“COMPARATIVE STUDY OF LACTATE FREE APASL-ACLF RESEARCH CONSORTIUM - ACUTE ON CHRONIC LIVER FAILURE SCORE (LaFAAS) VS. STANDARD PROGNOSTIC SCORES IN ACUTE ON CHRONIC LIVER FAILURE.”

By:

Dr. MANASA DIXIT C

Dissertation submitted to the

Sri Devaraj Urs Academy of Higher Education and Research,
Tamaka, Kolar, Karnataka,

In partial fulfillment of the requirement for the degree of

DOCTOR OF MEDICINE (M.D.)
IN
GENERAL MEDICINE

Under The Guidance Of
DR. PRABHAKAR K
PROFESSOR

DEPARTMENT OF GENERAL MEDICINE
SRI DEVARAJ URS MEDICAL COLLEGE, TAMAKA, KOLAR, KARNATAKA.
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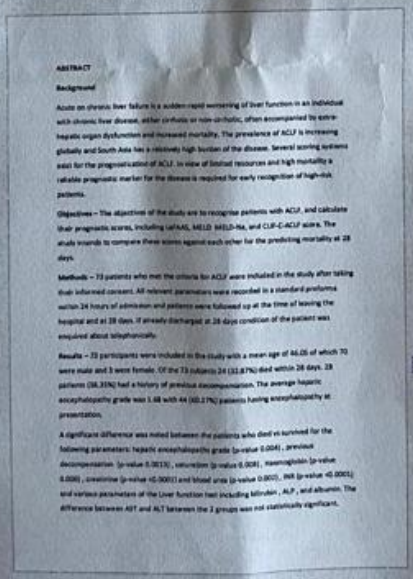

ABSTRACT

Background

Acute on chronic liver failure is a sudden rapid worsening of liver function in an individual with chronic liver disease, either cirrhotic or non-cirrhotic, often accompanied by extra-hepatic organ dysfunction and increased mortality. The prevalence of ACLF is increasing globally and South Asia has a relatively high burden of the disease. Several scoring systems exist for the prognostication of ACLF. In view of limited resources and high mortality a reliable prognostic marker for the disease is required for early recognition of high-risk patients.

Objectives – The objectives of the study are to recognise patients with ACLF, and calculate their prognostic scores, including LaFAAS, MELD, MELD-Na, and CLIF-C-ACLF score. The study intends to compare these scores against each other for the predicting mortality at 28 days.

Methods – 73 patients who met the criteria for ACLF were included in the study after taking their informed consent. All relevant parameters were recorded in a standard proforma within 24 hours of admission and patients were followed up at the time of leaving the hospital and at 28 days. If already discharged at 28 days condition of the patient was enquired about telephonically.

Results – 73 participants were included in the study with a mean age of 46.05 of which 70 were male and 3 were female. Of the 73 patients 24 (32.87%) died within 28 days. 28 patients (38.35%) had a history of previous decompensation. The average hepatic encephalopathy grade was 1.68 with 44 (60.27%) patients having encephalopathy at presentation.

A significant difference was noted between the patients who died vs survived for the following parameters: hepatic encephalopathy grade (p-value 0.004) , previous decompensation (p-value 0.0013) , saturation (p-value 0.028) , haemoglobin (p-value 0.008) , creatinine (p-value <0.0001) and blood urea (p-value 0.003) , INR (p-value <0.0001) and various parameters of the Liver function test including bilirubin , ALP , and albumin. The difference between AST and ALT between the 2 groups was not statistically significant.

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ACKNOWLEDGEMENT

No academic work is single handedly accomplished. This work is no exception. Words fail me in expressing my heartfelt and humble gratitude to thank the almighty for showering his blessings on me. I sincerely thank my guide, **DR. PRABHAKAR K.,** for their invaluable guidance and constant extended support with the timely advice which helped me with this study. Their encouragement, sense of punctuality, research-oriented approach, painstaking effort to weed out errors during the entire course of study leaves me permanently indebted to them.

I express my deep sense of gratitude and humble thanks to my senior Professors, **DR. RAGHAVENDRA PRASAD , DR. RAVEESHA A**, **DR VIDYASAGAR & DR. SRINIVASA .S.V** for their advice and encouragement throughout the study.

I am extremely indebted to and I thank my teachers**, DR. ANITHA. A, DR. MANJUNATH, DR PRAVEEN.P** for their constant support and encouragement throughout with patience and care. They have been my well wisher and a source of inspiration throughout my study.

My heartfelt thanks to all my teachers throughout my life for having made me what I am today for their practical tips, invaluable advice and constant encouragement.

I extend my sincere thanks to my seniors DR SASI , **DR. SANMITHA, DR. DHRUVANANDAN, DR.SREENATH, DR. KISHORE, DR. DEEPTHI, DR APARNA.R , DR HEMANTH** whose knowledge has guided and inculcated in me a sense of confidence. I am thankful for their valuable guidance and helping me with my dissertation.

I express my sincere thanks to my colleagues and dear friends **DR. SUJITHA.V, DR T.L.PAVAN, DR. AMULYA P , DR MANOHAR GOWDA, DR KAVYA B.K, DR**

POONGULALI, DR. INBA PRAVEEN for their co-operation and help in carrying out this study.

I would express my deepest gratitude to my beloved parents, **DR. CHANDRASHEKARA S** and DR. **RENUKA P** whose love, blessings and sacrifices made me the person I am today. Without them I would have never reached this level.

I am very much thankful to my sister **MEGHANA DIXIT** for her love and support.

I thank all my juniors interns and nursing and support staff of the ICU, MICU and the General ward for their help and assistance.

Last, but not the least, I thank my patients for providing me the opportunity to carry out my study.

Dr . MANASA DIXIT C

ABBREVIATIONS

ACLF: Acute on chronic liver failure
AARC: APASL Acute-on-Chronic Liver Failure Research Consortium
LaFAAS: Lactate-free APASL Acute on Chronic Liver Failure Research Consortium - Acute on Chronic Liver failure Score
MELD: Model for End stage Liver Disease
MELD-Na: Sodium MELD
CLIF-C-ACLF: Chronic Liver Failure (CLIF) Consortium - Acute on Chronic Liver Failure
CPT: Child-Pugh-Turcotte
APASL: Asian Pacific Association for the Study of the Liver
EASL: European Association for the Study of the Liver
EASL-CLIF: European Association for the Study of Chronic Liver Failure
NACSELD: North American Consortium for the Study for End-Stage Liver disease
COSSH: Chinese Group on the Study of Severe Hepatitis
CLIF-SOFA: chronic liver failure-sequential organ failure assessment
APACHE: ACUTE PHYSIOLOGY AND CHRONIC HEALTH EVALUATION
ASR: Age-standardized mortality rate
ALF: Acute liver failure
NAFLD: Non-alcoholic fatty liver disease
ALD: Alcohol-associated liver disease
VA: Veterans Affairs
AKI: Acute kidney injury
NIS: National Inpatient Sample
PAMPs: Pathogen-associated molecular patterns
DAMPs: Damage-associated molecular patterns
CRP: C reactive protein
IL: Interleukin
PRRs: Pattern-recognition receptors
TLRs: Toll-like receptors
MODS: Multiorgan dysfunction syndrome
ICU: Intensive care unit
LPS: Lipopolysaccharide
T2DM: Type 2 diabetes
HTN: Hypertension
IHD: Ischemic heart disease
SPO2: Oxygen saturation
WBC: White blood cell
A/G: Albumin/globulin
ALP: Alkaline Phosphatase
AST: Aspartate Transaminase
ALT: Alanine transaminase
INR: international normalised ratio
GGT: Gamma Glutamyl transferase

PT: prothrombin time
HE: Hepatic encephalopathy
PaO2/FiO2: Ratio of arterial oxygen partial pressure (PaO2 in mmHg) to fractional inspired oxygen
iNOS.: Inducible nitric oxide synthase
OxPhos: Oxidative phosphorylation
SNS: Sympathetic nervous system
RAAS: Renin-angiotensin-aldosterone system
ROC: receiver operating characteristic curve
AUC: Area under the ROC Curve

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ABSTRACT

Introduction :

Acute on chronic liver failure (ACLF) is a sudden rapid worsening of liver function in an individual with chronic liver disease, either cirrhotic or non-cirrhotic, often accompanied by extra-hepatic organ dysfunction. This entity has high morbidity and mortality within 3 months. The prevalence of ACLF is increasing globally and South Asia has a relatively high burden of the disease. Several scoring systems exist for the prognostication of ACLF. In view of limited resources and high mortality a reliable prognostic marker for the disease is required for early recognition of high-risk patients.

Objectives

The objectives of the study are to recognise patients with ACLF, and calculate their prognostic scores, including LaFAAS, MELD MELD-Na, and CLIF-C-ACLF score. The study intends to compare these scores against each other for the predicting mortality at 28 days.

Materials and Methods

73 patients who met the criteria for ACLF were included in the study after taking their informed consent. All relevant parameters were recorded in a standard proforma within 24 hours of admission and patients were followed up at the time of leaving the hospital and at 28 days. If already discharged at 28 days condition of the patient was enquired about telephonically.

Results

73 participants were included in the study with a mean age of 46.05 of which 70 were male and 3 were female. Of the 73 subjects 24 (32.87%) died within 28 days. 28 patients (38.35%) had a history of previous decompensation. The average hepatic encephalopathy grade was 1.68 with 44 (60.27%) patients having encephalopathy at presentation.

A significant difference was noted between the patients who died vs survived for the following parameters: hepatic encephalopathy grade (p-value 0.004) , previous decompensation (p-value 0.0013) , saturation (p-value 0.008) , Haemoglobin (p-value 0.006) , creatinine (p-value <0.0001) and blood urea (p-value 0.002) , INR (p-value <0.0001) and

various parameters of the Liver function test including bilirubin , ALP , and albumin. The difference between AST and ALT between the 2 groups was not statistically significant.

All the prognostic scores showed a significant statistical difference between the 2 groups. AUROC was calculated for the various scores where CLIF C ACLF had an AUC of 0.929, MELD of 0.938 , MELD Na of 0.91, LaFAAS of 0.898 and CPT of 0.874.

Conclusion

All the scoring systems used, the MELD score , LaFAAS , CLIF-C-ACLF, Child Pugh score and the MELD-Na were found to be effective tools at prognosticating ACLF. MELD score was found to be the better score among these. Although LaFAAS score had a lower discriminative factor than the standard scores it had a good sensitivity and is an effective easy to calculate scoring system for patients in ACLF.

INTRODUCTION

INTRODUCTION

Patients who have cirrhosis or chronic liver disease may experience a rapid and often life-threatening worsening of their clinical symptoms, known as acute-on-chronic liver failure (ACLF).[1] Acute decompensation of the liver disease, extrahepatic organ failure(s), along with significant mortality is the hallmarks of this syndrome. The pathophysiology of ACLF is defined by uncontrolled systemic inflammation together with paradoxical immunoparesis, and it is frequently brought on by persistent alcohol use, gastrointestinal bleeding, and/or infections. It can occur irrespective of the stage of cirrhosis, compensated, or decompensated, and can be precipitated by hepatic events such as toxin-induced injury or extrahepatic events such as infection.[2] In hospitalized cirrhotic patients with an acute liver disease complication, ACLF is a condition that occurs frequently and is the most frequent reason for death in these patients.[3] Hence early and rapid identification is necessary for patients with ACLF.[4]

Patients with decompensated cirrhosis were admitted with a 35% global frequency of ACLF, and a 58% 90-day death rate.[5] According to multicentre research conducted in India, individuals with ACLF 5 have a death rate of 42% within 8 days of being admitted.[6] In a nation like India, the bulk of these cases are handled in non-transplant settings due to a lack of resources. The condition must therefore be predicted quickly and accurately upon admission.

The current scoring systems used to prognosticate Liver disease include the Chronic Liver Failure (CLIF) Consortium - Acute on Chronic Liver Failure (CLIF-C-ACLF) score, the Model for End stage Liver Disease (MELD) and the MELD-Na(sodium MELD). APASL -Acute on Chronic Liver Failure Research Consortium - Acute on Chronic Liver failure (AARC-ACLF) score is a scoring system introduced by the Asian Pacific Association for the Study of the Liver (APASL) comprising of 5 parameters such as Total bilirubin, Hepatic encephalopathy grade, coagulopathy, Lactate, and renal for prognostication in ACLF.[7] This score takes into account lactate, which is not frequently evaluated in chronic liver disease patients, particularly in India. Therefore, a Lactate Free - AARC ACLF score (LaFAAS) approach would be more helpful in a country like India.

A pilot study by Chauhan et al has shown that LaFAAS is as accurate if not more accurate than the existing prognostic scoring systems at predicting mortality at 3 months

in patients who had alcohol-induced ACLF.[8] There is a lack of further studies with regard to this scoring system hence, the aim of this present study is to determine the patients' LaFAAS, MELD, MELD-Na, and CLIF C ACLF scores and assess LaFAAS' predictive significance for short-term (28-day) mortality in comparison to MELD, CLIF-C-ACLF and MELD-Na scores.

AIMS AND OBJECTIVES

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1. To identify the patients with acute on chronic liver failure as per the unified working definition given by APASL

2. To calculate the LaFAAS , MELD score, MELD-Na score, and CLIF C ACLF score of these patients.

3. To compare the prognostic value of the LaFAAS score as compared the to MELD score, MELD-Na score, and CLIF-C ACLF score for short-term (28-day) mortality

REVIEW OF LITERATURE

REVIEW OF LITERATURE

1. Definitions

Table 1: Definitions of ACLF[4]

Asian Pacific Association for the Study of the Liver (APASL) criteria
"An acute hepatic insult which manifests as jaundice (Bilirubin >5 mg/dL) and coagulopathy (INR>1.5) and is complicated within 4 weeks by clinical ascites and/or encephalopathy in a patient with previously diagnosed or undiagnosed CLD including cirrhosis"
European Association for the Study of Chronic Liver Failure (EASL-CLIF) criteria
"Acute deterioration of a pre-existing chronic liver disease that is usually related to a precipitating event and associated with increased mortality at 3 months due to multi-organ failure"
The North American Consortium for the Study for End-Stage Liver disease (NACSELD)
"A syndrome characterized by acute deterioration in a patient with cirrhosis due to infection presenting with two or more extra-hepatic organ failures."
Chinese Group on the Study of Severe Hepatitis (COSSH)
"A complicated syndrome with a high short-term mortality rate that develops in patients with HBV-related chronic liver disease regardless of the presence of cirrhosis and is characterized by acute deterioration of liver function and hepatic and/or extrahepatic organ failure."

Source; Abbas, 2022

1.1 Prevalence, Epidemiology, and mortality

There is limited available data with regard to the prevalence and mortality of ACLF and There is currently a lack of information on the epidemiology of ACLF, but the high mortality rates, lengthy hospital stays, and significant financial impact on healthcare systems brought on by the disorder show how critical it is to further our understanding of it.[9]

Cirrhosis mortality rose 47.15% globally between 1990 and 2017. India recorded the most fatalities in 2017. The United Arab Emirates was determined to have the biggest increase in mortality followed by Qatar and the Philippines. The age-standardized mortality rate

(ASR) of liver cirrhosis varies worldwide, ranging from 16.66 per 100,000 in 1990 to 17.31 per 100,000 as of 2017.[10] The basic idea behind the defining ACLF as a separate entity is to point out a subset of cirrhotic or chronic liver disease patients who have an unexpectedly quick and abrupt decompensation of the liver disease along with extrahepatic organ failure. With the normal course of cirrhosis with chronic decompensation, short-term mortality is significantly higher than those with acute liver failure (ALF).[11] Douglas et al, reported that in hospitalized cirrhotic patients, the prevalence of ACLF is between 12% to 40%.[12] ACLF is a serious medical issue that affects people all over the world, with prevalence rates in at-risk groups ranging from 20 to 35%. According to the EASL-CLIF Consortium definition, the reported mortality of ACLF globally varies between 30% and 50% and is highly correlated with the frequency of organ failures.[9] A CANONIC study by Moreau et al, reported patients without ACLF who had decompensated cirrhosis had a mortality rate of 1.9% at 28 days, while those with ACLF had a mortality rate of 32.8%.[13] A study analysing the United Network for Organ Sharing registry for a period of 12 years reported that the largest percentage increase in study population occurred among waitlist registrants for non-alcoholic fatty liver disease (NAFLD)-ACLF between 2005 and 2017, rising from 134 to 574 candidates, a rise of 331.6% and was related to greater risk of waitlist mortality; additionally, the number of candidates for alcohol-associated liver disease (ALD)-ACLF rose by 206.3%.[14] A study analysing cirrhosis patients in the Veterans Health Administration between 2008 and 2016 reported that among 80,383 patients, the incidence rate for APASL ACLF was 5.7 per 1,000 person-years and for EASL ACLF was 20.1. The mortality at 28 days and 90 days for APASL ACLF were 41.9% and 56.1%, respectively, and for EASL ACLF they were 37.6% and 50.4%.[15] A study using the US Department of Veterans Affairs (VA) Corporate Data Warehouse between January 1, 2004, and December 31, 2014, reported that 19,082 (26.4%) of the 72,316 patients hospitalized for decompensated cirrhosis satisfied the ACLF criteria upon admission. 12.8% of them experienced a single organ failure, 10.1% experienced two, and 3.5% had three or more. In this study,25.5% of ACLF cases were deceased within 28 days and 40% of ACLF patients passed away within 90 days following their hospitalisation.[16] A meta-analysis by Jiang et al reported that, acute kidney injury (AKI) complicates ACLF in about 40% of these patients, and significantly increases short-term mortality.[17] A study by Piano et al comprising 466 cirrhosis patients reported that 25% of patients developed ACLF while the probability of developing ACLF at 1 year was 14%, it was 29% at 5 years and 41% at

10 years.[18] A single centre study from Argentina comprising 100 cirrhotic patients reported that 29% patients developed ACLF and had a significantly elevated mortality rate.[19] Patients with chronic liver disease who are admitted for acute decompensations are also found to frequently develop ACLF, which is common, often fatal, and relates to the number of organs affected.[20] High mortality in the short-term was found in patients with ACLF who had multiple organ failure and a greater CLIF-SOFA score.[21] A study based on National Inpatient Sample (NIS) database from 2006 to 2014 reported that 29.599 (6.6%) of the 447,090 Alcohol-associated liver disease patients between 2006 and 2014 had ACLF.[22] A 2022 metanalysis study evaluating the burden of ACLF globally reported that In patients who had decompensated cirrhosis, the prevalence of ACLF was 35% (33% to 38% - 95% CI) globally, with an increasing incidence in East Asia (15%) and in South Asia (65%). Patients with ACLF had a 58% 90-day death rate worldwide vs only 14% in those patients who did not have ACLF. South America recorded the greatest death rate (73%) followed by South Asia (68%). The mortality rate at 28 days was 45% globally (95% CI: 41% to 48%). The findings from different subcontinents revealed South America had the greatest rate (63%, 95% Confidence Interval 54% to 71%) and North America had the least (28%, 95% CI 28% to 29%).[5] A study comprising patients from multiple tertiary care hospitals in Thailand reported a 54% incidence of ACLF and a 58% 30-day mortality rate, respectively.[21]

Premkumar et al reported that among 386 patients admitted to Rajiv Gandhi Government General Hospital, Chennai who were diagnosed with cirrhosis / decompensated cirrhosis, Acute or chronic liver failure, which had a prevalence of 39%, was diagnosed in 150 patients. The overall fatality rate was 83%, and it was shown that alcohol and infection were major contributing causes.[23] In a study comprising 1043 ACLF patients from 10 tertiary centres across India, Over a brief period of 8 days, the index admission's high (42%) in-hospital mortality rate.[24]

Pathophysiology

Pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns can both cause systemic inflammation (DAMPs).[25] Systemic inflammation is a defining feature of ACLF; patients with ACLF have higher white cell counts, increased inflammatory markers like C reactive protein (CRP), and elevated levels of cytokines such as interleukin (IL)-6, IL-1, and IL-8 than do patients without ACLF.[26]

