CLD and the median survival time was significantly higher for the viral group. Prolonged duration since diagnosis and the increment in AST level were found to increase the rate for incidence of acute in-hospital complications of CLD. Furthermore, increment in MCV level at admission was identified to increase the risk of in-hospital mortality. Finally, because of the small and unequal sample size used, the difference in clinical outcomes among patients with or without viral etiology cannot be concluded confidently; a further study with adequate sample size is recommended.

8 Recommendations

To improve clinical outcomes of CLD patients, involvement of different stakeholders like: health institutions, ministry of health, media personnel's and others are required. Based on the findings from our study, the following recommendations are forwarded.

Ethiopian Federal ministry of health (EFMOH)

- Given that, almost half of the CLD patients' in this study were with viral etiology, immunoprophylaxis should be promoted as it prevents progression.
- Since, improvement or even reverse in the progression of cirrhosis has been shown with treatments targeting the underlying cause; EFMOH should avail targeted treatment options with financial subside of the treatment.

Health care providers and health institutions

- Create awareness on CLD giving emphasis on prevention.
- Health care providers should be warranted on early detection and correction of hematologic abnormalities.

Media

- Should strengthen awareness creation on CLD and its prevention in collaboration with other concerned stakeholders.

Selected hospitals and others

- Since universities are strategic areas to promote public health concern; these University hospitals should use this opportunity to create awareness on CLD and its prevention.

Researchers

- Researchers are recommended to conduct further study on this topic with adequate sample size and possibly adequate resources for different work-up to come-up with concrete evidences.

References

1. Kasper D, Fauci A, Hauser S, Longo D, Jameson J, Loscalzo J. Chronic Hepatitis. Harrison's principles of internal medicine. 19th ed. 2015. p. 2031.
2. Nusrat S, Khan MS, Fazili J, Madhoun MF. Cirrhosis and its complications : Evidence based treatment. World J Gastroenterol. 2014;20(18):5442–60.
3. Samonakis DN, Koulentaki M, Coucoutsi C, Augoustaki A, Baritaki C, Digenakis E, et al. Clinical outcomes of compensated and decompensated cirrhosis : A long term study. WJH. 2014;6(7):504–12.
4. Garcia-Tsao G, Friedman S, Iredale J et al. . Now There Are Many (Stages) Where Before There Was One: In Search of a Pathophysiological Classification of Cirrhosis Guadalupe. Hepatology. 2010;51(4):1445–9.
5. Fagan K. J., Zhao E. Y. , Horsfall L. U. , Ruffin B. J. , Kruger M. S. , McPhail S. M. OP, Ballard E. IKM and PEE. Burden of decompensated cirrhosis and ascites on hospital services in a tertiary care facility : time for change ? Intern Med J. 2014;865–72.
6. Prowpanga Udompap, Donghee Kim and WRK. Current and Future Burden of Chronic Nonmalignant Liver Disease. Clin Gastroenterol Hepatol. 2015;13(12):2031–41.
7. Metrics GH. Global , regional , and national incidence , prevalence , and years lived with disability for 328 diseases and injuries for 195 countries , 1990 – 2016 : a systematic analysis for the Global Burden of Disease Study 2016. Lancet (London, England). 2017;390(10100):1211–59.
8. Reau, Archita P. Desai N. The Burden of Rehospitalization for Patients With Liver Cirrhosis. Hosp Pract. 2016;44:60–9.
9. Murphy SL, Xu J, Kochanek KD, Curtin SC, Arias E. Deaths: Final data for 2015. 2017.
10. Institute for Health Metrics and Evaluation (IHME). GBD Compare Data Visualization [Internet]. Seattle, WA: IHME,University of Washington. 2017. Available from: http://vizhub.healthdata.org/gbd-compare[Accessed on Feb.26,2018]
11. Wang F, Fan J, Zhang Z, Gao B, Wang H. The Global Burden of Liver Disease : Hepatology. 2014;60(6):2099–108.
12. World Health Organization. Global Health Sector Strategy On Viral Hepatitis 2016–2021 Towards Ending Viral Hepatitis. 2016.