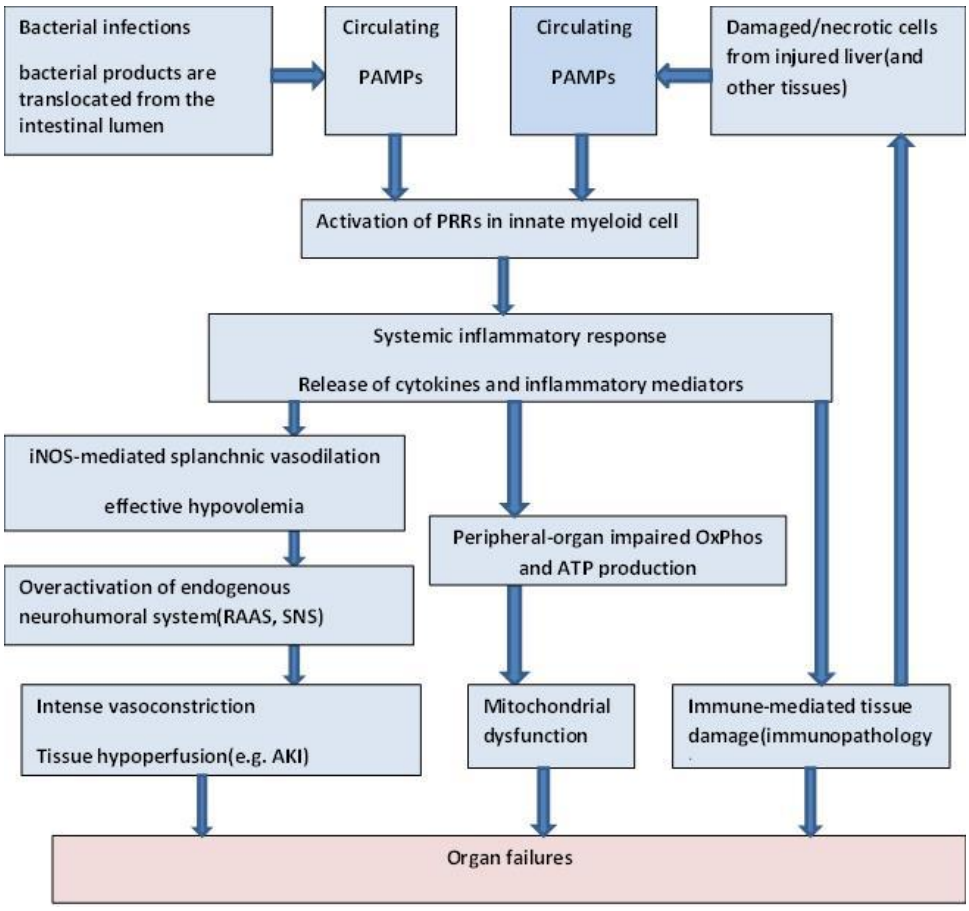
PAMPs, which are specific molecular structures expressed by microbes, is recognised by special pattern-recognition receptors (PRRs) such as Toll-like receptors (TLRs), for instance, which are expressed in neutrophils and monocytes, as well as other cells which are part of the innate immune response. As a result of intracellular signaling cascades being activated by the PRR, inflammatory mediators are eventually synthesised, and their transcripts are produced. The recognition and activity of TLR4 against lipopolysaccharides, a PAMP generated from the cell wall of gram-negative bacteria, serves as a classic example of these pathways by increasing the transcription and activity of several inflammatory mediators and cytokines. Cases of ACLF without active bacterial infections may be exacerbated by elevated levels of circulating PAMPs, most likely attributable to the translocation of bacterial products across the intestinal mucosa. Cases of ACLF with no identified precipitating cause may also be attributed to high levels of circulating PAMPs, which are primarily a result of the translocation of bacterial products from the intestinal lumen and are unrelated to ongoing bacterial infections. These translocated PAMPs occur as a result of intestinal bacterial overgrowth, increased intestinal mucosa permeability, and impaired local immune function of the gastrointestinal tract.[25] Even in the absence of an ongoing infection, systemic inflammation is still possible. As a result of dead or injured host cells releasing circulating DAMPs that bind to and activate particular PRRs, there is a sterile inflammation.[27,28] DAMPs are made up of components that are found inside the cell in diverse compartments. The DAMP release can occur as a result of several types of liver damage.[29,30,31]

Inducible nitric oxide synthase can be induced in the arteriolar walls of the splanchnic vasculature by PAMPs and inflammatory mediators. Due to the nitric oxide overproduction that results, the endogenous neurohumoral vasoconstrictor system becomes overactive due to homeostatic homeostasis, which lowers effective arterial blood volume. Then, neurohumoral mediators precipitate severe vasoconstriction, especially in the renal circulation, which leads to acute kidney damage, reduced glomerular filtration rate, and hypoperfusion of the kidneys (AKI). tissue harm caused by the immune system Similar to sepsis, ACLF is frequently accompanied by leukocytosis, which consists of immune cells that have been activated and may enter organs to induce immunopathology.[32] A study by Moreau et al comprising a large cohort of patients with acutely decompensated cirrhosis underwent high-throughput blood metabolomic and s

reported that peripheral organs in ACLF may have much less mitochondrial fatty acid -oxidation, which lowers oxidative phosphorylation and ATP generation.[33]

As evidenced by elevated levels of circulating cytokines, ACLF is linked to severe systemic inflammation. The Inflammatory cytokines cause SIRS and multiorgan dysfunction syndrome as well as mediate a number of the clinical signs of ACLF (MODS). Increased neutrophilia and lower frequencies of lymphocytes (T and B) , natural killer cells, and antigen-presenting cells are symptoms of the emergency granulocytopoiesis that is brought on by infection and cytokines. Infection clearance is hampered by pre-existing immune dysfunction brought on by cirrhosis, and the clinical picture of ACLF is made more challenging.[34]

Figure 1: Pathophysiology of acute-on-chronic liver failure[25]



AKI, acute kidney injury; DAMPs, damage-associated molecular patterns; PAMPs, pathogen-associated molecular patterns; PRRs, pattern-recognition receptors; iNOS, inducible nitric oxide synthase; OxPhos, oxidative phosphorylation; RAAS, renin-angiotensin-aldosterone system; SNS, sympathetic nervous system

1.4 Precipitating event

The precipitating events of ACLF vary geographically and can be categorised as extrahepatic or hepatic depending on where they originate. The frequent causes of ACLF in Asian countries are acute bacterial infection, acute hepatitis A or E infection, chronic HBV reactivation, acute alcoholic hepatitis, and acute viral infections. Active drinking and infections are the common precipitants in the western population, yet in a sizable number of individuals with ACLF, there is no apparent precipitating factor. Both in the east and the west, there hasn't been enough research done on the possible role of drug-induced liver injury as a contributing factor.[2]

Extrahepatic Precipitating Factors

Systemic Infection: Even though the frequency varies by region, infections are one of the primary causes of ACLF. According to the CANONIC study by Moreau et al in Europe, infection is thought to be the cause of close to 40% of instances with ACLF.[13] Similar rates can be found across the globe, with 35% of ACLF patients in a Chinese cohort being one example.[35] In patients with cirrhosis, a bacterial infection is common, frequently severe, and a major cause of AD. In 25% to 35% of individuals with cirrhosis, infection is present upon admission or develops while they are in the hospital. In addition to the previously mentioned translocation of bacteria and bacterial products, dysbiosis, and Cirrhosis-associated immune dysfunction, there are other predisposing variables that can explain why individuals with cirrhosis are more susceptible to infections. Bacterial infection, is a frequent and common cause of Acute decompensation overall (22% - 29% of AD cases and 33%–50% of ACLF cases), indicating that infection might cause severe forms of AD.[36,37,13] This idea is supported by the PREDICT study by Trebicka et al, showing a temporal correlation between episodes of viral infection and the development of ACLF.[38] A study by Nahon et al comprising individuals with severe alcoholic hepatitis showed that the only independent factor that was found to the onset of ACLF was the presence of preceding infection. The 5-year cumulative incidence of infections caused by bacteria in Cirrhotic patients was 13%. the infections generally occurred prior to and likely induced episodes of decompensation as was seen in a prospective trial of 1,672 patients with compensated (Child-Pugh A) cirrhosis due to hepatitis B or hepatitis C who did not have a history of previous decompensation.[39] Despite being a minor (5%) infectious precipitant of ACLF, fungi infections are linked to worse outcomes.[40, 41]

Variceal haemorrhage : Variceal or gastrointestinal bleeding may not be uniformly regarded as a cause of ACLF depending on the community. The EASL and NACSELD, on the other hand, consider variceal bleeding to be a precipitant in all cases, whereas the Asian Pacific Association for the Study of the Liver only does so if it causes liver failure.[42] In any case, it is thought that hepatic ischemia, enhanced bacterial translocation from the gut, and subsequent bacterial infections are the main causes of acute variceal bleeding that triggers ACLF.[43]

Invasive Procedures : 9% of all occurrences of ACLF in the CANONIC trial were caused by large-volume paracentesis, shunt procedures, and major surgery.[13] These made up 2% of the analysis from China.[35] Hepatocellular carcinoma treatments, such as radiofrequency ablation or transarterial chemoembolization, have been linked to ACLF in patients with Child-Pugh stage B or C cirrhosis and a diminished liver reserve.[42]

Intrahepatic Precipitating Factors

Alcohol: commonly seen intrahepatic precipitant of ACLF is active alcohol usage.[44] Geographical differences exist in the frequency of alcohol use being a precipitating factor. Active alcohol consumption—defined as "more than 14 units per week for women and more than 21 units per week for men"—was the precipitant in approximately 25% of patients with ACLF in the CANONIC study.[13] Alcohol accounted for over 50% of the hepatic precipitants of ACLF in research from the Asian Pacific Association for the Study of the Liver-Acute-on-Chronic Liver Failure Research Consortium (AARC).[7] Therefore, despite the fact that this load differs locally, it is nonetheless significant everywhere.

Viral Hepatitis: The most frequent virus that causes ACLF is HBV.[35] Approximately 35% of ACLF cases in Asia are caused by HBV, compared to 10% of cases in Europe and the US.[13,35] Acute HBV infection, HBV reactivation due to treatment interruption, HBV resistance, chemotherapy, or immunosuppression, or both, might result in ACLF.[35, 45] The development of ACLF may be influenced by excessive innate immune activity against viral antigens that are mediated by DAMPs and pathogen-associated molecular patterns (PAMPs).[13,46] It has also been demonstrated that some people are predisposed to ACLF caused by HBV due to host and viral genetic variables.[47,48] The most frequent causes of acute hepatitis in Asia are HAV and HEV, which are normally self-limiting diseases. However, they are responsible for ACLF in about 6%–19% of cases.[35,49]

Drug-Induced : The use of several potentially hepatotoxic substances, such as prescription pharmaceuticals, medication, and herbal or dietary supplements, can cause drug-induced liver injury(DILI).[50] Patients with the previous liver illness have been shown to have a greater DILI-related mortality rate than those without.[51] A previously compensated cirrhosis can decompensate as a result of DILI, and in the most severe cases, ACLF can also happen, carrying a substantial mortality risk.[52,53,54]

Unknown : Patients with ACLF do not necessarily have a known precipitating incident. The frequencies of unknown precipitants are actually quite high. The rate was >40% in the CANONIC investigation and 20% in the analysis of the AARC database.[13,26,55,35]

1.4 Role of Sepsis

Cirrhotic patients have a significantly higher risk of dying from sepsis and septic shock, two fatal disease categories. Cirrhosis of the liver increases the risk of infections and antibiotic resistance secondary to hemodynamic disturbances, immunological dysregulation, and prolonged systemic inflammation with changed gut flora and patients with cirrhosis experience recurring infections that are life-threatening and eventually lead to multiple organ failure.[56] There is evidence that in cirrhotic individuals , sepsis is accompanied by an imbalanced cytokine response ("cytokine storm"), converting normally beneficial responses required for fighting infections into an excessive and damaging inflammatory response. High levels of proinflammatory cytokines appear to contribute to the worsening of liver function and the emergence of organ/system failures affecting the cardiovascular system, coagulation, renal parameters, respiratory system, and nervous system in patients with cirrhosis and severe sepsis. These individuals may also have sepsis-induced hypoglycaemia or hyperglycemia, impaired arginine-vasopressin secretion, insufficient amounts of adrenal hormones, or compartment syndrome.[57] Lipopolysaccharide (LPS)-induced hepatocyte apoptosis and ischemic injury can both result from sepsis, which is a significant factor that can cause liver damage. According to some theories, the LPS present in bacteria damages the liver by causing apoptosis as well as ischemia harm from concomitant circulation abnormalities. The production of tumor necrosis factor enhances the apoptotic effects of LPS.[58] Acute decompensation from sepsis can lead to compensated cirrhosis, which can thereafter progress to ACLF. When sepsis occurs concurrently with decompensated cirrhosis, it can exacerbate pre-existing decompensation or cause new decompensation, both of which might result in ACLF.

Acute decompensation, ACLF, and sepsis are all conditions that can cause organ failure.[56] Sepsis in ACLF patients has a greater rate of morbidity and mortality, hence prognosis can be improved with early recognition and treatment of sepsis in these patients.[59]

2.1 Diagnosis

Patients with ACLF will exhibit acute hepatic decompensation symptoms. Long-term coagulopathy (INR >/= 1.5, frequently elevated bilirubin and liver enzymes, thrombocytopenia, anaemia, hypoglycemia, hyperammonaemia, signs of acute kidney injury and dyselectrolytaemia (hypokalaemia, hypophosphatemia) are also frequent. Imaging may be needed to confirm the clinical findings and to identify infections, organs involved, or multiple organ failure. It is crucial to perform abdominal imaging to check for evidence of portal hypertension, hepatocellular carcinoma, venous thrombosis, lymphadenopathy, and splenomegaly. If renal damage and vascular thrombosis are present simultaneously in a patient, abdominal ultrasonography with Doppler may be recommended. Radiological imaging of the chest will assist rule out pulmonary edema or pneumonia, while radio imaging of the brain is important to exclude other organic aetiology for altered sensorium.[60]

The CANONIC study set out to develop diagnostic standards for ACLF in 2013, using data from patients who had organ failure as measured by the CLIF-SOFA score. According to the study, young drinkers with concomitant bacterial infections, leucocytosis, and higher C-reactive protein (CRP) levels made up the majority of the ACLF patients. Leukocyte counts and the CLIF-SOFA score, both of which were greater in patients with ACLF, were independent predictors of mortality in these individuals.[61,13]

Table 2: CLIF-SOFA Score[13]

Organ/system	0	1	2	3	4
Liver (bilirubin, mg/dL)	<1.2	≥1.2 to ≥2.0	≥2.0 to <6.0	≥6.0 to <12.0	**≥12.0**
Kidney (creatinine, mg/dL)	<1.2	≥1.2 to ≥2.0	**≥2.0 to <3.5**	**≥3.5 to <5.0 or use of renal replacement therapy**	**≥5.0**
Cerebral (HE grade)	No HE	I	II	**III**	**IV**
Coagulation (international normalized ratio)	<1.1	≥1.1 to <1.25	≥1.25 to <1.5	≥1.5 to >2.5	**≥2.5 or platelet count ≤20×10^9/L**
Circulation (mean arterial pressure, mm Hg)	≥70	**<70**	**Dopamine ≤5 or dobutamine or terlipressin**	**Dopamine >5 or E ≤0.1 or NE ≤0.1**	**Dopamine >15 or E>0.1 or NE >0.1**
Lungs **PaO/FiO2 or** **SpO2/FiO2**	>400 >512	**300 to** ≤400 >357 to ≥512	>200 to ≤300 >214 to ≤300	>100 to ≤200 >214 to ≤357	≥100 ≥89

SpO2: Oxygen saturation, PaO2/FiO2: ratio of arterial oxygen partial pressure (PaO2 in mmHg) to fractional inspired oxygen

Diagnostic criteria for ACLF as considered in Japan:[62]

- "ACLF can be considered in patients with cirrhosis and a Child-Pugh score of 5–9, When a decline in liver function (serum bilirubin level of 5.0 mg/dl or more, prothrombin time value of 40% or less of the standardised values, and/or international normalisation rates [INRs] of 1.5 or more) brought on by severe liver damage appears within 28 days of an acute insult, such as alcohol abuse, bacterial infection, gastrointestinal bleeding, and the exacerbation of cirrhosis."

2.1 Differential diagnosis[60]

- Paracetamol toxicity
- Acute fatty liver of pregnancy , HELLP syndrome
- Toxins
- Cholestasis
- Infections – Ebola , Marburg
- Galactosemia
- Haemolysis
- Hypersensitivity
- Severe acute hepatitis

2.2 Assessment of prognosis and ACLF grade

Clinicians are able to evaluate the prognosis by grading ACLF and Prognosis was observed to be predicted by renal failure which is defined as a serum creatinine concentration of 1.5-1.9 mg/dL and/or brain dysfunction when combined with a single Organ failure. No ACLF is based on a single nonrenal organ failure without cerebral dysfunction and renal dysfunction or no organ failure.[60,63]

ACLF is categorised into 3 grades depending on severity:[60]

Grade-1 ACLF:

- Single renal failure
- Single liver, circulatory, coagulation, or lung failure which is associated with a serum creatinine level of 1.5 to 1.9 mg/dL and/or hepatic encephalopathy grade 1 or grade 2
- A single brain failure with a serum creatinine level of 1.5 to 1.9 mg/dl

Grade-2 ACLF: 2 organ failures of any combination

Grade-3 ACLF: There are three or more organ failures of any combination

3. Prognostic scores

Research into the identification of distinct markers of severity and outcome predictors has been restricted by the differences in defining and varying classification of ACLF, and therefore the varied characteristics of the study population. The severe condition known as ACLF occasionally shows signs of reversibility in around half the patients, and in other instances, it can become life-threatening. The ability to identify patients who are at high risk and those who may need intensive care, as well as the ability to make clear clinical decisions to optimise management and reduce unnecessary and expensive care, are therefore of utmost importance.[64] There are a number of prognostic models available to prognosticate ACLF because there isn't a single prognostic model that is universally acknowledged for the condition.

3.1 AARC-ACLF and Lactate free APASL ACLF research consortium - acute on chronic liver failure score (LaFAAS)

The APASL ACLF Research Consortium (AARC) ACLF score is created using data from the AARC database, which was prospectively compiled from several centers.[7]

Table 3 : AARC score and ACLF grade[7]

AARC score					
Points	Total bilirubin (mg/dl)	HE grade	PT-INR	Lactate (mmol/l)	Creatinine (mg/dl)
1	<15	0	<1.8	<1.5	<0.7
2	15–25	I–II	1.8–2.5	1.5–2.5	0.7-1.5
3	>25	III–IV	>2.50	>2.5	>1.5
Minimum 5, maximum 15					
AARC ACLF grade					
Grade			Score		
I			5–7		
II			8–10		
III			11–15		

PT: prothrombin time INR: international normalized ratio, HE: Hepatic encephalopathy

Among Asians with ACLF, it has proven to have good predictive value. Using a combination of lactate for perfusion, hepatic encephalopathy grade for CNS involvement, INR for coagulopathy, bilirubin for hepatic failure, and serum creatine levels for renal failure, it provides a straightforward predictive model that is simple to implement. Studies by Alam et al and Lal et al confirmed the utility of the AARC ACLF score in predicting the course of cirrhosis in children.[65,66] However, many facilities do not routinely test patients' serum lactate levels. As a result, the Lactate-free AARC ACLF score (LaFAS), a variation of the aforementioned score, was developed and investigated in patients with alcoholic liver disease and liver failure. They received the same number of points as in AARC score, with the exception of serum lactate. The minimum score is 3, and the maximum is 12.[67]

3.2 MELD and MELD-Na score

To assess the reserve of hepatic function in individuals with cirrhosis, the model for end-stage liver disease (MELD) score was developed. It has the benefit of using total bilirubin, international normalised ratio (INR), and creatinine levels as three straightforward and objective measures. In cirrhotic patients having a transjugular intrahepatic portosystemic shunt, the MELD score is used to predict survival. Additionally, it has been used to forecast

the post-operative course of cirrhotic patients undergoing surgical treatments and to assign priority on wait lists for liver transplants.[68,69,70,71]

The components of the score are:[72]
serum creatinine (mg/dl)
total bilirubin (mg/dl)
INR
These variables are used to calculate the score :
MELD = (0.957 x ln [Cr]) + (0.378 x ln [bilirubin]) + (1.120 x ln [INR]) + 0.643
(ln = log to the base of e, loge)

Since hyponatraemia is a significant predictor of death among liver transplant waitlist patients, a modified score that incorporates serum sodium, known as the "MELD sodium" score (MELD-Na), was developed as an alternative to the MELD score and introduced for liver transplant allocation in 2016.[73,74] The MELD/Na score is a method for assessing the severity of chronic liver disease and predicting survival using measurements such as blood bilirubin, serum creatinine, and the international normalised ratio for prothrombin time and sodium. In 2016 the MELD score itself was edited to include sodium as a correcting factor in a different equation only if the original MELD score was more than 12.[75]

Table 4 : MELD/Na score[75]

Score	Mortality(%)
MELD/Na score >40	71.3
MELD/Na score 30-39	52.6
MELD/Na score 20-29	19.6
MELD/Na score 10-19	6
MELD/Na score <9	1.9

MELD-Na: Sodium MELD

3.3 CLIF-OF score and CLIF-C ACLF score

The EASL defined ACLF as “Acute deterioration of a pre-existing chronic liver disease that is usually related to a precipitating event and associated with increased mortality at 3 months due to multi-organ failure”. The organ failure is assessed using a modified SOFA score [13,76] Mortality depends on the ACLF grade and ranges from 23.3% at 28 days in grade 1 to 75.5% at 28 days in grade 3. The majority of ACLF patients require intensive care and organ support.[13,77,78]

The CLIF collaboration developed and validated a new score, the CLIF-C ACLF score, to better mortality prediction. The CLIF-C ACLF score creates a composite score of 0-100 in a linear range by combining the CLIF-OF score, patient age, and white blood cell (WBC) count. This score was substantially more reliable than the Child-Pugh score, the MELD, and the MELD-Na score at predicting mortality in ACLF. Short-term mortality was predicted by the CLIF-C ACLF score 25% more accurately than by any other score. Mortality at 28 days varied greatly from less than 20% in patients who had scores of <45 to greater than 80% in patients with scores of ≥65.[76]

3.4 APACHE(acute physiology and chronic health evaluation)II

In order to categorise patient groups according to the severity of their illnesses, the first APACHE score was created in 1981. It was composed of two sections: the physiological score to evaluate acute illness and preadmission part the chronic health status. The initial model was updated and made simpler in 1985 to produce APACHE II, now the most often used score worldwide to assess illness severity. There are only 12 physiological factors in APACHE II as opposed to 34 in the initial score. A single score is produced by explicitly incorporating the impacts of age and chronic health status into the model and weighting them in accordance with their respective importance. The primary diagnosis that caused the patient to be admitted to the ICU is added as a category weight so that the expected mortality is determined using the patient's APACHE II score and primary diagnosis. The reason for ICU admission is a significant factor in predicting mortality.[79]

3.5 CTP

To predict mortality in cirrhotic patients, the Child-Pugh scoring system—also called the Child-Pugh-Turcotte score—was developed. It was first conceived by Child and Turcotte in 1964 to help select patients who were likely to benefit from elective surgery for portal decompression. Patients were divided into three categories: A, which denoted good hepatic

function, B, which denoted moderately impaired hepatic function, and C, which denoted advanced hepatic dysfunction. Serum bilirubin, serum albumin, ascites, neurological disease, and clinical nutrition status were the five clinical and laboratory criteria they utilised in their original scoring system to divide patients into different categories. Pugh et al. later changed the grading system, replacing prothrombin time for clinical nutrition status. They also added changeable points for each requirement, with points increasing in severity.[80]

4. Comparing different prognostic scores in acute on chronic liver failure

A Retrospective cohort study comprising 177 patients by Barosa et al reported that High mortality patients who were admitted to the ward were identified by CLIF scores, which also had good performance and were more accurate in predicting short- and medium-term death than their forerunners MELD, MELD-Na, and CTP.[81] A study by Zhang et al comprising 102 ACLF patients reported that The prognosis of ACLF patients can be accurately predicted using the CTP score, MELD score, MELD-Na, CLIF-C OF score, CLIF-SOFA score, and CLIF-ACLF score. For the assessment of mortality in the short-term, the CLIF-SOFA score offers greater discriminative potential.[82] Chen et al Compared eight Prognostic Scores in Two hundred forty-nine ACLF patients in the ICU. The study reported that according to their experience, the APACHE III score and CLIF-C ACLF score among these frequently employed prognostic scores were significantly better than others in predicting overall mortality.[83] A study by Liu et al assessed prediction Effect for Mortality at 28 days in 89 patients with ACLF. The study reported that the MELD score exhibits poorer prediction compared to the CLIF-SOFA score score . The best prognostic model compared to ALBI and MELD was the CLIF-SOFA score.[84] Kuo et al compared three prognostic scores which were variations of the CLIF-C ACLF score in 135 ACLF patients admitted to the ICU. The study reported in critically ill patients with liver cirrhosis with ACLF, CLIF-C ACLF, and CLIF-C ACLF-D scoresise significant outcome predictors.[85] A study by Dhiman et al comparing CLIF-SOFA and APASL reported that In order to categorise patients into ACLF based on their prognosis, CLIF-SOFA criteria are preferable to APASL. The best indicator of mortality in the short term is the CLIF-SOFA score.[86] Song et al reported in a study that the diagnostic performance of the lactate-free AARC-ACLF score for predicting 28-day and 90-day mortality in Korean patients with alcohol-related liver failure and ACLF according to AARC definition was comparable to that of MELD-Na and CLIF-SOFA.[87] A single prospective observational study carried out at a tertiary care centre not equipped for transplant by

Chauhan et al compared Standard scores MELD, MELD-Na, Maddreys' discriminant function, CLIF-OF &CLIF-C ACLF scores, APACHE II, ALBI, PALBI and LaFAAS for predicting short term mortality in 67 cases of alcohol induced ACLF. For predicting mortality at 3 months ALBI and LaFAAS performed best among the other models. When it comes to predicting death after three months, the LaFAAS has the best sensitivity and specificity among the scores, followed closely by ALBI and CLIF-OF. When compared to LaFAS, CLIF-OF demonstrated equal sensitivity but lower specificity. LaFAAS performed well against common validated scores.[8]

MATERIALS AND METHODS

MATERIALS AND METHODS

Study design:

A tertiary care center-based prospective observational study.

Period of study:

Jan 2021 to october 2022

Source of the data:

Patients admitted to R L Jalappa Hospital, Kolar, a tertiary care hospital in Karnataka, India, fulfilling the inclusion criteria during the study diagnosed as Acute on Chronic Liver failure.

Inclusion criteria:

1. Adult patients (age > 18 years), with hepatic or extrahepatic insults, with or without prior decompensation, and satisfying APASL criteria for ACLF.

2. **Exclusion criteria:**

1. patients with pregnancy related liver diseases

2. patients with hepatocellular carcinoma

Method of data collection:

Patients received a thorough explanation of the entire procedure and informed consent was taken in their own understandable language. A detailed clinical examination, routine investigations, and specific investigations were performed. Prognostic scores were calculated and followed up for outcome during a hospital stay, at discharge, and at 28 days from the day of admission.

Ethical Consideration:

The study was approved by the institutional ethics committee. Informed written consent was taken from all the study participants and only those participants who signed the informed consent were included in the study.

Sample size: (no)

The sample size estimate was based on the sensitivity of the LaFAAS score was 95.5% for cut-off value 7 in predicting mortality at 3month as reported by a study done by Chauhan SG et al using the below formula.[8]

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

Where P^ is the pre-determined value of sensitivity (or specificity) that is ascertained by previously published data or clinician experience/judgment and for α = 0.05, Zα2 is inserted by 1.96.

P^ = 95.5% or 0.955
d = 5% or 0.05.

Using the above values at a 95% Confidence level a sample size of 66 subjects will be included in the study. Considering a 10% Non-response rate a sample size of 66+ 6.6 = 73 subjects minimum to be included in the study.

Data collection tool:

After informed consent parameters including demographics, test results examination findings and outcome at discharge and at 28 days were collected in a proforma.

STATISTICAL ANALYSIS

Data were analysed using excel data analysis (Excel 2019). Graphs were plotted using Python (version: 3.10.0) in the Jupyter Notebook (version: 6.2.0) and mortality were analysed using receiver operating characteristic curves (ROCs), in Epitools(https://epitools.ausvet.com.au/roccurves)and LaFAAS score was compared to other prognostic scores. The computation of sensitivity, specificity, and positive and negative predictive values were done using the receiver operating characteristic (ROC) and the best cut-off points. A test with an area under the ROC curve of 0.5 predicts a result no better than by chance. Graphical representations of data such as count plot and box plot were obtained through MS Excel and MS word. P value (Probability that the result is true) of <0.05 was considered statistically significant after assuming all the rules of statistical tests.

RESULTS

RESULTS

The study population

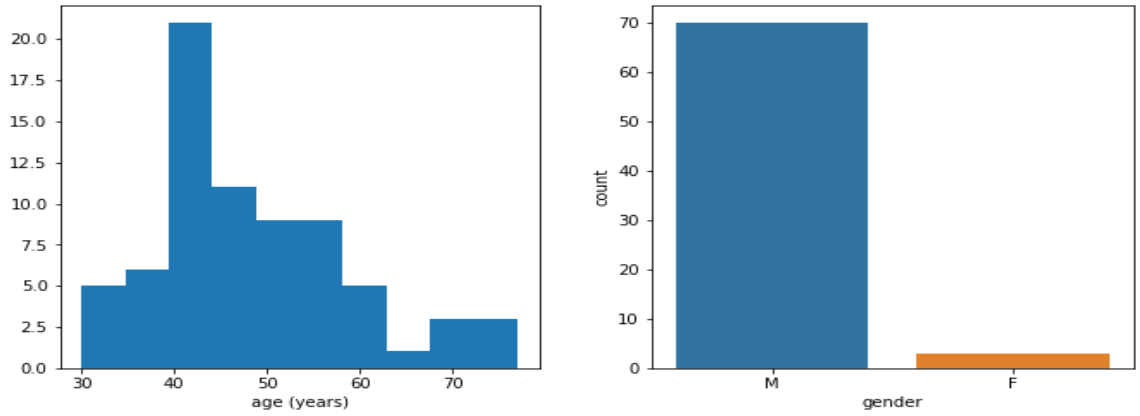
The study included a total of 73 subjects between 30-77 years with a mean age of 46.05. The corresponding number of male and female subjects enrolled were 70 (95.89%) and 3 (4.10%)(Table 5, Fig 2).

Table 5: Descriptive statistical analysis of demographic features of the study population

Variables	Total Patient(N=73)
Age	46.05±10.79(30-77)
Gender(M/F)	70(3)

Values presented as Mean±SD (Range) or number(%)

Figure 2: Demographic characteristics of the study population



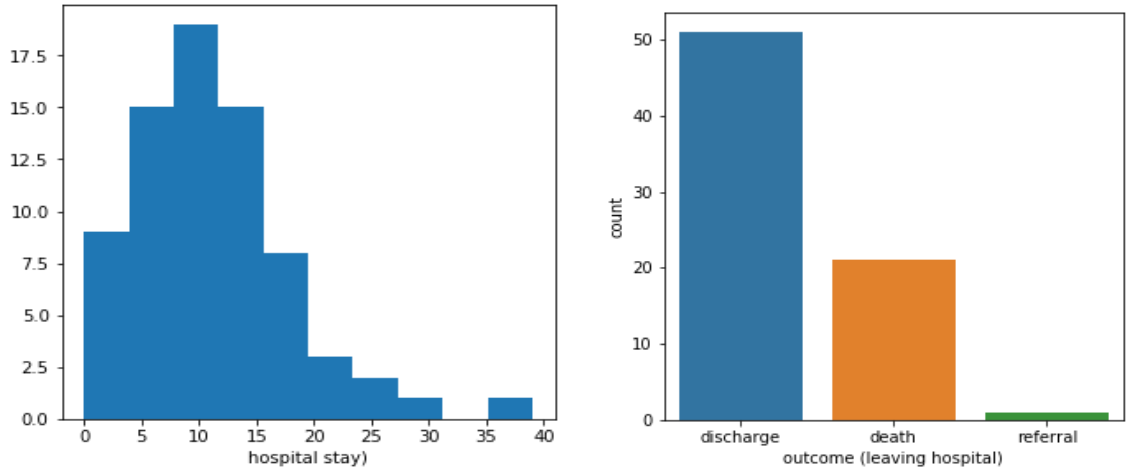
The mean hospital stay noted among the study subjects was 5.89±7.05. In terms of patients leaving the hospital, 21(28.76%) patients were dead, 51(69.86%) were alive and 1(1.36%) of the subjects were referred to another hospital%)(Table 6, Fig 3).

Table 6: Descriptive analysis of Hospital stay and outcome in the study population

Variables	Total Patient(N=73)
Hospital Stay	5.89±7.05(1-39)
Outcome (leaving hospital)	
Death	21(28.76%)
Alive	51(69.86%)
Referral	**1(1.36%)**

Values presented as Mean±SD (Range) or number(%)

Figure 3: Hospital stay and outcome of the study population



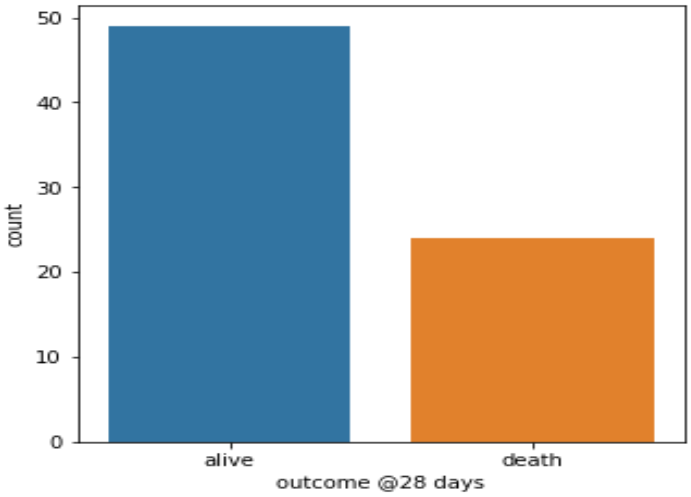
With regard to the outcome at 28 days, death was reported in 24(32.87%) of the subjects whereas 49(67.12%) were reported to be alive%)(Table 7, Fig 4).

Table 7: Descriptive analysis of 28 days outcome in the study population

Variables	Total Patient(N=73)
Outcome at 28 days	
Death	24(32.87%)
Alive	49(67.12%)

Values are presented as number(%)

Figure 4: 28 days outcome of the study population



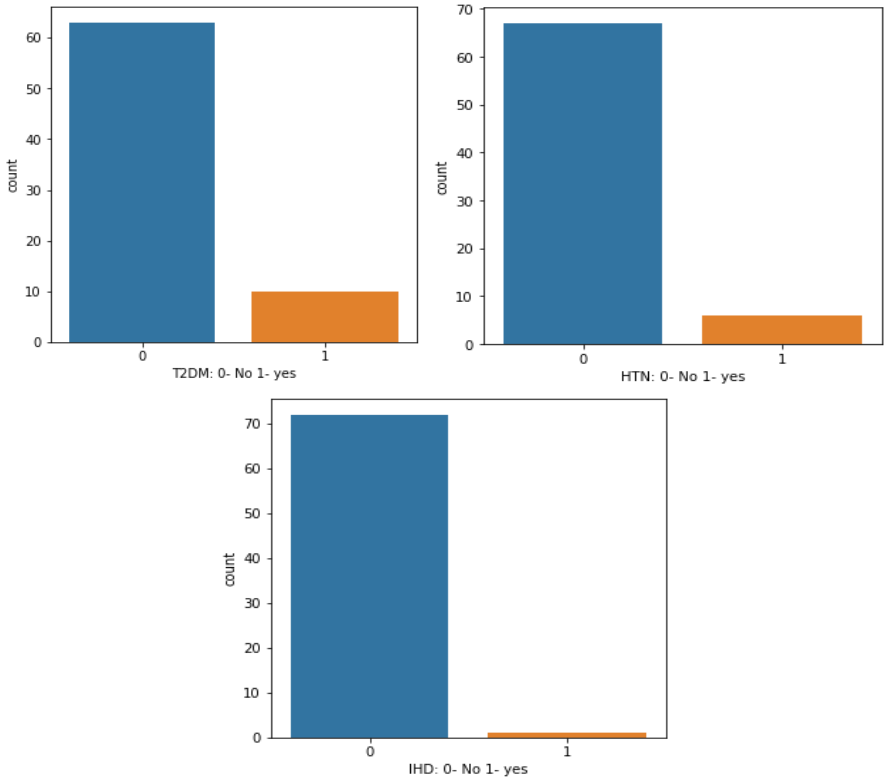
A total of 10(13.69%) patients were diabetic, 6(8.22%) patients had hypertension, ischemic heart disease(IHD) was noted in 1(1.36%) (Table 8, Fig 5).

Table 8: Descriptive statistics of comorbidities in the study population

Variables	Total Patient(N=73)
T2DM	10(13.69%)
HTN	6(8.22%)
IHD	1(1.36%)

Values are presented as number(%), T2DM: Type 2 diabetes, HTN: Hypertension, IHD: ischemic heart disease

Figure 5: Comorbidities in the study population



The mean hepatic encephalopathy grade noted among the study population was 1.68±0.95.

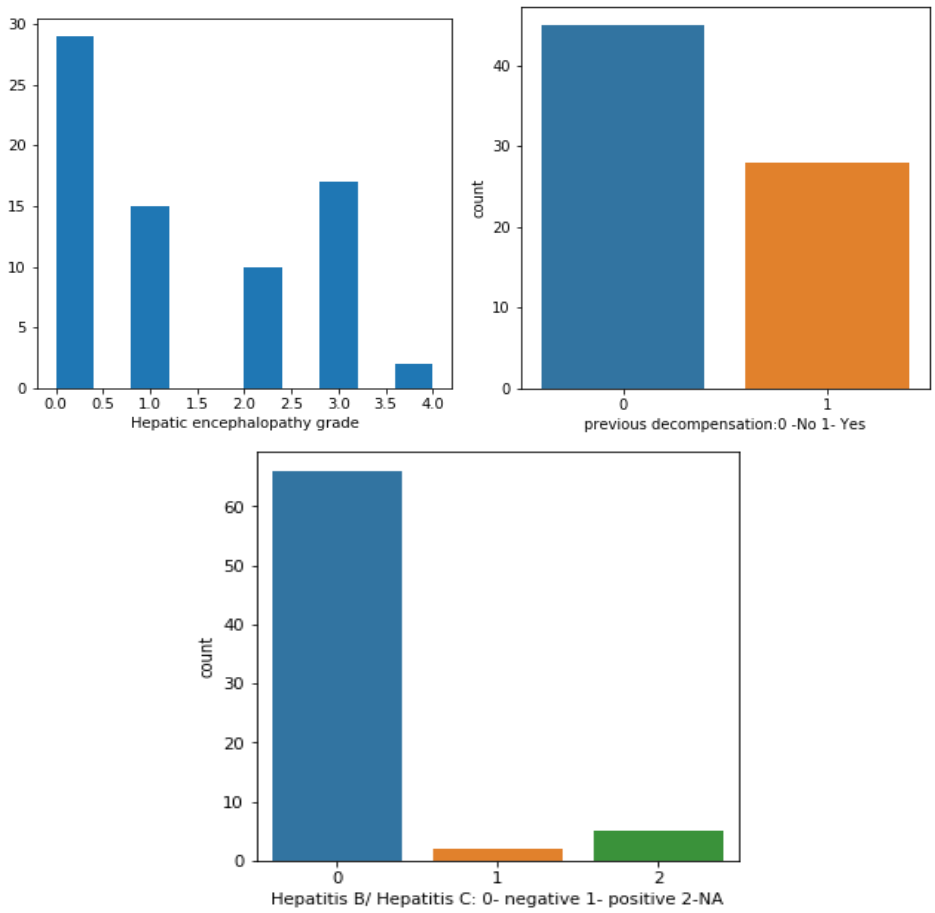
2(2.94%) subjects were positive for hepatitis B, none were positive for hepatitis C and 28 (38.35%) had a history of previous decompensation(Table 9, Fig 6).