13. World Health Organization. Global Hepatitis Report. 2017;1–68.
14. Garcia-Tsao G, Friedman S, Iredale J et al. Now there are many stages where before there was one: in search of pathophysiological classification of cirrhosis. Hepatology. 2010;51:1445–9.
15. Pinzani M, Rosselli M ZM. Liver cirrhosis. Best Pr Res Clin Gastroenterol. 2011;25:281–90.
16. Ginés P, Quintero E, Arroyo V, Terés J, Bruguera M R, A, Caballería J, Rodés J RC. Compensated cirrhosis: natural history and prognostic factors. Hepatology. 1987;7:122–8.
17. Amico GD, Morabito A, Amico MD, Pasta L, Rebora P, Valsecchi MG. Clinical states of cirrhosis and competing risks. J Hepatol. 2017;1–59.
18. Fagan K. J., Zhao E. Y. , Horsfall L. U. , Ruffin B. J. , Kruger M. S. , McPhail S. M. OP, Ballard E. IKM and PEE. Burden of decompensated cirrhosis and ascites on hospital services in a tertiary care facility: time for change? Intern Med J. 2014;865–72.
19. Garcia-tsao G, Abraldes JG, Berzigotti A, Bosch J. Portal Hypertensive Bleeding in Cirrhosis : Risk Stratification , Diagnosis , and Management : 2016 Practice Guidance by the American Association for the Study of Liver Diseases A . Purpose and Scope. Hepatology. 2017;65(1):310–35.
20. Gines P, Quintero E, Arroyo V, Teres J, Bruguera M R, A, Caballeria J et a. Compensated cirrhosis: natural history and prognostic factors. Hepatology. 1987;7:12–8.
21. Lucena MI, Andrade RJ, Tognoni G, Hidalgo R de la, Cuesta FS, Fraile JM, Cabella R et al. Multicenter hospital study on prescribing patterns for prophylaxis and treatment of complications of cirrhosis. Eur J Clin Pharmacol. 2002;58:435–40.
22. Groszmann RJ WS. The hepatic venous pressure gradient: anything worth doing should be done right. Hepatology. 2004;39:280–2.
23. Borzio M, Salerno F, Piantoni L, Cazzaniga M AP, Bissoli F, Boccia S et al. Bacterial infection in patients with advanced cirrhosis: a multicentre prospective study. Dig Liver Dis. 2001;33:41–8.
24. Fernández J GT. Management of bacterial infections in cirrhosis. Hepatology. 2012;56(Suppl 1: S1-12).
25. Goel GA, Deshpande A, Lopez R, Hall GS V, Duin D CW. Increased rate of spontaneous bacterial peritonitis among cirrhotic patients receiving pharmacological

acid suppression. Clin Gastro Hep. 2012;10:422–7.

26. Poordad F. F. Review article: the burden of hepatic encephalopathy. Aliment Pharmacol Ther. 2007;25(1):3–9.
27. American Association for the Study of Liver Diseases and European Association for the Study of the Liver. Hepatic Encephalopathy in Chronic Liver Disease : 2014 Practice Guideline by the European Association for the Study of the Liver and the American Association for the Study of Liver Diseases. J Hepatol. European Association for the Study of the Liver; 2014;61(3):642–59.
28. Cordoba J, Ventura-cots M, Simón-talero M, Amorós À, Pavesi M, Vilstrup H, et al. Characteristics , risk factors , and mortality of cirrhotic patients hospitalized for hepatic encephalopathy with and without acute-on-chronic liver failure (ACLF). J Hepatol. European Association for the Study of the Liver; 2014;60(2):275–81.
29. Merli M, Nicolini G, Angeloni S, Rinaldi V DSA, Merkel C, Attili AF RO. Incidence and natural history of small esophageal varices in cirrhotic patients. Hepatology. 2003;38:266–72.
30. Zoli M, Merkel C, Magalotti D, Gueli C, Grimaldi M G, A BM. Natural history of cirrhotic patients with small esophageal varices: a prospective study. Gastroenterol Am J. 2000;95:503–8.
31. D'Amico G DFR. Upper digestive bleeding in cirrhosis. Post-therapeutic outcome and prognostic indicators. Hepatology. 2003;38:599–612.
32. Serste T, Melot C, Francoz C, Durand F, Rautou P-E V, D, Moreau R et al. Deleterious effects of beta-blockers on survival in patients with cirrhosis and refractory ascites. Hepatology. 2010;52:1017–22.
33. Mandorfer M, Bota S, Schwabl P, Bucsics T PN, Kruzik M et al. Nonselective beta blockers increase risk for hepatorenal syndrome and death in patients with cirrhosis and spontaneous bacterial peritonitis. Gastroenterology. 2014;146:1680–90.
34. Bang UC, Benfield T, Hyldstrup L, Jensen JB BF. . Effect of propranolol on survival in patients with decompensated cirrhosis: a nationwide study based Danish patient registers. Liver Int. 2016;36:1304–12.
35. Madsen BS, Nielsen KF, Fialla AD KA. Keep the sick from harm in spontaneous bacterial peritonitis: Dose of beta blockers matters. J Hepatol. 2016;64:1455–6.
36. Onyekwere CA, Ogbera AO, Hameed L. Chronic liver disease and hepatic encephalopathy : Clinical profile and outcomes. Niger J Clin Pract. 2011;14(2):181–5.
37. Udompap P, Kim D, Kim WR. Current and Future Burden of Chronic Nonmalignant

Liver Disease. Clin Gastroenterol Hepatol. 2015 Nov 17;13(12):2031–41.