Table 9: Descriptive statistics of hepatic conditions in the study population

Variables	Total Patient(N=73)
Hepatic encephalopathy grade	1.68±0.95(1-4)
Previous decompensation	28 (38.35%)
hepatitis B / hepatitis C*	2(2.94%)

Values presented as Mean±SD (Range) or number(%), *hepatitis B / hepatitis C (N=68)

Figure 6: Hepatic conditions in the study population



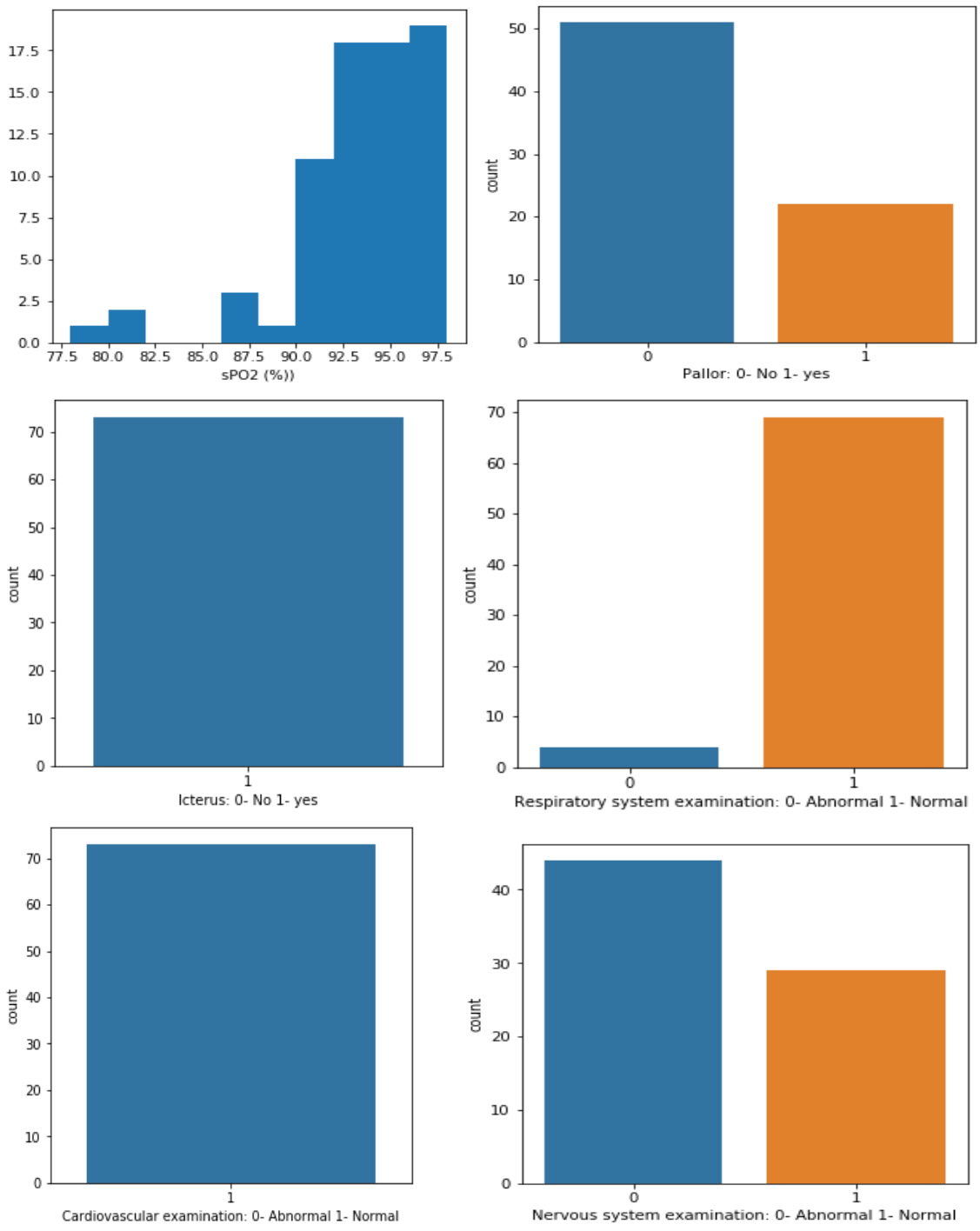
The mean SPO2 % noted among the study population was 92.60±3.91. Pallor and Icterus were noted in 22(30.14%) and 73(100%) patients, respectively. Respiratory and nervous system examinations showed abnormal results in 4(5.47%) and 44(60.27%) patients(Table 10, Fig 7).

Table 10: Descriptive statistics of General examination in the study population

Variables	Total Patient(N=73)
SPO2 %	92.60±3.91(78-98)
Pallor	22(30.14%)
Icterus	73(100%)
Respiratory system examination (abnormal)	4(5.47%)
Cardiovascular system examination (abnormal)	0
Nervous system examination (abnormal)	44(60.27%)

Values presented as Mean±SD (Range) or number(%), SPO2: Oxygen saturation

Figure 7: General examination of the study population



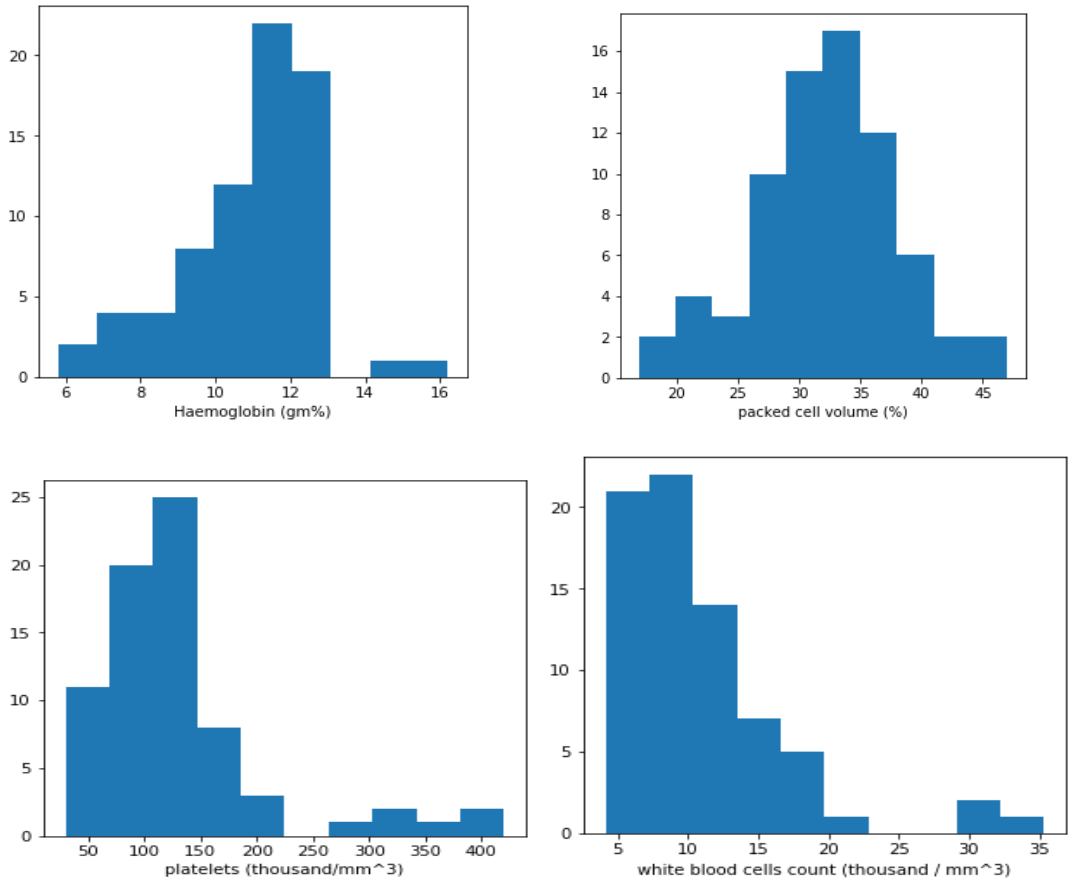
Descriptive analysis of the blood parameters revealed the mean haemoglobin of the study subjects as 10.55±1.86 gm%. The corresponding mean packed cell volume, platelets, and white blood cells count, reported were 30.75±5.86%, 97.40±79.23 thousand/mm^3, and 8.77±6.08 thousand/mm^3 (Table 11, Fig 8).

Table 11: Descriptive statistics of blood parameters in the study population

Variables	Total Patient(N=73)
Haemoglobin (gm%)	10.55±1.86(5.8-16.2)
Packed cell volume (%)	30.75±5.86(16.9-47)
Platelets (thousand/mm^3)	97.40±79.23(30-420)
White blood cells count (thousand / mm^3)	8.77±6.08(4.12-35.34)

Values are presented as Mean±SD (Range)

Figure 8: Blood parameters in the study population



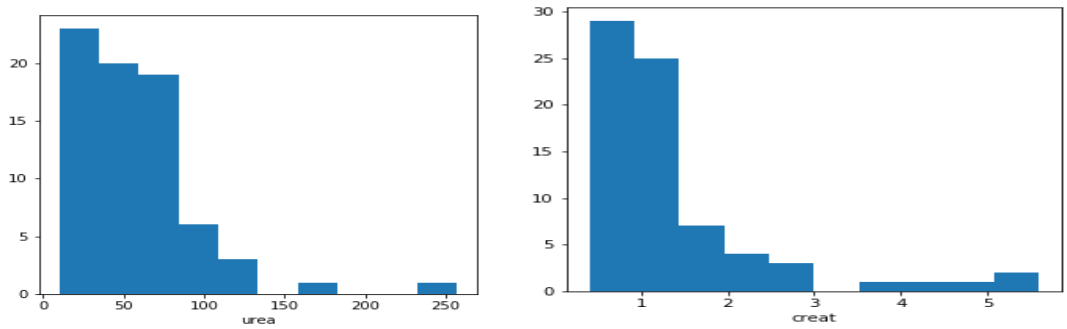
The mean creatinine noted among study subjects was 1.02±1.06 mg/dl, and the mean blood urea level was 38.38±39.48 mg/dl(Table 12, Fig 9).

Table 12: Descriptive analysis of the Renal profile distribution in the study population

Variables	Total Patient(N=73)
Blood Urea (mg/dl)	38.38±39.48(10-257)
Creatinine (mg/dl)	1.02±1.06(0.4-5.6)

Values are presented as Mean±SD (Range)

Figure 9: Renal profile distribution graph in the study population



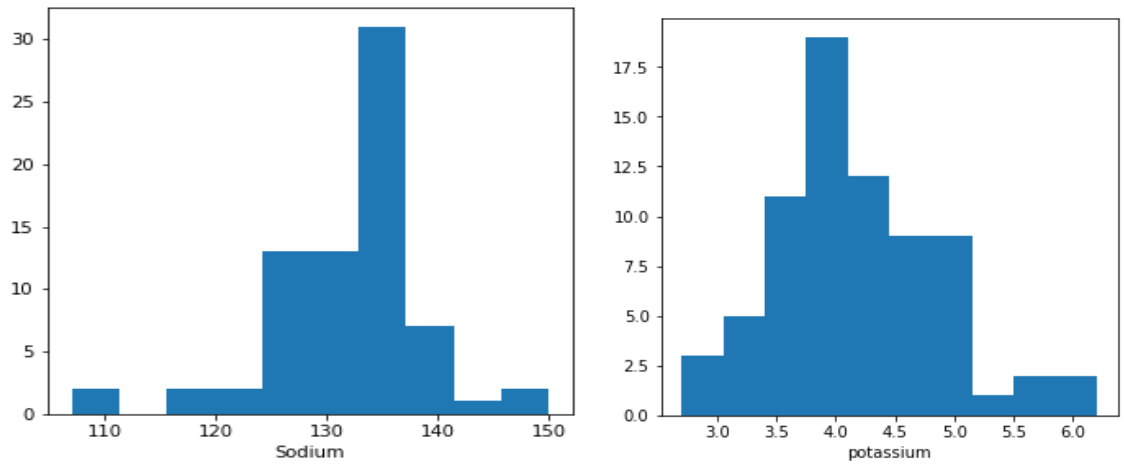
Descriptive analysis of the serum electrolytes revealed a mean serum sodium of 131.77±6.77 mEq/L and serum potassium of 4.02±0.70 mEq/L(Table 13, Fig 10).

Table 13: Descriptive analysis of the Serum Electrolytes in the study population

Variables	Total Patient(N=73)
Sodium(mEq/L)	131.77±6.77(107-150)
Potassium (mEq/L)	4.02±0.70(2.7-6.2)

Values are presented as Mean±SD (Range)

Figure 10: Serum Electrolytes distribution graph in the study population



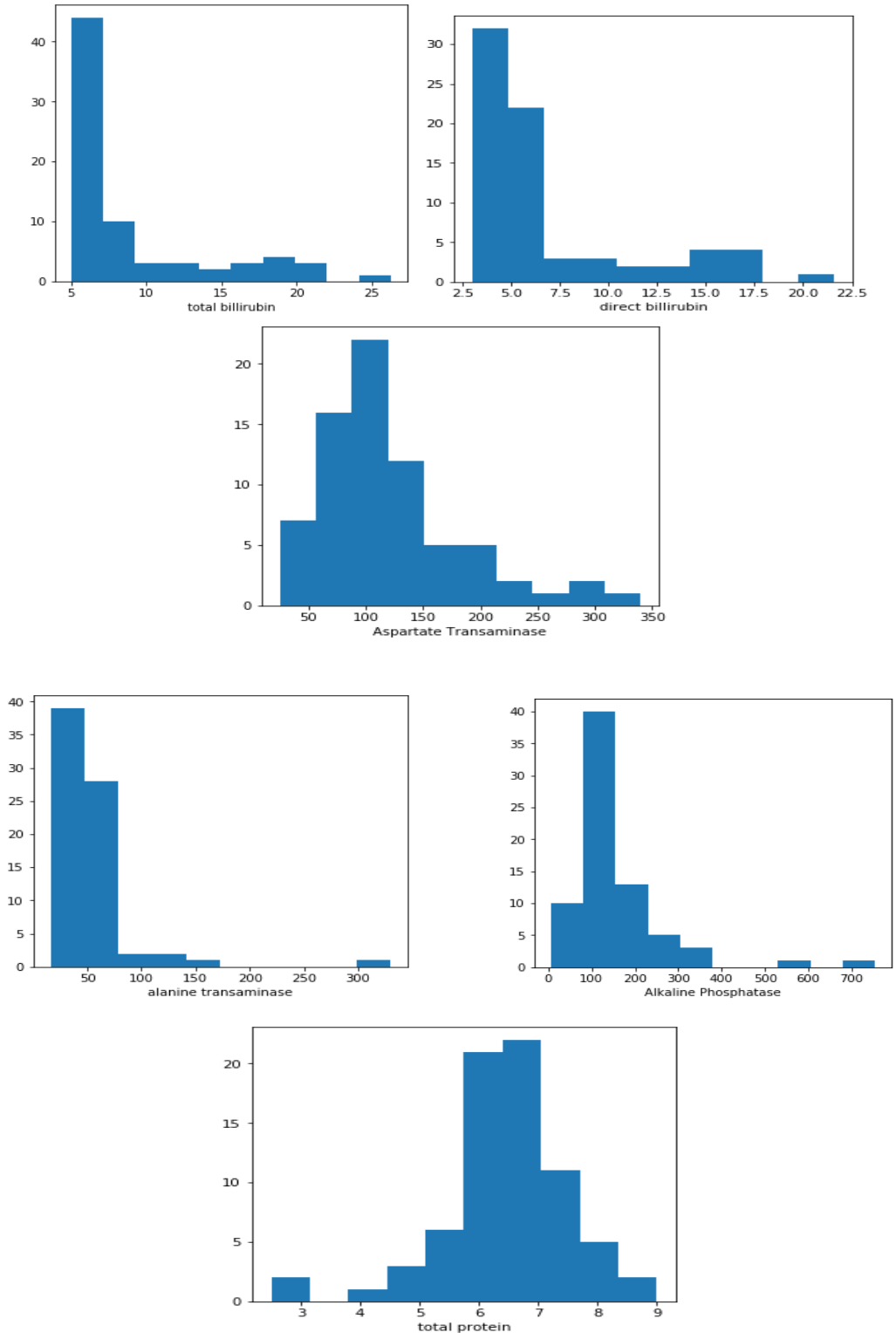
The corresponding mean total bilirubin and direct bilirubin noted among the study subjects were 7.33±5.01 and 5.23±4.30 mg/dl. The mean Aspartate Transaminase, Alanine transaminase, Alkaline Phosphatase, total protein, albumin, globulin, albumin/globulin (A/G) ratio, Prothrombin time, activated Plasma thromboplastin time and international normalised ratio reported were 92.84±62.45 U/L, 41.47±40.54 U/L, 93.97±110.25 U/L, 6.14±1.07 g/dl, 2.63±0.57 g/dl, 3.57±0.62 g/dl, 0.72±0.17, 112.49±170.02 U/L, 21.91±6.72 sec, 37.36±18.05 sec and 1.96±0.83 respectively(Table 14, Fig 11).

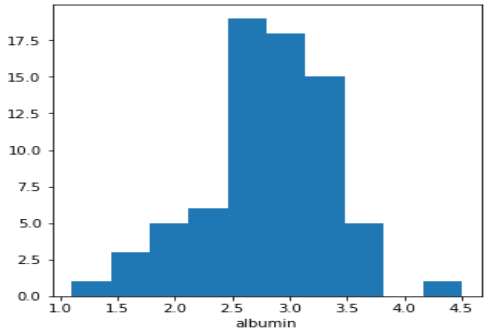
Table 14: Descriptive analysis of the Liver Profile parameters in the study population

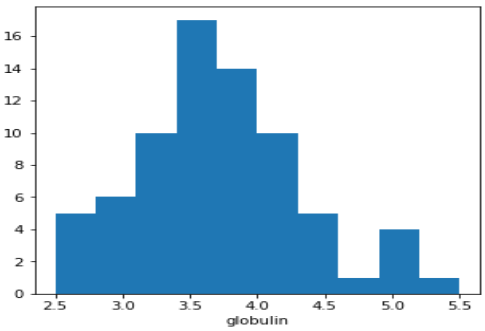
Variables	Total Patient(N=73)
Total bilirubin (mg/dl)	7.33±5.01(5-26.3)
Direct bilirubin (mg/dl)	5.23±4.30(3-21.6)
Total protein (g/dl)	6.14±1.07(2.5-9)
Albumin (g/dl)	2.63±0.57(1.1-4.5)
globulin (g/dl)	3.57±0.62(2.5-5.5)
Albumin/globulin (A/G) ratio	0.72±0.17(0.4-1.2)
Aspartate Transaminase (U/L)	92.84±62.45(25-340)
Alanine transaminase (U /L)	41.47±40.54(16-330)
Alkaline Phosphatase (U/L)	93.97±110.25(5.5-754)
Gamma Glutamyl Transferase (U/L)	112.49±170.02(18-806)
Prothrombin time (sec)	21.91±6.72(12.8-45)
Activated Plasma Thromboplastin time (sec)	37.36±18.05(24.8-128)
international normalised ratio	1.96±0.83(1.5-6)

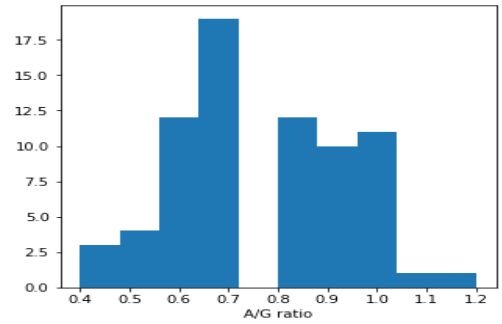
Values are presented as Mean±SD (Range)

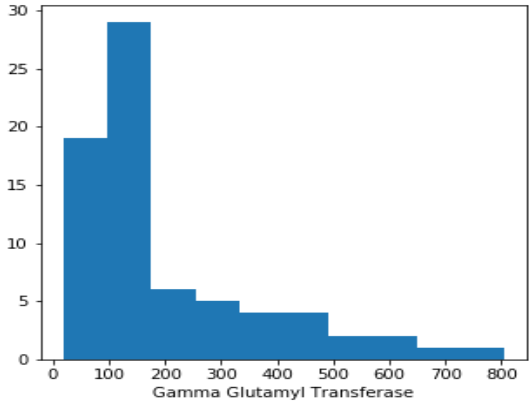
Figure 11: Liver Profile parameters in the study population

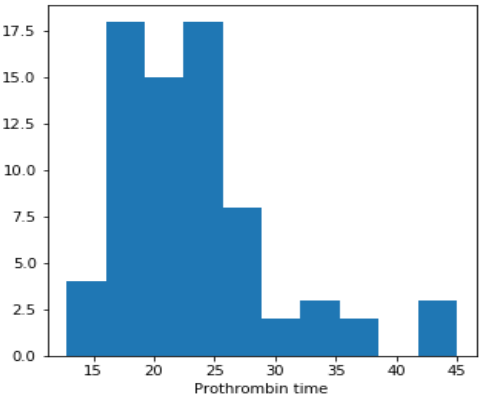


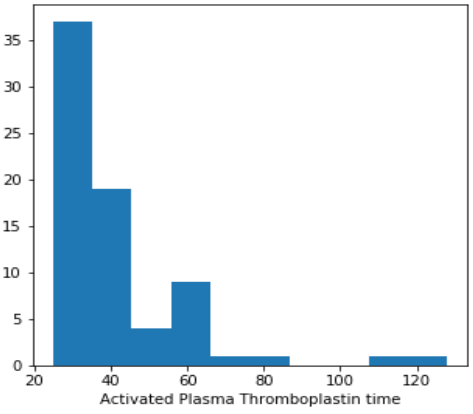

albumin

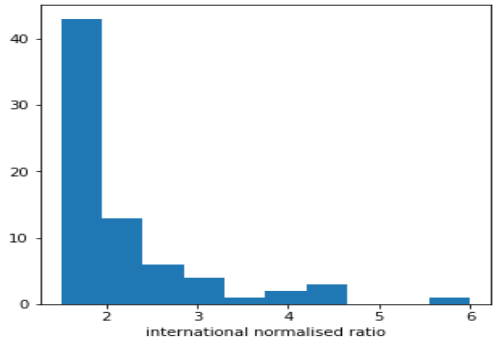

globulin


A/G ratio


Gamma Glutamyl Transferase


Prothrombin time


Activated Plasma Thromboplastin time



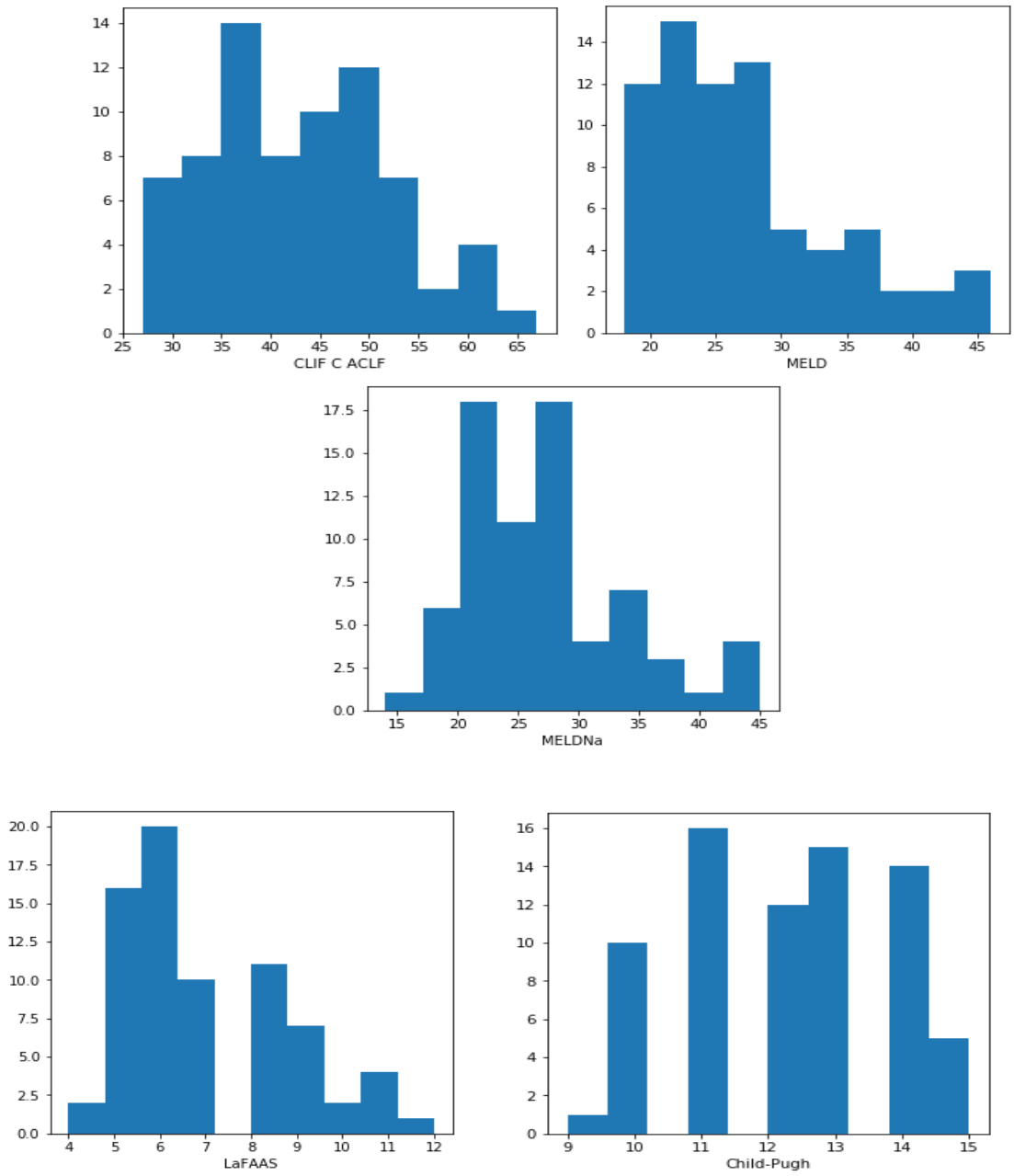
Descriptive analysis of the predictive scores revealed mean CLIF C ACLF, MELD, MELDNa, LaFAAS, and CPT of 25.73±6.97, 25.96±6.51, 6.48±1.85 and 12.06±1.56 respectively (Table 15, Fig 12).

Table 15: Descriptive analysis of the Risk Prediction Scores in the study population

Variables	Total Patient(N=73)
CLIF C ACLF	40.82±8.98(27-67)
MELD	25.73±6.97(18-46)
MELDNa	25.96±6.51(14-45)
LaFAAS	6.48±1.85(4-12)
CPT	12.06±1.56(9-15)

Values are presented as Mean±SD (Range), CLIF: chronic liver failure, ACLF: Acute-on-chronic liver failure MELD: Model for End-Stage Liver Disease, CPT: Child-Pugh-Turcotte

Figure 12: Risk Prediction Scores in the study population



Comparison between the death and alive study population

The total patients(73) were further divided into death and alive study groups. There were 24 patients in the death group and 49 in the alive group, respectively.

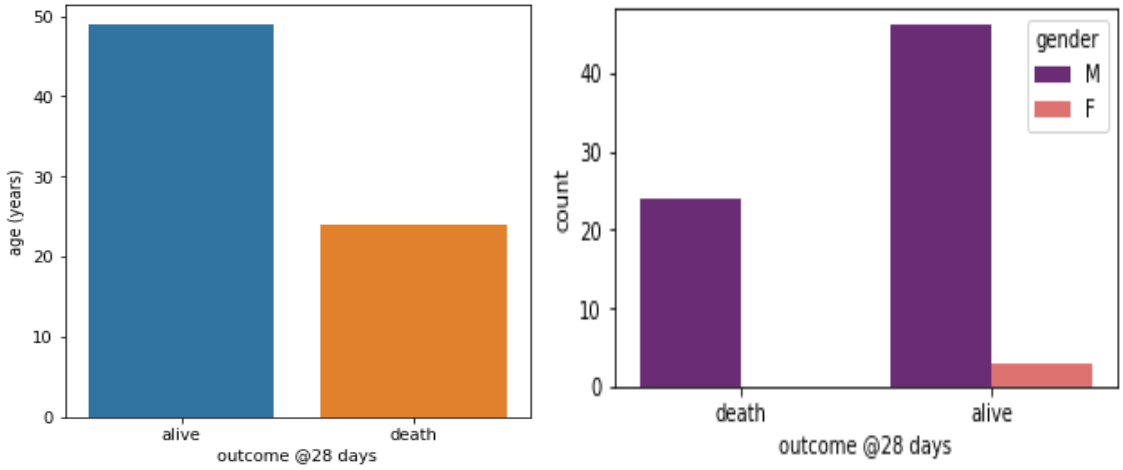
There was a non-significant statistical difference in age (P 0.174), and gender (P 0.546), between the death and alive groups (Table 16, Fig 13).

Table 16: Comparison of demographic parameters between death and alive group

Variables	Death(N=24)	Alive(N=49)	P- value
Age	47.06±14.23(30-77)	45.57±8.55(32-70)	0.174[#]
Gender	24	46(3)	0.546[$]

Values presented as Mean±SD (Range) or number(%)

Figure 13: Boxplot graph comparing demographic parameters between death and alive group



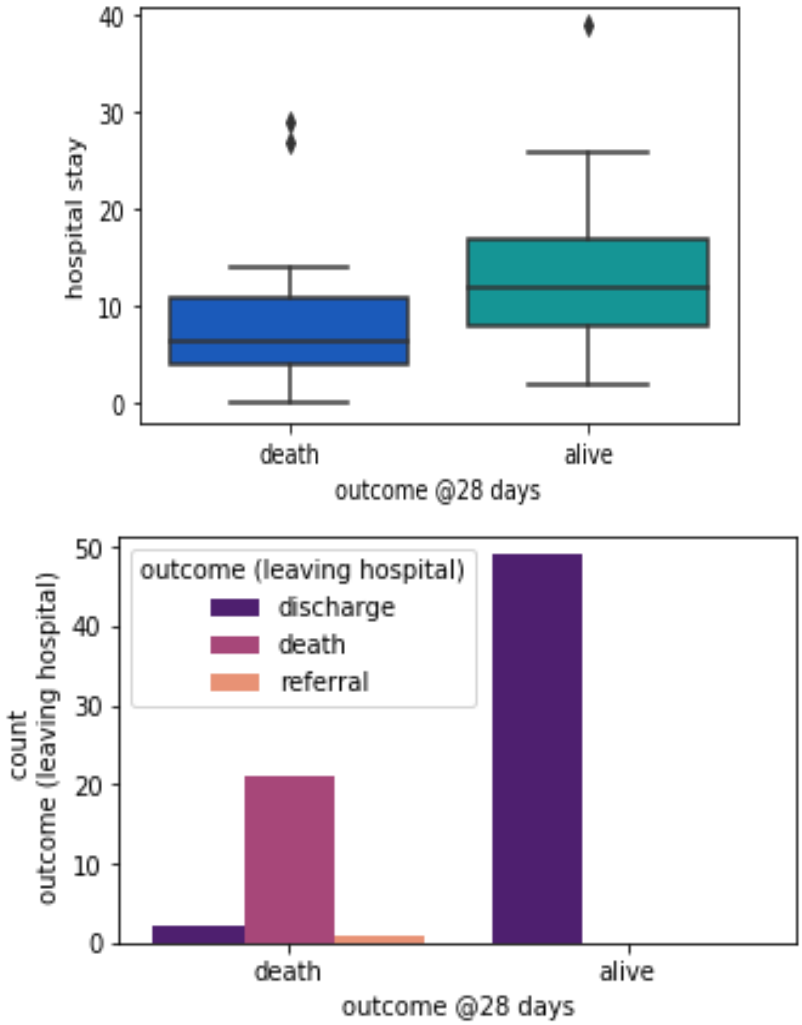
A significant statistically significant difference was noted for hospital stay(P 0.033) and outcome(P <.0001) between the death and alive groups (Table 17, Fig 14).

Table 17: Comparison of hospital stay and outcome between death and alive group

Variables	Death(N=24)	Alive(N=49)	P- value
Hospital Stay	3.87±7.15(1-29)	7.80±6.77(2-39)	0.033[#]
Outcome (leaving hospital)			
Death	21(87.50%)	0	
Alive	2(8.33%)	49	<.0001[$]
Referral	1(4.16%)	0	

Values presented as Mean±SD (Range) or number(%)

Figure 14: Boxplot graph comparing hospital stay and outcome between death and alive group



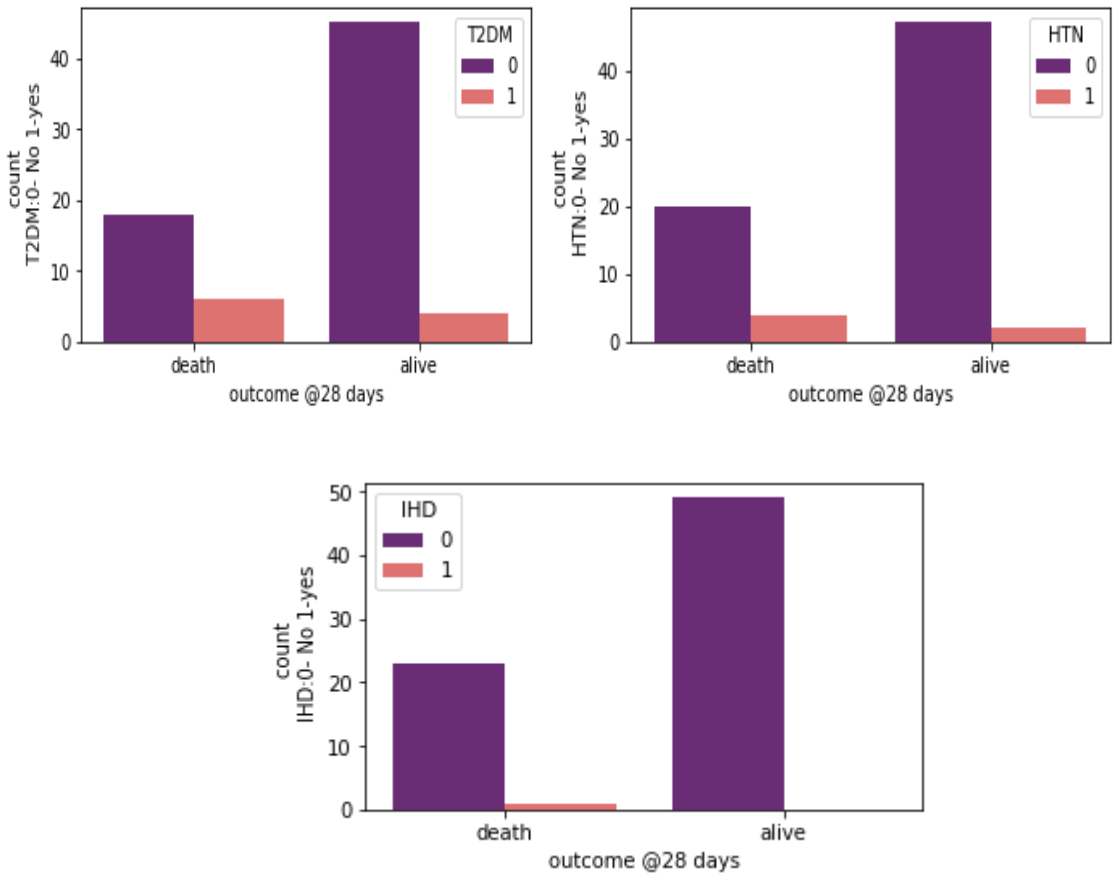
There was a non-significant statistical difference in Type 2 diabetes (P, 0.071) Hypertension(P, 0.086), and ischemic heart disease(P 0.328) between the death and alive groups (Table 18, Fig 15).

Table 18: Comparison of comorbidities between death and alive group

Variables	Death(N=24)	Alive(N=49)	P- value
T2DM	6(25%)	4(8.16%)	0.071[$]
HTN	4(16.66%)	2(4.08%)	0.086[$]
IHD	1(4.16%)	0	0.328[$]

Values are presented as number(%), T2DM: Type 2 diabetes, HTN: Hypertension, IHD: ischemic heart disease

Figure 15: Boxplot graph comparing comorbidities between death and alive group



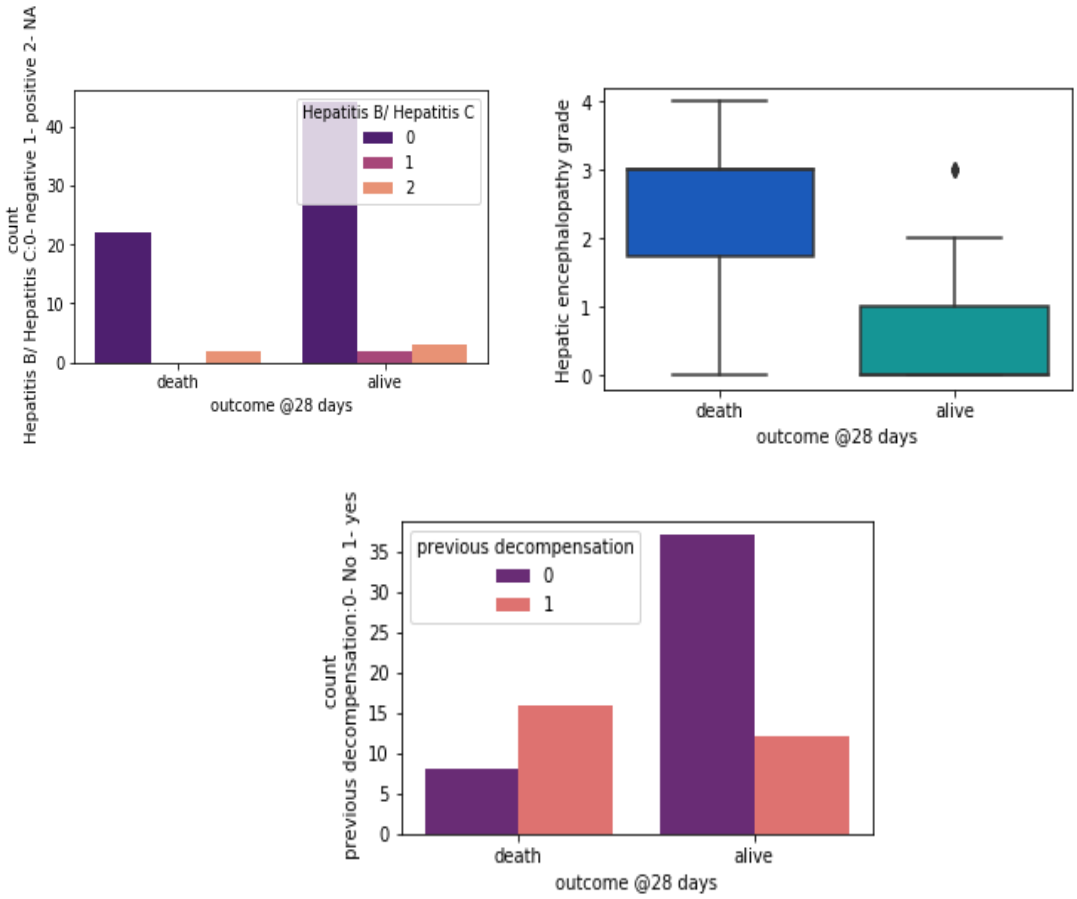
A non-significant statistical difference was noted for hepatitis B / hepatitis C (P 0.55) between the death and alive groups, whereas a significant statistical difference was noted for Hepatic encephalopathy grade(P 0.004) and Previous decompensation(P 0.0013) between the two groups(Table 19, Fig 16).