38. Tsega E, Nordenfelt E, Hansson BG, Mengesha B LJ. Chronic liver disease in Ethiopia: a clinical study with emphasis on identifying common causes. Ethiop Med J. 1992;30(2):1–33.
39. Ashenafi W, Eshetu F, Assefa N, Oljira L, Dedefo M, Zelalem D, et al. Trend and causes of adult mortality in Kersa health and demographic surveillance system (Kersa HDSS), eastern Ethiopia : verbal autopsy method. BMC. Population Health Metrics; 2017;15:1–10.
40. Weldearegawi B, Ashebir Y, Gebeye E, Gebregziabiher T, Mussa S, Berhe H, et al. Emerging chronic non-communicable diseases in rural communities of Northern Ethiopia : evidence using population-based verbal autopsy method in Kilite Awlaelo surveillance site. Health Policy Plan. 2013;28(January):891–8.
41. Mulugeta Adhanom HD. Magnitude, Clinical Profile and Hospital Outcome of Chronic Liver Disease at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia. Ethiop Med J. 2017;55(4):267–72.
42. Magnus S, Orlien S, Ismael NY, Ahmed TA, Berhe N, Lauritzen T, et al. Unexplained chronic liver disease in Ethiopia : a cross-sectional study. BMC Gastroenterol. BMC Gastroenterology; 2018;18(27):1–12.
43. Moriwaki H, Shiraki M, Iwasa J, Terakura Y. Hepatic encephalopathy as a complication of liver cirrhosis : An Asian perspective. J Gastroenterol Hepatol. 2010;25:858–63.
44. Kooffreh-ada M, Okpara H, Oku A, Ihekwaba PA. Risk factors of chronic liver disease amongst patients receiving care in a Gastroenterology practice in Calabar. IOSR-JDMS. 2015;14(12):6–13.
45. Hsiang JC, Bai WW, Raos Z, Stableforth W, Upton A, Selvaratnam S, et al. Epidemiology , disease burden and outcomes of cirrhosis in a large secondary care hospital in South Auckland , New Zealand. Intern Med J. 2014;160–9.
46. Giannousis IP, Papatheodoridis G V, Deutsch MJ, Manolakopoulos SG, Manesis EK, Koskinas JS, et al. The burden and recent epidemiological changes of the main chronic liver diseases in a Greek referral tertiary centre. Eur J Gastroenterol Hepatol. 2010;22:172–9.
47. Mukherjee PS, Vishnubhatla S, Amarapurkar DN. Etiology and mode of presentation of chronic liver diseases in India : A multi centric study. PLoS One. 2017;10(12):1–13.
48. Bernard B, Cadranel J, Valla D, Escolano S, Jarlier V, Opolon P. Prognostic

Significance of Bacterial Infection in Bleeding Cirrhotic Patients : A Prospective Study. Gastroenterology. 1995;108:1828–34.

49. Bajaj JS, O'Leary JG, Tandon P et al. Hepatic Encephalopathy Is Associated With Mortality in Patients With Cirrhosis Independent of Other Extrahepatic Organ Failures. Clin Gastroenterol Hepatol. 2017;15(4):565–74.
50. Warren A, Soulsby CR, Puxty A, Campbell J, Shaw M, Quasim T, et al. Long-term outcome of patients with liver cirrhosis admitted to a general intensive care unit. Ann Intensive Care [Internet]. Springer Paris; 2017;7(37).
51. Miguel Hernan Vicco, Luz Rodeles, Franco Ferini, Ana Karina Long HMM. In-hospital mortality risk factors in patients with ascites due to cirrhosis. REV ASSOC MED BRAS. 2015;61(1):35–9.
52. R. Zubieta-Rodríguez, J. Gómez-Correa, R. Rodríguez-Amaya, K.A. Ariza-Mejia NAT-C. Hospital mortality in cirrhotic patients at a tertiary. Integr Med Res [Internet]. Asociación Mexicana de Gastroenterología; 2017;82(3):203–9.
53. Gomez EV, Rodriguez YS, Bertot LC, Gonzalez AT, Perez YM, Soler EA, et al. The natural history of compensated HCV-related cirrhosis : A prospective long-term study. J Hepatol. 2013;58(3):434–44.
54. Charif I, Saada K, Mellouki I, Yousfi M El, Benajah D, Abkari M El, et al. Predictors of Intra-Hospital Mortality in Patients with Cirrhosis. Open J Gastroenterol. 2014;4(March):141–8.
55. Bruns T, Zimmermann HW, Stallmach A. Risk factors and outcome of bacterial infections in cirrhosis. World J Gastroenterol. 2014;20(10):2542–54.
56. Hyung-Jin Yoon, Kyaehyung Kim, You-Seon Nam, Minseon Park J-MY. Mean corpuscular volume levels and all-cause and liver cancer mortality. Clin Chem Lab Med. 2015;54(7):p9.
57. Ethiopia Demographics [Internet]. [cited 2018 Feb 27]. Available from: https://www.google.com.et/search
58. Review World Population. Ethiopia Population 2018 [Internet]. 2018. Available from:
59. Ethiopian data portal. World GDP per Capita Ranking 2017 | Data and Charts | Forecast [Internet]. 2017 [cited 2018 Feb 27].
60. Federal Democratic Republic of Ethiopia. Health and Development [Internet]. 2009 [cited 2018 Feb 27]. p. 2–3. Available from: http://www.who.int/countryfocus
61. Jimma university HMIS. Hospital Profile. 2017.
62. St Paul's Millennium Medical College. Who we are [Internet]. [cited 2018 Feb 28].