Table 19: Comparison of hepatic conditions between death and alive group

Variables	Death(N=24)	Alive(N=49)	P- value
hepatitis B / hepatitis C*	0	2(4.34%)	0.55$
Hepatic encephalopathy grade	2.21±0.86(1-4)	1.38±0.82(1-3)	0.004#
Previous decompensation	16(66.66%)	12(24.48%)	0.0013*

Values are presented as Mean±SD (Range), *hepatitis B / hepatitis C (N, death:22, alive: 46)

Figure 16: Boxplot graph comparing hepatic conditions between death and alive group



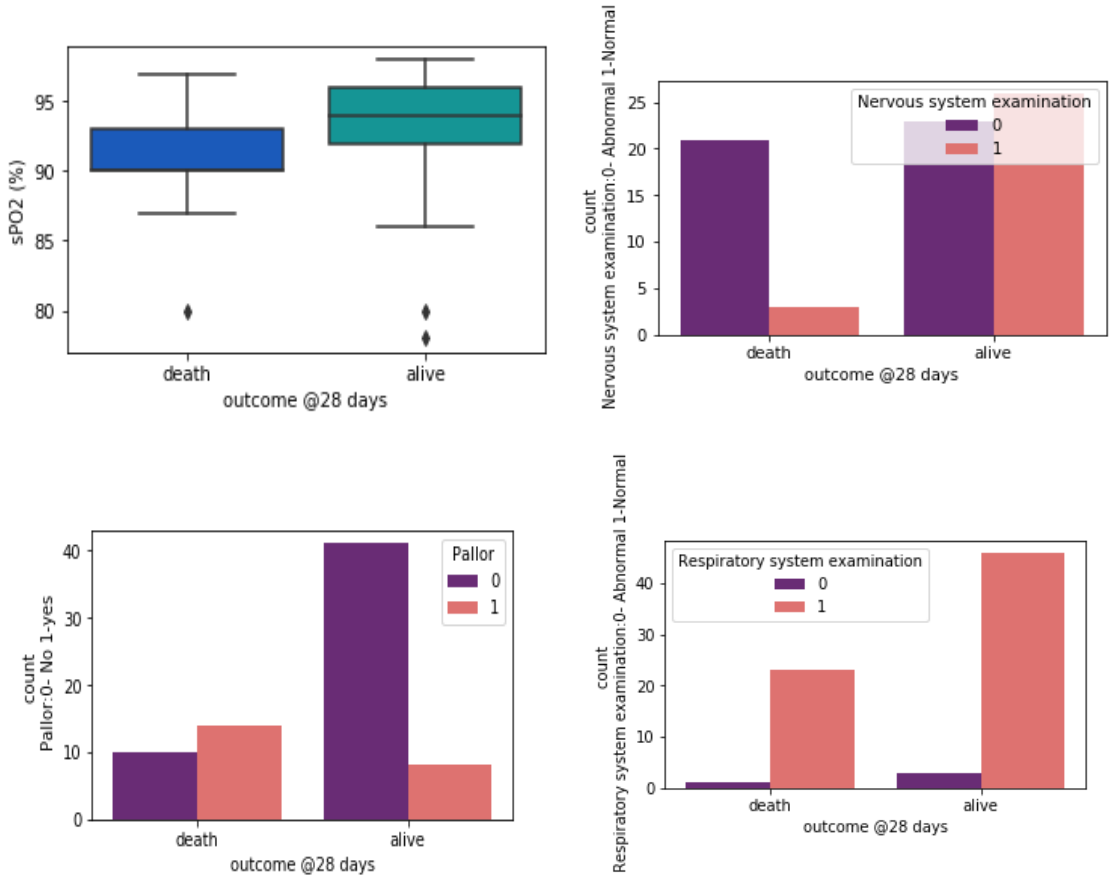
A significant statistical difference was noted for SPO2 % (P 0.008), nervous system examination (P 0.008), and pallor (P 0.008), between the death and alive groups whereas Respiratory system examination was not significantly different between them (P 1), (Table 20, Fig 17).

Table 20: Comparison of general examination between death and alive group

Variables	Death(N=24)	Alive(N=49)	P- value
SPO2 %	90.93±3.62(80-97)	93.44±3.81(78-98)	0.008#
Nervous system examination(abnormal)	21(87.50%)	23(46.93%)	0.0008$
Pallor	14(58.33%)	8(16.32%)	0.0007*
Respiratory system examination(abnormal)	1(4.16%)	3(6.12%)	1$

Values presented as Mean±SD (Range) or number(%)

Figure 17: Graph comparing general examination between death and alive group



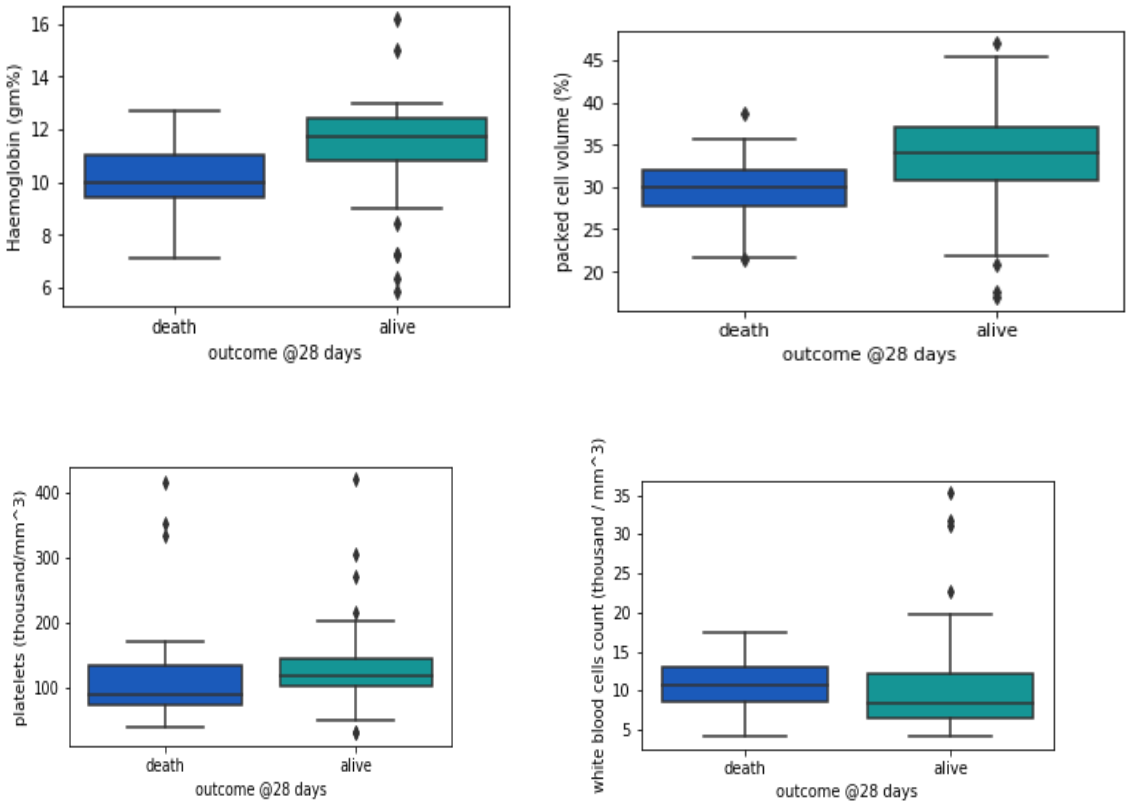
A significant statistical difference was noted for haemoglobin (P 0.006), and packed cell volume(P 0.01), between the death and alive groups whereas platelets(P 0.778), and total white blood cell count (P 1), were not significantly different. (Table 21, Fig 18).

Table 21: Comparison of blood parameters between death and alive group

Variables	Death(N=24)	Alive(N=49)	P- value
Haemoglobin (gm%)	9.86±1.47(7.1-12.7)	10.92±1.91(5.8-16.2)	0.006#
packed cell volume (%)	28.94±4.15(21.4-38.8)	31.71±6.24(16.9-47)	0.01#
platelets (thousand/mm^3)	88.39±99.47(38-415)	102.52±68.30(30-420)	0.778#
WBC count (thousand / mm^3)	9.44±3.86(4.12-17.5)	8.47±6.95(4.23-35.34)	1#

Values are presented as Mean±SD (Range), WBC: white blood cell

Figure 18: Boxplot graph comparing blood parameters between death and alive group



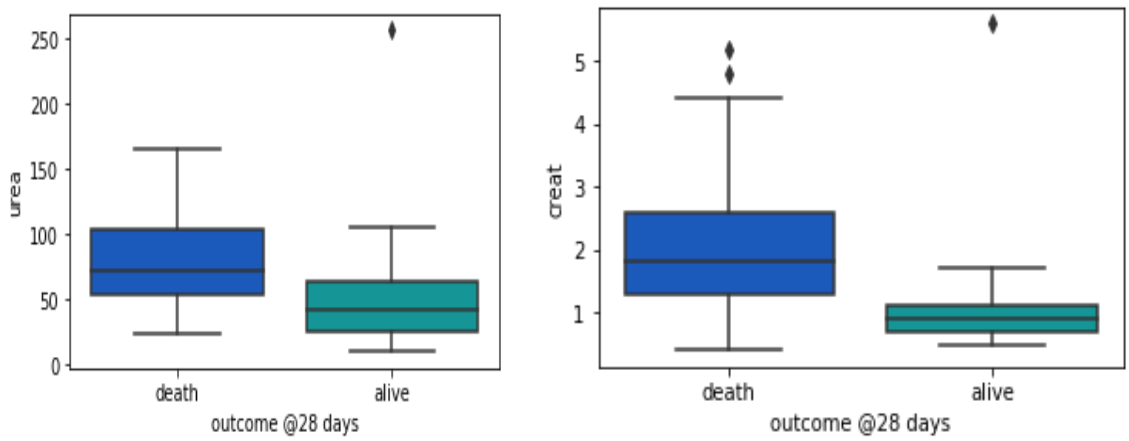
A significant statistical difference was noted for creatinine (P <.0001), and blood urea nitrogen level (P 0.002), between the death and alive groups (Table 22, Fig 19).

Table 22: Comparison of renal profile distribution between death and alive group

Variables	Death(N=24)	Alive(N=49)	P- value
Creatinine	1.48±1.28(0.4-5.2)	0.88±0.71(0.5-5.6)	<.0001#
Blood urea nitrogen level	61.02±36.18(24-166)	32.48±37.71(10-257)	0.002#

Values are presented as Mean±SD (Range)

Figure 19: Boxplot graph comparing renal profile distribution between death and alive group



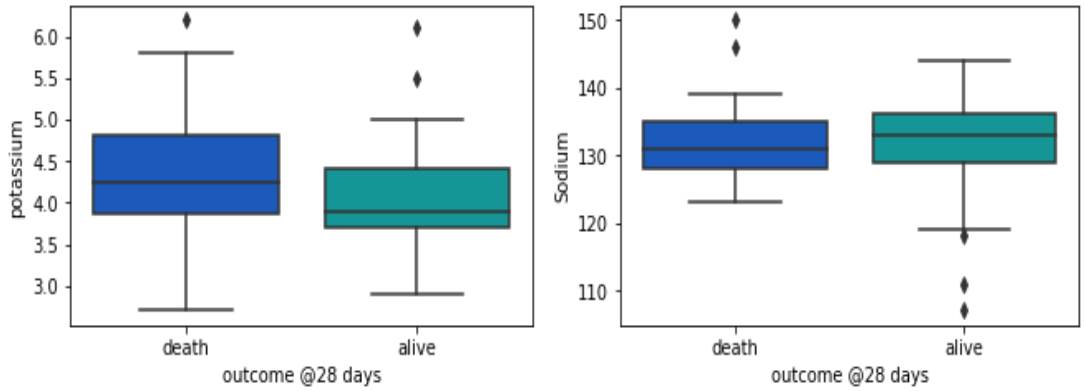
A statistically non-significant difference was noted for potassium (P <.0001), and sodium(P 0.33) between the death and alive groups (Table 23, Fig 20).

Table 23: Comparison of serum electrolytes between death and alive group

Variables	Death(N=24)	Alive(N=49)	P- value
Potassium	4.17±0.84(2.7-6.2)	3.96±0.61(2.9-6.1)	0.09#
Sodium	132.36±6.17(123-150)	131.48±7.09(107-144)	0.672#

Values are presented as Mean±SD (Range)

Figure 20: Boxplot graph comparing serum electrolytes between death and alive group



A statistically significant difference was noted for total bilirubin (P <.0001), direct bilirubin(P <.0001), alkaline phosphatase(P 0.035), albumin(P 0.002), albumin/globulin (A/G) ratio(P 0.004), Prothrombin time (P <.0001), activated plasma thromboplastin time(P <.0001) and the international normalised ratio(P <.0001) between the death and alive groups. Whereas a non-significant statistical difference was noted for aspartate Transaminase (P 0.055) , Alanine transaminase (P 0.123) , Total protein (P 0.152) , globulin (P 0.26) and glutamyl Transferase (P 0.561) (Table 24, Fig 21).

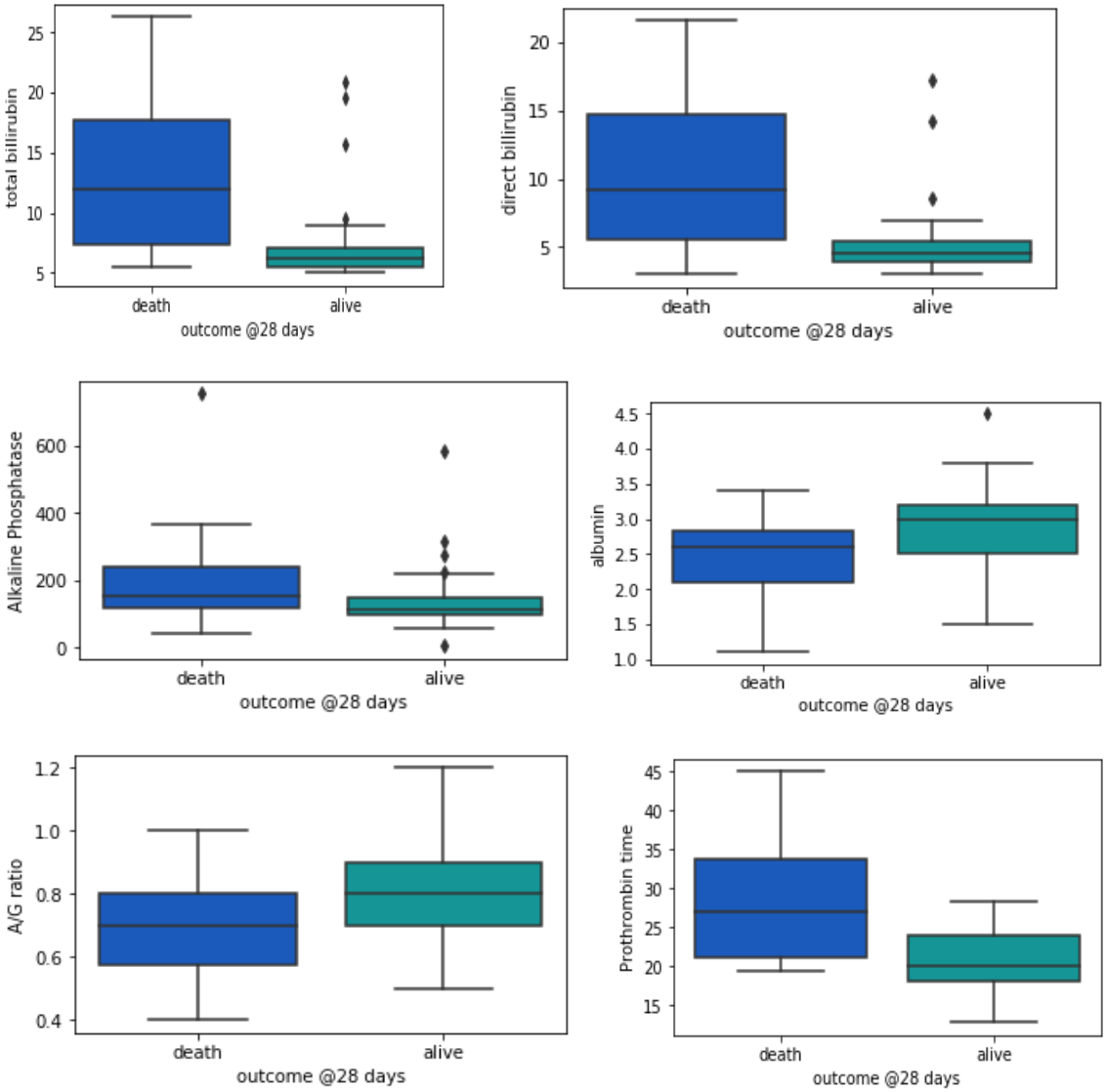
Table 24: Comparison of Liver Profile parameters between death and alive group

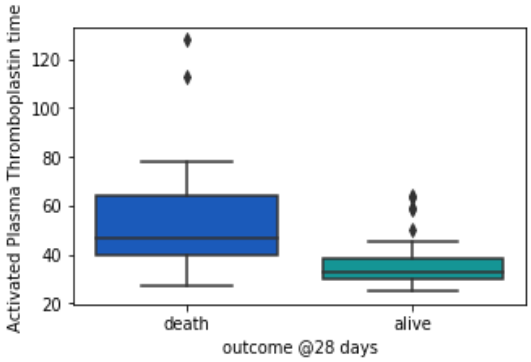
Variables	Death(N=24)	Alive(N=49)	P-value
Total bilirubin	10.10±5.98(5.5-26.3)	6.46±3.21(5-20.8)	<.0001#
Direct bilirubin	7.19±5.36(3-21.6)	4.61±2.48(3-17.2)	<.0001#
Alkaline Phosphatase	131.88±144.18(45-754)	82.37±84.62(5.5-582)	0.035#
Albumin	2.32±0.56(1.1-3.4)	2.81±0.52(1.5-4.5)	0.002#
Albumin/globulin (A/G) ratio	0.63±0.17(0.4-1)	0.77±0.16(0.5-1.2)	0.004
Prothrombin time	26.89±8.23(19.4-45)	20.08±3.53(12.8-28.4)	<.0001#
Activated Plasma Thromboplastin time	46.85±24.53(27.1-128)	33.99±9.30(24.8-64.2)	<.0001#
international normalised ratio	2.46±1.14(1.6-6)	1.79±0.28(1.5-2.56)	<.0001#
Aspartate Transaminase	90.32±79.49(25-340)	94.13±50.26(40-277)	0.055
Alanine transaminase	43.07±61.76(16-330)	40.72±23.58(17-147)	0.123#

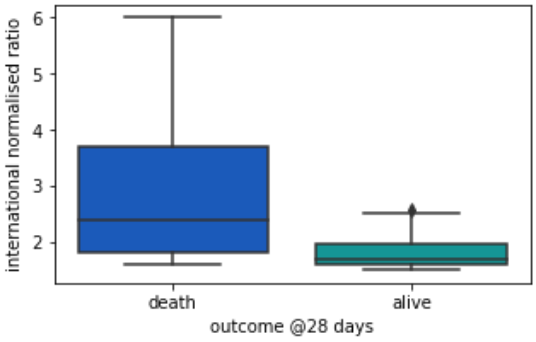
Total protein	5.85±1.13(2.8-8.1)	6.29±1.02(2.5-9)	0.152[#]
Globulin	3.65±0.75(2.5-5.5)	3.54±0.55(2.5-5.1)	0.26[#]
Gamma Glutamyl Transferase	111.22±159.68(34-572)	113.12±175.88(18-806)	0.561[#]

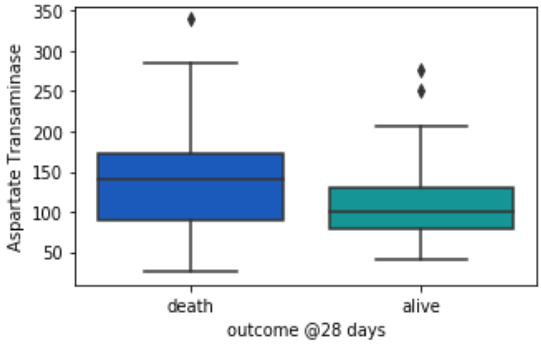
Values are presented as Mean±SD (Range)