Available from: https://www.sphmmc.edu.et/

63. Sik B, Kim M, Li BT, Engel A, Samra JS, Clarke S, et al. Diagnosis of gastrointestinal bleeding : A practical guide for clinicians. World J Gastrointest Pathophysiol. 2014;5(4):467–78.
64. NICE. Liver disease Quality standard. 2017;1–26.
65. Heidelbaugh JJ, Sherbondy M. Cirrhosis and Chronic Liver Failure: Part II. Complications and Treatment. Am Fam Physician [Internet]. 2006;74(5):767–76.
66. Jepsen P. Comorbidity in cirrhosis. World J Gastroenterol 2014. 2014;20(23):7223–30.
67. Okçu N, Bilen N. The Frequency of Complications and the Etiology of Disease in Patients with Liver Cirrhosis in Erzurum. Eurasian J Med. 2014;46:110–5.
68. Møller S, Henriksen JH, Bendtsen F. Extrahepatic complications to cirrhosis and portal hypertension : Haemodynamic and homeostatic aspects. World J Gastroenterol. 2014;20(42):15499–517.
69. Ahmed Imran Siddiqi, Musfireh Siddiqeh, Asif Mehmood AMS. Alanine aminotransferase / aspartate aminotransferase ratio reversal and prolonged prothrombin time : a specific indicator of hepatic cirrhosis. J Ayub Med Coll Abbottabad. 2007;19(3):22–4.
70. Gkamprela E, Deutsch M, Pectasides D. Iron deficiency anemia in chronic liver disease : etiopathogenesis , diagnosis and treatment. Ann Gastroenterol. 2017;30(4):405–13.
71. Bernard, B., Grangé, J.D., Nguyen Khac, E., Amiot, X., Opolon, P. and Poynard T. Antibiotic Prophylaxis for the Prevention of Bacterial Infections in Cirrhotic Patients with Gastrointestinal Bleeding: A Metaanalysis. Hepatology. 1999;29:1655–61.
72. Francoz C, Nadim MK, Durand F. Review Kidney biomarkers in cirrhosis. J Hepatol [Internet]. European Association for the Study of the Liver; 2016;65(4):809–24.
73. Abid S, Anis K, Ahmad A, Jafri W. Factors predicting in-hospital mortality in patients with cirrhosis hospitalized with gastro-esophageal variceal hemorrhage. Indian Soc Gastroenterol. 2006;25:240–3.
74. Tanaka A, Azuma T. Screening tool of neuropsychiatric test detecting minimal hepatic encephalopathy of cirrhotic patients. Hepatol Res. 2015;45:994–1003.

Annexes

Jimma University

Institute of Health, Department of Pharmacy

I. Patient Information Sheet

Study Title: Clinical Outcomes of patients admitted with Chronic Liver Disease: Prospective cohort study

Name of the investigator: Behailu Terefe Tesfaye

Name of study area: Jimma University Medical Center (JUMC), St. Paul's Hospital Millennium Medical College (SPHMMC), and Hiwot Fana University Hospital (HFSUH)

Research budget covered by: Jimma University

Research objective: To assess Clinical Outcomes and its associated factors among Chronic liver disease patients admitted to medical wards from April 1- October 5, 2018.

Study procedure: Data was collected both from the patient and active patient chart using a checklist developed by the principal investigator. Data collectors extracted data on socio-demography, clinical and laboratory. Furthermore, data collectors took patients/caregivers phone number at discharge from the hospital and at 30-day post discharge data on status was obtained. These data were kept confidential in a way that no other person had access. If patients were willing to participate in this project, they were informed the need to understand and sign the agreement form

Risks: this study didn`t impose any significant risk on participants.

Participant's right: The patient had a full right to withdraw from this study at any time and not to allow review of his/her chart, or to skip any question that he/she does not want to answer.

Benefit: the outcome of this study was expected to identify common etiology of CLD thereby indicating point of intervention, improve care of Chronic liver disease patients, including those participants survived after completion of this study.

Incentives: Patients were not provided any specific incentive for taking part in the research other than an acknowledgment.

Confidentialities: The study result didn`t included patient's name, and any personal details that may lead to identification of patient. The informations collected during the study period were kept confidential. Information that will be collected from the study will be stored in a file, which will not have your name on it, but a code number assigned to it.