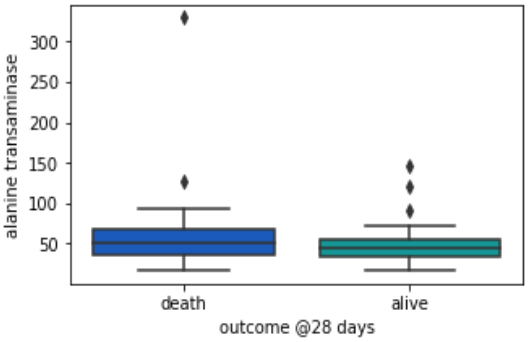
Figure 21: Boxplot graph comparing Liver Profile parameters between death and alive group

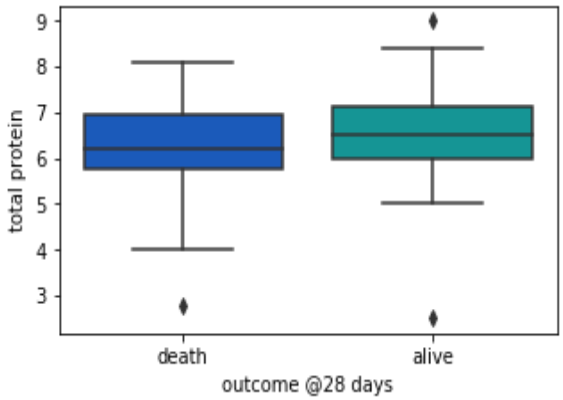


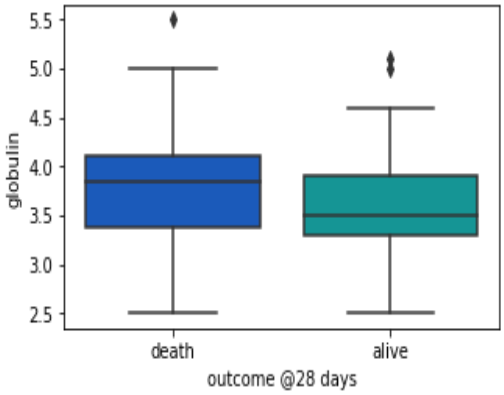

Activated Plasma Thromboplastin time
120
100
80
60
40
20
death
alive
outcome @28 days

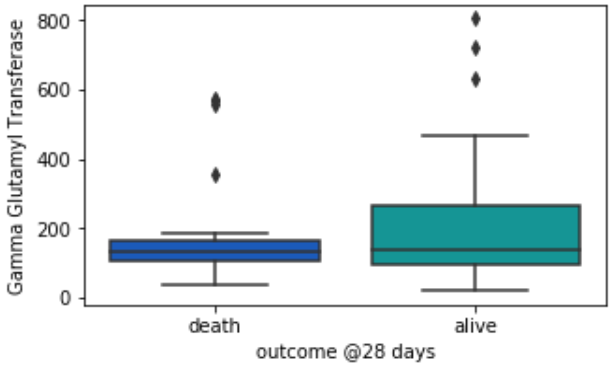

international normalised ratio
6
5
4
3
2
death
alive
outcome @28 days


Aspartate Transaminase
350
300
250
200
150
100
50
death
alive
outcome @28 days


alanine transaminase
300
250
200
150
100
50
death
alive
outcome @28 days


total protein
9
8
7
6
5
4
3
death
alive
outcome @28 days


globulin
5.5
5.0
4.5
4.0
3.5
3.0
2.5
death
alive
outcome @28 days


Gamma Glutamyl Transferase
800
600
400
200
0
death
alive
outcome @28 days

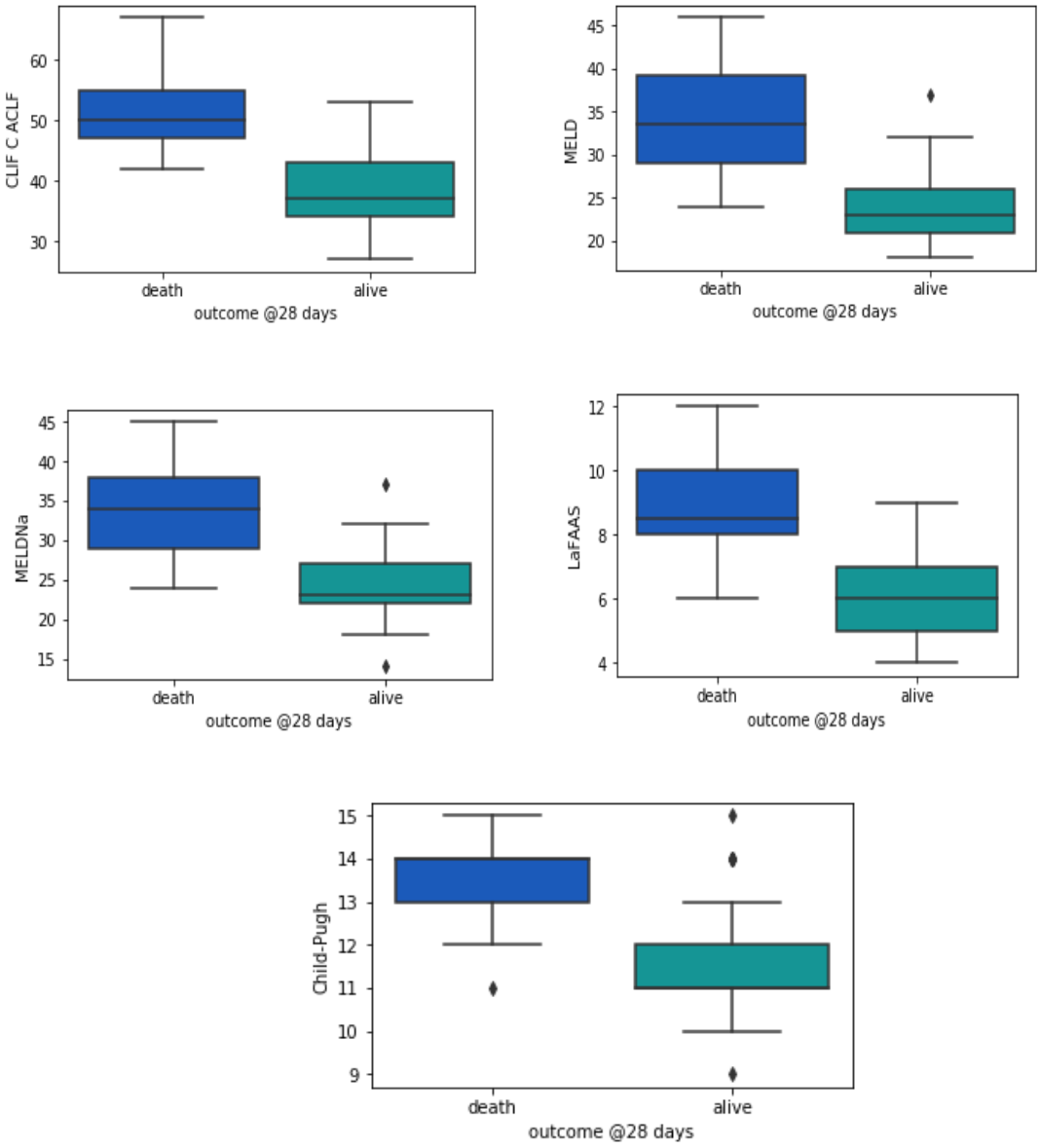
A statistically significant difference was noted for CLIF C ACLF(P <.0001) , LaFAAS(P <.0001), MELD (P <.0001), MELDNa (P <.0001), CPT (P <.0001), between the death and alive groups (Table 25, Fig 22).

Table 25: Comparison of prediction models between death and alive group

Variables	Death(N=24)	Alive(N=49)	P-value
CLIF C ACLF	50.83±6.51(42-67)	37.23±6.43(27-53)	<.0001#
MELD	33.30±6.33(24-46)	23.15±3.97(18-37)	<.0001#
MELDNa	32.65±6.01(24-45)	23.59±4.07(14-37)	<.0001#
LaFAAS	13.55±0.96(11-15)	11.44±1.35(9-15)	<.0001#
CPT	8.38±1.70(6-12)	5.83±1.17(4-9)	<.0001#

Values are presented as Mean±SD (Range), MELD: Model for End-Stage Liver Disease, CPT: Child-Pugh-Turcotte, CLIF C ACLF: Chronic Liver Failure (CLIF) Consortium - Acute on Chronic Liver Failure, MELDNa: Sodium MELD, LaFAAS: Lactate-free Acute on Chronic Liver Failure Research Consortium - Acute on Chronic Liver failure Score

Figure 22: Boxplot graph comparing prediction models between death and alive group



Comparison of predictive models for 28-day mortality

The MELD had the highest Area under the curve (AUC) achieved of 0.938 compared to other prediction models. The AUC of CLIF C ACLF, MELDNa, LaFAAS and CPT were 0.929, 0.91, 0.898, and 0.874, respectively. The CPT model had the lowest AUC achieved among the prediction models(Table 26).

Table 26: Area under the curve of the prediction models

Variables	Area under curve (AUC)	95% CI for AUC
CLIF C ACLF	0.929	0.874-0.983
MELD	0.938	0.884-0.991
MELDNa	0.91	0.843-0.977
LaFAAS	0.898	0.825-0.97
CPT	0.874	0.795-0.954

MELD: Model for End-Stage Liver Disease, CPT: Child-Pugh-Turcotte, CLIF C ACLF: Chronic Liver Failure (CLIF) Consortium - Acute on Chronic Liver Failure, MELDNa: Sodium MELD, LaFAAS: Lactate-free Acute on Chronic Liver Failure Research Consortium - Acute on Chronic Liver failure Score

The ROC curve method was used to evaluate the obtained prediction models. ROC cut-offs for the variables at 90% sensitivity, MELD demonstrated good sensitivity(0.917) and specificity(0.837). The MELDNa demonstrated good sensitivity of 0.917 whereas the specificity was 0.694. The CLIF C ACLF demonstrated good sensitivity of 0.958 whereas the specificity was 0.735. The CPT demonstrated good sensitivity of 0.917 whereas the specificity was 0.755. The LaFAAS demonstrated good sensitivity of 1 whereas the specificity was poor with a value of 0.367(Table 27).

Table 27: Predictive value of 28-day mortality of the prediction model at 90% sensitivity cut-off

			Cut-off	Target	0.9		
Variables	**Cut point**	**Sensitivity**	**Se Lower 95%CL**	**Se Upper 95% CL**	**Specificity**	**Sp Lower 95% CL**	**Sp Upper 95% CL**
CLIF C ACLF	43	0.958	0.798	0.993	0.735	0.597	0.838
MELD	28	0.917	0.742	0.977	0.837	0.71	0.915
MELDNa	27	0.917	0.742	0.977	0.694	0.555	0.805
LaFAAS	6	1	0.862	1	0.367	0.247	0.507
CPT	13	0.917	0.742	0.977	0.755	0.619	0.854

MELD: Model for End-Stage Liver Disease, CPT: Child-Pugh-Turcotte, CLIF C ACLF: Chronic Liver Failure (CLIF) Consortium - Acute on Chronic Liver Failure, MELDNa: Sodium MELD, LaFAAS: Lactate-free Acute on Chronic Liver Failure Research Consortium - Acute on Chronic Liver failure Score

ROC cut-offs for the variables at 80% sensitivity, MELD demonstrated good sensitivity at 0.917 whereas the specificity was 0.837. The MELDNa demonstrated a sensitivity of 0.833 whereas the specificity was 0.776. The CLIF C ACLF demonstrated a sensitivity of 0.833 whereas the specificity was 0.878. The CPT demonstrated good sensitivity of 0.917 whereas the specificity was 0.755. The LaFAAS demonstrated a sensitivity of 0.875 whereas the specificity was 0.714 (Table 28).

Table 28: Predictive value of 28-day mortality of the prediction model at 80% sensitivity cut-off

			Cut-off	Target	0.8		
Variables	**Cut point**	**Sensitivity**	**Se Lower 95% CL**	**Se Upper 95%CL**	**Specificity**	**Sp Lower 95% CL**	**Sp Upper 95% CL**
CLIF C ACLF	47	0.833	0.641	0.933	0.878	0.758	0.943
MELD	28	0.917	0.742	0.977	0.837	0.71	0.915
MELDNa	28	0.833	0.641	0.933	0.776	0.641	0.87
LaFAAS	7	0.875	0.69	0.957	0.714	0.576	0.822
CPT	13	0.917	0.742	0.977	0.755	0.619	0.854

MELD: Model for End-Stage Liver Disease, CPT: Child-Pugh-Turcotte, CLIF C ACLF: Chronic Liver Failure (CLIF) Consortium - Acute on Chronic Liver Failure, MELDNa: Sodium MELD, LaFAAS: Lactate-free Acute on Chronic Liver Failure Research Consortium - Acute on Chronic Liver failure Score

ROC cut-offs for the variables at 90% specificity, MELD demonstrated good specificity at 0.918 whereas the sensitivity was 0.708. The MELDNa demonstrated a good specificity of 0.939 whereas the sensitivity was 0.667. The CLIF C ACLF demonstrated a good specificity of 0.918 whereas the sensitivity was 0.625. The CPT demonstrated good specificity of 0.98 whereas the sensitivity was poor at 0.167. The LaFAAS demonstrated a good specificity of 0.959 whereas the sensitivity was low at 0.5 (Table 29).

Table 29: Predictive value of 28-day mortality of the prediction model at 90% specificity cut-off

			Cut-off	Target	0.9		
Variables	**Cut point**	**Specificity**	**Sp Lower 95% CL**	**Sp Upper 95% CL**	**Sensitivity**	**Se Lower 95% CL**	**Se Upper 95% CL**
CLIF C ACLF	48	0.918	0.808	0.968	0.625	0.427	0.788
MELD	30	0.918	0.808	0.968	0.708	0.508	0.851
MELDNa	30	0.939	0.835	0.979	0.667	0.467	0.82
LaFAAS	9	0.959	0.863	0.989	0.5	0.314	0.686
CPT	15	0.98	0.893	0.996	0.167	0.067	0.359

MELD: Model for End-Stage Liver Disease, CPT: Child-Pugh-Turcotte, CLIF C ACLF: Chronic Liver Failure (CLIF) Consortium - Acute on Chronic Liver Failure, MELDNa: Sodium MELD, LaFAAS: Lactate-free Acute on Chronic Liver Failure Research Consortium - Acute on Chronic Liver failure Score

ROC cut-offs for the variables at 80% specificity, MELD demonstrated specificity at 0.837 whereas the sensitivity was high at 0.917. The MELDNa demonstrated a specificity of 0.857 whereas the sensitivity was 0.792. The CLIF C ACLF demonstrated a specificity of 0.837 whereas the sensitivity was 0.875. The CPT demonstrated a specificity of 0.898 whereas the sensitivity was poor at 0.583. The LaFAAS demonstrated a specificity of 0.878 whereas the sensitivity was 0.792 (Table 30).

Table 30: Predictive value of 28-day mortality of the prediction model at 80% specificity cut-off

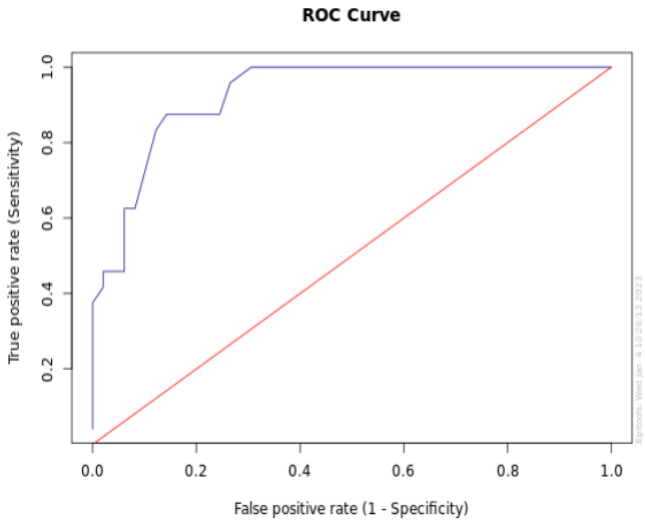
			Cut-off	Target	0.8		
Variables	**Cut point**	**Specificity**	**Sp Lower 95% CL**	**Sp Upper 95% CL**	**Sensitivity**	**Se Lower 95% CL**	**Se Upper 95% CL**
CLIF C ACLF	45	0.837	0.71	0.915	0.875	0.69	0.957
MELD	28	0.837	0.71	0.915	0.917	0.742	0.977
MELDNa	29	0.857	0.733	0.929	0.792	0.595	0.908
LaFAAS	8	0.878	0.758	0.943	0.792	0.595	0.908
CPT	14	0.898	0.782	0.956	0.583	0.388	0.755

MELD: Model for End-Stage Liver Disease, CPT: Child-Pugh-Turcotte, CLIF C ACLF: Chronic Liver Failure (CLIF) Consortium - Acute on Chronic Liver Failure, MELDNa: Sodium MELD, LaFAAS: Lactate-free Acute on Chronic Liver Failure Research Consortium - Acute on Chronic Liver failure Score

All prediction scores had reliable performance in terms of AUC. Among all the prediction scores, the MELD score had the superior AUC of 0.94, followed by CLIF C ACLF with an AUC of 0.93. The AUC of MELDNa, LaFAAS, and CPT were 0.91, 0.898 and 0.874, respectively.

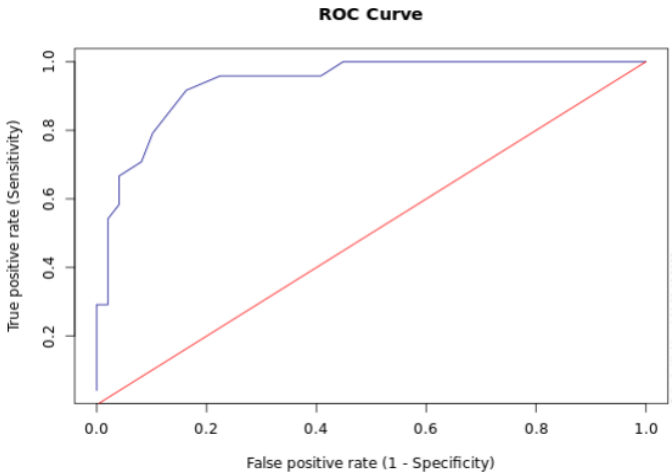
The ROC curve for predicting 28 days of mortality by CLIF C ACLF score showed an AUC of 0.93 and a 95% confidence interval of 0.874-0.983(Figure 23).

Figure 23: ROC curve : prediction of 28-day mortality by CLIF C ACLF score



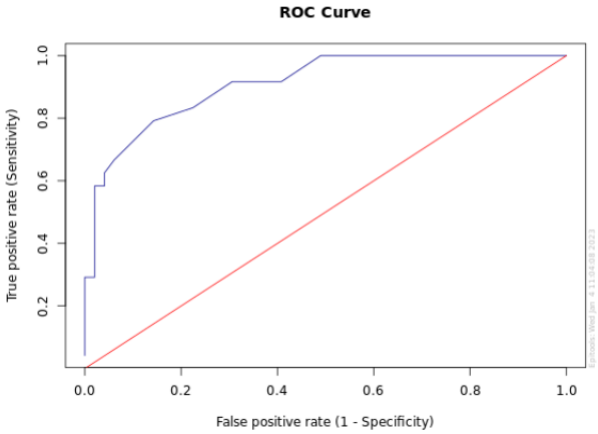
The ROC curve for predicting 28 days of mortality by MELD score showed an AUC of 0.94 and a 95% confidence interval of 0.884-0.991 (Figure 24).