Contact address to access the principal investigator (PI): contact address was provided to contact the principal investigator if there is any inconvenience or doubt about the study.

Mr. Behailu Terefe Tesfaye:

Phone No: 0943302087, E-mail: terefebh@gmail.com or behailu.terefe@ju.edu.et

II. Patient Written Consent Form

Dear Sir/madam;

My name is Behailu Terefe Tesfaye. I am a Master's Degree student in clinical pharmacy in Jimma University. As part of my academic requirements, I am expected to conduct a research. This study is aimed at assessing Clinical Outcomes of Patients admitted with Chronic Liver Disease. The information obtained from this study will facilitate clinicians to improve the provision of care and policy makers in their planning activities. Your participation in this study is voluntary and all data provided will be treated as confidential and anonymous. You have a right not to participate in this study. Therefore; we politely request your cooperation to participate in this study. But your input has great value for the success of the objectives the research.

So, do you agree? 1. Yes 2. No

Thank you for your cooperation!!!

Consent Form

While putting my signature in this sheet, I am giving my consent to participate in this study.I have been informed that the purpose of this study is to assess Clinical Outcomes of Patients admitted with Chronic Liver Disease and I have understood that participation in this study is entirely voluntarily. I have been told that my answers and other profiles to the questions will not be given to anyone else and no reports of this study ever identify me in any way. I have also been informed that my participation or non-participation or my refusal to participate in this study will have no effect on me. I understood that participation in this study does not involve risks.

Participant/caregiver`s	***Data collector***	***Supervisor***
Sign……..	Sign……	Sign……
Phone number: …….. ..	Phone number……	Phone number…….

III. Patient Information sheet: -Afan Oromo Version

Odeefannoo hirmaataa

Maqaa Qorataa: Bahaayiluu Tarrafa Tesfaayee

Bakka qorannoo: Gidduu alaa fayyaa Yunivarsiitii Jimmaa, Hospitaala qulqulluu Paawulos, Hospitaala Hiwoot faanaa.

Baasii qorannoo Kan haguugu: Jimmaa yunivarsiitii

Kaayyoo qorannoo: Hospitaalota fayyaa ibsaman keessatti dhuukkubsattota tiiruu haammaataa dhaan ciisanii kutaa yaalaa dhibee keessoo keessatti yaalaman eerga galanii booda bu`aa argamee fi murtessitoota isaa adda baasuu ta'a.

Haala adeemsa qorannoo: qorannoo kanarratti akka hirmaattaniif isin affeeraa, fedha yoo qabaattan qofa waliigaltee qophaa'e hubattanii malatteesitu. Jalqabarratti odeeffanoo hawaasummaa itti aansuun waa'ee dhukkuba tiiruu fi amaloota isa faana hidhata qaban fi firii laaborattorii isin gaafachuun fi chaartii keessan irraa ni fudhamaa. Oddeeffanoo isinirraa argannee, kaayyoo isinnitti himameen ala waanna biraaf gonkuma hin fayyadamnu.

Rakkoo qorannootiin dhukkubsatootarra ga'u: qooranicharratti hirmaachuutiin rakkoon isinirra ga'u hin jiru.

Mirga qoranicharratti hirmaachuu dhiisuu yookiin erga jalqabanii addaan kutuu: qoranichi fedhii guutuu hirmaataa irratti kan hundaa'eedha. Qoranicharratti hirmaachuuf dirqama hin qabdani. Gaaffii hin barbaannee dhiisuu ni dandeessu. Akkasumas qoranicha irratti hirmaachuu dhiisuu keessaniitiin tajaajila fayyaa hin dhabdan yookiin rakkinni kamiyyuu isinirra hin ga'u. Akkasumas yeroo barbaddanitti qoranicharraa addaan kutuu dandessu.

Qoranicha irratti hirmaachuun faayida inni qabu: qarannoo kanarratti yoo hirmattan dhukkuba tiiru haammaataa wajjin walqabatee akkamitti akka ittiisuu fi bu`aa isaa foyyeessuu danda`aamu wanta barbachisa ta`aan argachuuf fayyadaa.

Fayidaa: dhukkubsataa galateefachuun ala hirmaachuudhaaf kaffaltiin addaa hin kennamu.

Iciitii: qoorannoo kanarraa kan argamu odeeffanoon kamiyyuu iciitiin isaa ni eegama. Maqaan hirmaataa hin caafamuu. Oddeffanoo argamees qorataa fi oggessa fayyaa ala namni beekuu hin jiru. Odeeffannoon qorannicharraa argamus iciitiin isaanii ni eegama.

Waliigaltee: qoranicharratti hirmaachuuf dhukkubsatichi walii galtee guutuu gochuu qaba.

Qoranicharratti yaadaa fi gaaffiif: qoranicharrati yaada barbaadaniif teessoo kanaa na dubbisuu dandeessu.

Bahaayiluu Tarrafa Tasfaayee, lakkoofsa mobaayilii +25194302087 yookiin

Imeelii;-**terefebh@gmail.com or behailu.terefe@ju.edu.et**

IV. Patient Informed consent:-Afan Oromo Version

Gucca waliigaltee

Kabajamoo hirmaattoota qorannoo

Maqaan koo Bahaayiluu Tarrafa Tasfaayee jedhama. Waraqaa eebbaa Digirii lammaffaa koo hospitaalota fayyaa sadii keessatti dhuukkubsattota tiiruu haammaataa dhaan ciisanii kutaa yaali dhibee keessoo keessatti yaalamanirraa eerga galanii booda bu`aa fi murtessitoota isaa adda baasuudhaaf qorachuurran jira. Kaayyoon qorannoo kanaas buufata fayyaa ibsaman keessatti dhuukkubsattota tiiruu haammaataa dhaan ciisanii kutaa yaala dhibee keessoo keessatti yaalamanirraa eerga galanii booda bu`aa argamee fi murtessitoota isaa adda baasuu ta'a.

Haa ta'u malee kaayyoowwan armaan olitti himamani galmaan gahuuf deeggarsi fi gargarsi keessan murteessadha. Odeeffannoon funanamani iciitiin isaanii eegamadha. Akkasumas qoranicharrati mirgi hirmaachuu dhiisuu fi yeroo barbaadanitti addaan kutuu keessan eegamaadha. Kana caalaas gaaffilee deebisuu hin barbanne irra taruu ni dandeessu.

Kaayyoo qorannoo kanaa hubattanii hirmaachuudhaaf eeyyamamaa waan tataniif duraan dursee galatooma jechuun barbaada.

Qorannoo kana irratti hirmaachuu akkan barbaadu mallattoo kiyyaan mirkaneessera

Hirmaataa/fira	***Odeeffannoo funnaana***	***To`ataa***
Mallattoo ……..	Mallattoo ……	Mallattoo ……
Laak. Bilbillaa : ……..	Laak. Bilbillaa ……	Laak. Bilbillaa…….
Guyyaa ____ ji'a____bara____	Guyyaa ____ ji'a___bara	Guyyaa ____ ji'a___ bara___

Deeggarsaa fi Hirmaannaa keessaniif Galatooma!!

V. Patient Information Sheet: Amharic Version

የተሳታፊዎች መረጃ ቅጽ

ዋና ተመራማሪ፡ በሃይሉ ተረፈ ተስፋዬ

ምርምሩ የሚካሄድበት ቦታ፡ ጅማ ዩኒቨርሲቲ የህክምና ማእከል፡ ቅዱስ ፓዉሎስ/ሆ/ሚ/ሜ/ኮ፡ ሂዎት ፋና ዩኒቨርሲቲ ሆስፒታል

የጥናቱን ወጪ የሚሸፍነው ድርጅት፡ ጅማ ዩኒቨርስቲ

የጥናቱ ዓላማ ፤ በተጠቀሱት የጤና ማእከል እና ሆስፒታች ሜዲካል ክፍል ዉስጥ ተኚተዉ የሚታከሙ ስር የሰደደ የጉበት ህሙማን የህክምና ዉጤት በተመለከተ ጥናት ለማድረግ

የአሰራር ቅደም ተከተል፡ በዚህ ጥናት እንዲሳተፉ በአክብሮት አየጋበዝን ፍቃደኛ ከሆኑ የመግባቢያ ስምምነትዎን ተረድተው ይፈርማሉ፡፡ በመጀመሪያ ስነ-ህዝብ እና ማህበራዊ ጉዳዮችን የተመለከቱ ጥያቄዎችን፣ በመቀጠልም ከህምሞ ጋር የተያያዙ ጥያቄዎችን እንጠይቆታለን፡እንዲዉም የተለያዩ የላብራቶሪ ዉጤቶችን ከህክምና ከካርድዎ እንዎስዳለን፡፡

በጥናቱ ምክንያት ሊደርስ የሚችል ጉዳት፡ በጥናቱ በመሳተፍዎ የሚደርስብዎት ጉዳት የለም

በጥናቱ ያለመሳተፍ ወይም ከገቡ በኋላ የመውጣት መብት፡ ጥናቱ በሙሉ ፍቃደኝነት ላይ የተመሰረተ ነው፡፡ በጥናቱም የመሳተፍ ግዴታ የለብዎትም፡፡ ለመመለስ ያልፈለጉትን ጥያቄ ማለፍ ይችላሉ፡፡ በተጨማሪ ባለመሳተፍዎ የሚያገኙት የጤና አገልግሎት ጥቅም ላይ ምንም አይነት ችግር አያስከትልብዎትም፡፡ እንዲሁም በማንኛውም ሰዓት ከተሳታፊነት ማቋረጥ ይችላሉ፡፡

በጥናቱ መሳተፍ ያለው ጥቅም፡ በዚህ ጥናት ቢሳተፉ የቆይ የጉበት በሽታ ህክምና ዉጤትለማሻሻል እና ለመከላከል ይረዳል፡፡

ጥቅማጥቅም፡ በጥናቱ ላይ በመሳተፍዎ ከምስጋና በዘለለ የሚያገኙት የክፍያ ጥቅም አይኖርም፡፡

ሚስጥራዊነት፡ በዚህ ምርምር የሚገኝ ማናቸውም መረጃ በሚስጢር ይጠበቃል፡፡ የተሳታፊው ስም አይፃፍም፡፡ ከተመራማሪውና የጤና ባለሙያው በስተቀር ሌላ ሰው አያየውም፡፡ ከጥናቱ የምናገኛቸው መረጃዎች ሚስጢርነታቸው የጠበቀ ነው፡፡

ስምምነት፡ በዚህ ጥናት ላይ የሚሳተፉ ታካሚዎች ሙሉ ፍቃደኛ መሆን አለባቸው፡፡

በጥናቱ ዙሪያ የበለጠ መረጃ ቢያስፈልግዎ፡ በጥናቱ ዙሪያ የበለጠ መረጃ ከፈለጉ የሚመለከተውን ግለሰብ ማነጋገር ይችላሉ፡፡

በሃይሉ ተረፈ ተስፋዬ ስልክ፡+251943302087 ወይም

የኢሜል አድራሻ፡ **terefebh@gmail.com or behailu.terefe@ju.edu.et**

VI. Patient Informed consent Amharic Version

የስምምነት ሰነድ

ዉድ ተሳታፊዎች

ስሜ በሃይሉ ተረፈ ተስፋዬ ይባላል፡፡ የሁለተኛ ድግሪ የመመረቂያ ጥናቴን በሶስት የጤና መዐከላት ሜዲካል ክፍል ዉስጥ ተኺተዉ በሚታከሙ ህሙማን መካከል ስር የሰደደ ጉበት በሽታ የህክምና ዉጤት ያተኮረ ነው፡፡ የዚህ ጥናት አላማ ሊስተካከሉ የሚችሉ ሁኔታዎች መለየት እና የበሽታውንም ባህርይ በመረዳት ስር የሰደደ ጉበት በሽታ ህሙማንን አጠቃላይ የጤና ሁኔታን ማሻሻል ነው፡፡ ፡

በመሆኑም ከላይ የተጠቀሱትን አላማዎች ለማሳካት የእርሰዎ ትብብር እና ተሳትፎ በጣም አስፈላጊ ነዉ፡፡ የሚሰጡት መረጃ ሚስጥራዊነቱ የተጠበቀ ነዉ፡፡ እንዲሁም በጥናቱ ያለመሳተፍ እና በፈለጉት ሰአት ከጥናቱ የመዉጣት መብትዎ የተጠበቀ ነዉ፡፡ ከዚህም ባሻገር መመለስ ያልፈለጉትን ጥያቄ መተዉ ይችላሉ፡፡

ይህን የጥናት አላማ ተረድተዉ ተሳታፊ ለመሆን ፍቃደኛ ስለሆኑ በቅድሚያ ምስጋናዬን አቀርባለሁ፡፡

በጥናቱ ላይ ለመሳተፍ መስማማቴን አረጋግጣለሁ፡፡

የተሳታፊው ፊርማ/የጣት አሻራ ----------

ቀን----------ወር----------ዓ.ም.----------

የመረጃ ሰባሳቢው ስም እና ፊርማ----------

ቀን----------ወር----------ዓ.ም.----------

ስለትብብርዎ በድጋሜ አመሰግናለሁ፡፡

VII. Data collection tool

Data collection tool on Clinical Outcomes of admitted chronic liver disease patients.

Patient medical Card number: ……..

I. Socio-demographic characteristics of the patient

C.N:_____

1. **Age (years):____**
2. **Sex:** □ M □ F
3. **Admission date: _____**
4. **Residence:** □ Urban □ Rural
5. **Age at diagnosis(years):_____**
6. **Marital status:** □ Single □ Married □ Divorced □ Widowed
7. **Religion:** □ Orthodox □ Catholic □ Protestant □Muslim □ Traditional □ Other
8. **Educational status:** □ Informal □ Primary □ Secondary □ Tertiary □unable to read and write
9. **Occupation:** □Civil servant □Military□ Health worker □Retired □Self-employed □Daily labor □No work
10. **Average monthly income (birr):_____**
11. **Cigarette Smoking history:** □ Yes □No
12. **Alcohol drinking habits:** □ Active alcoholic □ Inactive alcoholic □Denied
13. **Khat Chewing history** □Yes □No
14. **Herbal medication use history:** □ Yes □ No

II. Baseline Clinical characteristics of the patient

15. **Past medication history (history of medication use in the past 03 months):** □Yes □No

16. **What is the etiology of chronic liver disease in this patient?**

□Alcoholism	□HBV	□HCV	□Cryptogenic
□Hepatic schistosomiasis	□Other(s), _____		

17. **What is the reason(s) for current hospital admission (chief compliant)?**

18. **What is the full working Diagnosis of the patient?**

19. **Which type of CLD complication(s) does the patient have at presentation?**

Complication(s)	**Method of diagnosis**	**Treatment given including paracentesis**
□ **Ascites**		□Dietary sodium restriction(only tick) □Furosemide □Paracentesis □Spironolactone □Other(s)_____
□**Esophageal varices**		□Propranolol (primary prophylaxis) □Omeprazole

Variceal bleeding or Gastrointestinal bleeding	Clinical Endoscopy	Propranolol Omeprazole Blood transfusion
HE **Grade:** I II III IV		Metronidazole Lactulose Bisacodyl Other(s)_____
Spontaneous bacterial peritonitis	clinical laboratory	Ceftriaxone Cefotaxime Norfloxacin Other(s)_____
Hepatocellular carcinoma	US	
Others (please specify)		

20. Blood pressure, signs and symptoms at presentation

Blood pressure (mm Hg)	**1**	**2**	**3**

Signs and symptoms:

Ultrasound finding(s):

21. Laboratory results (with date)

Complete blood count (CBC)	WBC	RBC	Hgb	Hematocrit	PLT	Neutrophil
	Lymphocytes	Monocytes	Basophils	Eosinophil	MCV	MCH
	MCHC					
Liver related parameters	ALT	AST	ALP	Remark		
Coagulation Profile	PT	INR	APTT	Remark		
Serum Albumin (g/dl):				**Serum Bilirubin**		

ASCITIC FLUID ANALYSIS

Cell count	Lymphocytes	Neutrophils	RBCs	LDH	Gram stain	Glucose
AFB	Protein(albumin)					
Renal Function Test(RFT)	Scr(mg/dl)	BUN				
Serologic Tests	HBsAg	HCVAb	Liver autoimmune serology (ANA)		HIV(PIHCT) Reactive Non-reactive	

22. Does the patient have active Medical comorbidities currently? Yes No

23. If the answer to no. 47 is yes please specify the disease

24. Please specify any other medication(s) the patient take while in hospital

a) _____,date_____

b) _____,date_____

c) _____,date_____

III. In-hospital and 28-day outcome, and 30-day post discharge outcomes

25. Did the patient developed acute complication of chronic liver disease while in-hospital? ☐Yes ☐No

26. If the answer is yes to no. 48, what is the type of complication(s) observed?

Major Acute complication of Chronic liver disease	**Diagnosis method**	**Date event is diagnosed**	**Treatments given**
☐**Gastrointestinal (Variceal bleeding)**	☐Clinical ☐Endoscopy		☐Propranolol ☐omeprazole ☐other(s)_____
☐**Hepatic encephalopathy** **Grades** ☐ I ☐ II ☐ III ☐ IV			☐Metronidazole ☐Lactulose ☐Bisacodyl ☐other(s), please specify_____
☐**Spontaneous bacterial peritonitis**	☐Clinical ☐laboratory		☐Ceftriaxone ☐Norfloxacin ☐Other(s), please specify,_____
☐**Hepatorenal syndrome**			
☐**Other(s), please specify _____**			

27. What is the final in-hospital outcome of the patient?

☐**Patient improved and discharged**	Date of discharge	
☐**Patient discharged without improvement**		
☐**Referred/worsened**	Referral date	
☐ **Patient Left against medical advice**		
☐ **patient lost on follow-up**	Date the patient lost	
☐**Patient is still in-hospital at the end of the study period**	The final contact date	

28. 30 days post discharge outcome

☐Patient died	☐Patient survived	☐Not responded

Note: **US**-ultrasound, **PMN**-Polymophonuclear**, NAFLD**-Non Alcoholic liver Disease, **AIH**-Autoimmune hepatitis,, **ANA**-anti-nuclear antibody

Declaration

Here with my signature, I declare that this research paper entitled by "**Clinical outcomes of patients with chronic liver disease admitted to selected tertiary care hospitals, Ethiopia: Prospective cohort study",** is done under my advisor ship and I have approved that this draft is the final draft thesis for submission to the school of pharmacy, Student Research Project office of Jimma University.

NAME_____ Signature _____

Here with my signature, I declare that this research paper has been examined by me and I have checked that the student has corrected the comment that I forwarded before final submission.

NAME_____ Signature _____

Here with my signature, I declare that this research paper is done by me as a principal researcher and I assure that this research paper is the final draft for submission to the school of pharmacy, Student Research Project (SRP) office of Jimma University.

NAME_____ Signature _____