Figure 24: ROC curve : prediction of 28-day mortality by MELD score



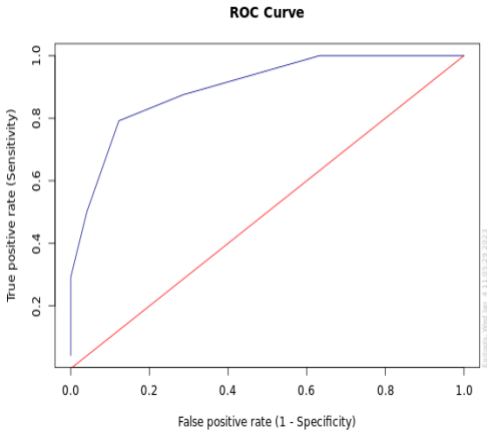
The ROC curve for predicting 28 days of mortality by MELDNa score showed an AUC of 0.91 and a 95% confidence interval of 0.843-0.977 (Figure 25).

Figure 25: ROC curve : prediction of 28-day mortality by MELDNa score



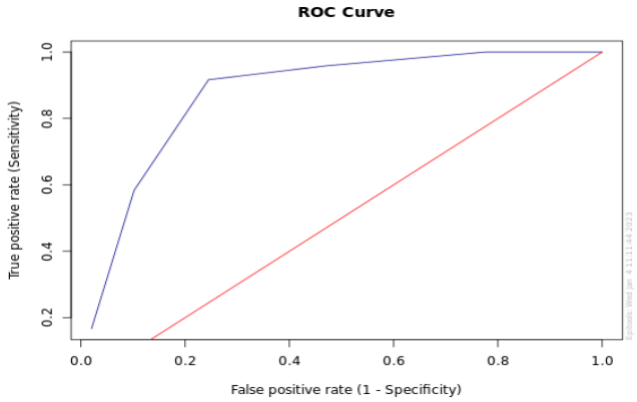
The ROC curve for predicting 28 days of mortality by LaFAAS score showed an AUC of 0.898 and a 95% confidence interval of 0.825-0.97 (Figure 26).

Figure 26: ROC curve : prediction of 28-day mortality by LaFAAS score



The ROC curve for predicting 28 days of mortality by CPT score showed an AUC of 0.874 and a 95% confidence interval of 0.795-0.954 (Figure 27).

Figure 27: ROC curve : prediction of 28-day mortality by CPT score



DISCUSSION

DISCUSSION

The prospective observational study was conducted at R L Jalappa Hospital, Kolar, a tertiary care hospital in Karnataka. The study included 73 patients with ACLF and followed up for 28 days. The study's key objective was to calculate the patients' LaFAAS, MELD, MELD-Na, and CLIF SOFA scores, and compare LaFAAS' predictive value to MELD, MELD-Na, and CLIF SOFA scores for 28-day mortality. The study considered patients aged between 30-77 with the mean age being 46.05. A mean hospital stays of 5.89 was noted among the study subjects. In 28 days, outcome, 67.12% were alive and 32.87% were dead. A mean score of 40.82 for CLIF C ACLF was noted among the subjects. A mean score of 25.73 for MELD was noted among the subjects. A mean score of 25.96 for MELDNa was noted among the subjects. A mean score of 6.48 for LaFAAS was noted among the subjects. A mean score of 12.06 for CPT was noted among the subjects.

In the present study, there was no statistically significant difference noted for age and gender between the death and alive groups. A study by Chen et al reported a significant statistical difference between the survivors and non-survivors in ACLF patients whereas it was non-significant for gender.[83] Similar results were shown by a study by Kuo where a significant statistical difference was noted for age whereas in terms of gender, it was non-significant.[85] A study by da Silva et al reported a significant statistical difference in age and female gender between the survivors and non-survivors in ACLF patients.[88] A study by Yu et al reported a significant statistical difference in age between ACLF patients who survived and those who did not, however, male gender was non-significant.[89] Liu et al reported a non-significant statistical difference in age and male(gender) between survivors and non-survivors.[84] A study by Zakareya et al also reported significant statistical differences in age however gender was non-significant.[90] Méndez-Guerrero et al reported a non-significant statistical difference in age and gender between the survivors and non-survivors in ACLF patients.[91] In the present study a significant statistical difference in hospital stay and a non-significant statistical difference for type 2 diabetes was noted between the death and alive groups. A similar result was observed in a study by Boteon et al, where the length of hospital stay was significant and a non-significant statistical difference was noted between survivors and non-survivors.[88] In the present study significant statistical difference was found for Hepatic encephalopathy grade between the death and alive group, whereas a non-significant statistical difference was noted for it between survivors and non-survivors in a study by Chen et al.[83] The WBC count

difference was statistically non-significant in our study, whereas a significant statistical difference was observed for it between survivors and non-survivors in a study by Chen et al[83], Kuo et al[85], Boteon et al[88], Yu et al[89], Liu et al[84], Zakareya[90]. In the present study, for platelet, a significant statistical difference was noted for death and alive group, a similar result was displayed by studies by Yu et al[89], Liu et al[84,] and Zakareya et al[90] between the survivors and non-survivors. In terms of creatinine a significant statistical difference was noted between the dead and alive, a similar result was obtained by studies by Chen et al[83], Kuo et al[85], Yu et al[89], Zakareya et al[90] between the survivors and non-survivors, whereas a non-significant statistical difference was noted for creatinine between the survivors and non-survivors in a study by Liu et al.[84]In terms of blood urea nitrogen a significant statistical difference was noted between the death and alive, similar result was obtained by studies by Yu et al between the survivors and non-survivors[89], whereas a study by Liu et al reported a non-significant statistical difference for blood urea nitrogen between the survivors and non-survivors.[84] A statistically non-significant difference was noted for sodium between death and alive group in the present study, similar result was obtained by studies by Chen et al[83], and Kuo et al[85] between the survivors and non-survivors. In the present study, a statistically significant difference was noted for alkaline Phosphatase(ALP), and albumin between the death and alive group, whereas it was non-significant for whereas it was non-significant for aspartate Transaminase(AST), alanine transaminase(ALT), and gamma Glutamyl Transferase(GGT). A study by Yu et al reported significant statistical differences for albumin and a non-significant difference for AST, ALT, GGT, and ALP between the survivors and non-survivors.[89] Another study by Liu et al reported significant statistical differences for albumin, ALT, AST, and ALP between the survivors and non-survivors whereas it was non-significant for GGT.[84] Chen et al reported significant statistical differences for albumin between the survivors[83], and non-survivors whereas it was non-significant in a study by Kuo et al.[85] In the present study, significant statistical differences were noted for CLIF C ACLF, MELD, MELDNa, LaFAAS, and CPT between the death and alive group. In a study by Zhang et al, significant statistical differences for CLIF C ACLF, MELD, LaFAAS, and CPT and non-significant for MELDNa were noted between survivors and non-survivors.[82] A significant statistical difference for CLIF C ACLF, MELD, and CPT was noted between survivors and non-survivors in a study by Chen et al.[83] A significant statistical difference for MELDNa, MELD, and CPT was noted between survivors and non-survivors in a study by Yu et al.[89] A significant statistical differences for CLIF C ACLF, MELD, and CPT was noted between survivors and non-survivors in a study by Zakareya et al.[90]

Early prediction scores that can recognise high-risk patients for mortality, early in the disease course are required to decrease mortality. These scores allow for the early administration of appropriate medication. Prognostication done early is therefore essential for ACLF patients as the clinical syndrome is associated with a high mortality risk and is characterised by the emergence of acute decompensation and organ failure.[13] However, because to various factors, including aetiology, illness stage, and comorbidities, the prognosis for specific patients in the clinical context is frequently difficult to predict. Numerous other measures have been demonstrated in prior research to have predictive significance for death in these patients. It is crucial to select the most accurate score for predicting mortality in Asian patients receiving clinical care. Patients with ACLF in Asia exhibit entirely distinct clinical traits from those in Europe and America. In the present study, the predictive value of five scores CLIF C ACLF, MELD**,** MELDNa**,** LaFAAS and CPT was compared at 28 days. The ROC curve for predicting 28-day mortality demonstrated AUC of 0.94, 0.93, 0.91, 0.898 and 0.874 for MELD, CLIF C ACLF, MELDNa, LaFAAS, and CPT respectively. In a study by Chen et al, the AUROC of CTP, MELD, CLIF-C ACLF were 0.810, 0.815, and 0.827 to predict 28-day mortality.[83] In a study by Zhang et al, the AUROC for CTP, MELD, and MELD-Na, were 0.707, 0.673, and 0.606 to predict 28-day mortality.[82] In a study by Liu et al, the AUROC for MELD was 0.670 for predicting 28-day mortality.[84] In a study by Lin et al, the AUROC for CTP, MELD, and MELD-Na was 0.688, 0.753 and 0.747 to predict 28-day mortality.[92] In a study by Maipang et al, the AUROC of CTP, MELD, MELD-Na, CLIF-C ACLF were 0.70, 0.63, 0.63 and 0.79 to predict 28-day mortality.[93] In a study by Raveendran et al, the AUROC of CTP, MELD and CLIF-C ACLF were 0.737, 0.789, and 0.843 to predict 28-day mortality.[94]

In the present study, at 90% sensitivity cut-off MELD, MELDNa, CLIF C ACLF, CPT, and LaFAAS showed a sensitivity of 0.917, 0.917, 0.958, 0.917, 1 and specificity of 0.837, 0.694, 0.735, 0.755 and 0.367. at 80% sensitivity cut-off MELD, MELDNa, CLIF C ACLF, and CPT showed a sensitivity of 0.917, 0.833, 0.833, 0.917, 0.875 and specificity of 0.837, 0.776, 0.878, 0.755 and 0.714. at 90% specificity cut-off MELD, MELDNa, CLIF C ACLF, and CPT showed a sensitivity of 0.708, 0.667, 0.625, 0.167, 0.5 and specificity of 0.918, 0.939, 0.918, 0.98 and 0.959. at 80% specificity cut-off MELD, MELDNa, CLIF C ACLF, and CPT showed sensitivity 0.917, 0.792, 0.875, 0.583, 0.792 and specificity of 0.837, 0.857, 0.837, 0.898 and 0.878. In a study by Zhang et al, CTP, MELD, and MELD-Na showed a sensitivity of 57.78, 84.44, 71.11 and specificity of 74.47, 59.57, and 59.57.1. In a study by

Liu et al, the sensitivity and specificity for MELD were 59.57 and 83.33.[84] In a study by Barosa et al, CTP, MELD, MELD-Na, and CLIF-C ACLF demonstrated sensitivity of 48.4, 69.0, 79.3, 73.1 and specificity of 74.8, 80.6, 78.7 and 74.1.[81] In a study by Lin et al, MELD and MELD-Na demonstrated sensitivity of 0.72, 0.75 and specificity of 0.68, and 0.64.[92]

In the present study, MELD had supremacy in predicting 28 days mortality when compared to other prediction scores MELDNa, CLIF C ACLF CPT, and LaFAAS. In contrast to our study, the MELD had a poor performance in predicting 28-day mortality in a study by Liu et al.[84] After MELD, the CLIF C ACLF had the highest AUC in the present study**.** In a study by Barosa et al and Maipang et al, compared to CTP, MELD, and MELD-Na, the CLIF-C ACLF score was considerably better in predicting 28-day mortality with AUROC 0.799.[81,93] In our study LaFAAS score had less supreme than CLIF C ACLF, MELD, MELDNa in predicting 28-days mortality. In contrast to our study, a study by Chauhan et al reported that LaFAAS score had supremacy in predicting mortality at 3 months compared to CLIF C ACLF, MELD, MELDNa.[8]

Although in our study LaFAAS score had less supreme than CLIF C ACLF, MELD, and MELDNa however it demonstrated good performance for predicting 28 days mortality and it can be a useful tool to predict 28-day mortality in ACLF patients.

CONCLUSION

CONCLUSION

Our analysis demonstrated that the MELD, MELDNa, CLIF C ACLF, CPT, and LaFAAS scores are effective for predicting 28-days mortality in patients with ACLF. The MELD score has better discriminative power for the evaluation of 28 days mortality compared to other scores and may help in better utilisation of resources and in managing ACLF patients. The present study findings could pave the way for further research for the implementation of such predictive scores to determine prognosis early and lead to better management of ACLF.

LIMITATIONS

LIMITATIONS AND RECOMMENDATIONS

The study only included patients from a single centre in southern India and may not be generalisable to other ethnicities, races, or regions. Patients were followed up for a period of 28 days only and outcomes at 3 months and 1 year where ACLF generally has a higher mortality were not checked at which the other scoring systems might have performed better. The APASL definition of ACLF was considered and performance by the scores may have been different if other definitions such as the EASL or NACSELD were used. Further studies with longer follow up, a consensus definition for ACLF and a larger population under study are required to arrive at a conclusion.

SUMMARY

SUMMARY

The present prospective observational study was conducted on 73 ACLF patients at R L Jalappa Hospital, Kolar during the academic year Jan 2021 to June 2022. Adult patients (age > 18 years), with hepatic or extrahepatic insults, with or without prior decompensation, and satisfying APASL criteria for ACLF were included in the study. All the patient data were collected on Microsoft windows excel sheet and the statistical analysis was performed using Excel 2019, Python (version: 3.10.0) in the Jupyter Notebook and Epitools.

Our study calculated prognostic scores LaFAAS, MELD MELD-Na, and CLIF-C-ACLF score and compared these scores against each other for predicting mortality at 28 in ACLF patients.

A total of 73 patients fulfilling the inclusion criteria were divided into two groups Death(24)and alive(49).

Participants aged between 30-77 with the mean age being 46.05

Among the participants, 70 were male and 3 were female.

There was no statistically significant difference noted for age and gender between the death and alive groups.

In the present study, a statistically significant difference was noted for alkaline Phosphatase(ALP), and albumin between the death and alive group, whereas it was non-significant for whereas it was non-significant for aspartate Transaminase(AST), alanine transaminase(ALT), and gamma Glutamyl Transferase(GGT).

All the predictive score performed well in predicting 28 days mortality in ACLF patients. MELD had supremacy in predicting 28 days mortality when compared to other prediction scores MELDNa, CLIF C ACLF CPT, and LaFAAS.

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ANNEXURES

PROFORMA

Name:

Age:

Sex:

Occupation:

UHID number:

Phone number:

Address:

Date of Admission:

Date of Discharge:

Complaints with duration:

Previous history of Decompensation-

Past history:

HbSAg/HCV status (if available)

Family history:

History of Alcohol consumption

Duration

Quantity

Last drink

GENERAL PHYSICAL EXAMINATION:

- Built and nourishment:
- Pallor/Cyanosis/Icterus/Clubbing/edema/Generalized lymphadenopathy

VITAL DATA

- Pulse:
- sPO2 -
- BP:
- Respiration rate

Systemic examination

- Per abdomen:
- Respiratory system:
- Cardio vascular system:
- Central nervous system:

INVESTIGATIONS:

Routine:

CBC with Peripheral Smear

RFT

Blood Urea

Serum Creatinine

Serum Electrolytes

Sodium

Potassium

ECG

Chest X ray

Specific:

LFT

PT

APTT

INR

USG Abdomen & Pelvis

CLIF-SOFA score -

MELD score -

MELD-Na score -

LaFAAS score –

CPT score -

PATIENT INFORMATION SHEET

STUDY TITLE: COMPARATIVE STUDY OF LACTATE FREE APASL-ACLF RESEARCH CONSORTIUM - ACUTE ON CHRONIC LIVER FAILURE SCORE (LaFAAS) VS. STANDARD PROGNOSTIC SCORES IN ACUTE ON CHRONIC LIVER FAILURE.

STUDY CONDUCTED BY : DR. Manasa Dixit C
STUDY LOCATION: R L Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar.
Acute on chronic liver failure (ACLF) is a clinical syndrome of sudden hepatic decompensation observed in patients with pre-existing chronic liver disease and associated with one or more extrahepatic organ failures and increased mortality. Early intervention is therefore essential. Prognostic scores aid in early decision making. To compare these prognostic scores is the intention of this study.

The purpose of the study is explained in detail to us and that all information collected is for study purpose only. The data collected is submitted to the department of general medicine, SDUMC, Kolar and confidentiality is ensured. The merits and demerits of the study have been explained to us.

All patients diagnosed with acute on chronic liver failure will be included in this study. Patients in this study will undergo routine investigations like CBC, LFT , RFT , Serum Electrolytes , prognostic scores calculated and correlation of clinical and pathological factors with outcome at the end of 28 days will be done to find a significant correlation. Standard of the care will be maintained throughout the study.

Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in the study, we will collect information (as per proforma) from you or a person responsible for you or both. Relevant history will be taken. This information collected will be used only for dissertation and publication.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. This study has been reviewed by the Institutional

Ethics Committee and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

For further information contact:
Dr. Manasa Dixit C [post graduate]
Department of General Medicine
SDUMC, Kolar

left thumb impression/signature of the patient

left thumb impression / signature of the witness

Phone number

9902011512

INFORMED CONSENT FORM

Title: - COMPARATIVE STUDY OF LaFAAS (LACTATE FREE APASL-ACLF RESEARCH CONSORTIUM - ACUTE ON CHRONIC LIVER FAILURE SCORE) VS. STANDARD PROGNOSTIC SCORES IN ACUTE ON CHRONIC LIVER FAILURE.

Principal investigator: Dr. Manasa Dixit C

I, Mr/Mrs/Ms. …….. have been explained in my own understandable language, that I will be included in a study which is COMPARATIVE STUDY OF LaFAAS (LACTATE FREE APASL-ACLF RESEARCH CONSORTIUM - ACUTE ON CHRONIC LIVER FAILURE SCORE) VS. STANDARD PROGNOSTIC SCORES IN ACUTE ON CHRONIC LIVER FAILURE.in RL Jalappa Hospital.

I have been explained that my clinical findings, investigations and outcome will be assessed and documented for study purpose.

I have been explained that my participation in this study is entirely voluntary and I can withdraw from the study at any time and this will not affect my relation with my doctor or treatment for my ailment.

I have been explained about the risk/benefit of the study.

I understand that the medical information produced by this study will become part of institutional records and will be kept confidential by said institute.

I agree not to restrict the use of any data or result that arises from this study provided such a use is only for scientific purpose(s).

I have the principal investigator's mobile number for enquiries.

I have been informed that standard of care will be maintained throughout the treatment period.

I, in my sound mind, give full consent to be added as the part of this study.

Investigator: Dr. Manasa Dixit C

Phone number : 9902011512

Participant’s signature/ thumb impression

Name:

Signature/thumb impression of the witness: Date:

Name:

Relation to patient

ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳ

ಅಧ್ಯಯನದ ಶೀರ್ಷಿಕೆ : ಲಾಫಾಸ್‌ನ (ಲ್ಯಾಕ್ಟೇಟ್ ಉಚಿತ ಎ.ಪಿ.ಎ.ಎಸ್.ಎಲ್-ಎ ಸಿ ಎಲ್ ಎಫ್ ಸಂಶೋಧನಾ ಕನ್ಸೋರ್ಟಿಯಂ - ಕ್ರೋನಿಕ್ ಯಕೃತ್ತು ವೈಫಲ್ಯದ ಸ್ಕೋರ) ವಿರುದ್ಧ ಕ್ರೋನಿಕ್ ಯಕೃತ್ತು ವೈಫಲ್ಯದ ಮೇಲೆ ಪ್ರಮಾಣಿತ ಪ್ರೊಗ್ನೋಸ್ಟಿಕ್ ಸ್ಕೋರ್ಗಳ ತುಲನಾತ್ಮಕ ಅಧ್ಯಯನ

ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ: ಡಾ. ಮಾನಸ ದೀಕ್ಷಿತ್ ಸಿ

ಅಧ್ಯಯನ ಸ್ಥಳ: ಕೊಲಾರದ ತಮಕಾದ ಶ್ರೀ ದೇವರಾಜ್ ಉರ್ಸ್ ವೈದಯಕೋಯ ಕಾಲೇಜು - ಆರ್ ಎಲ್ ಜಾಲಪ್ಪ ಆಸ್ಪತ್ರೆ.

ತೀವ್ರವಾದ ಪಿತ್ತಜನಕಾಂಗದ ವೈಫಲ್ಯ (ಎ.ಸಿ.ಎಲ್.ಎಫ್) ಎಂಬುದು ಹಠಾತ್ ಯಕೃತ್ತಿನ ವಿಭಜನೆಯ ಕ್ಲಿನಿಕಲ್ ಸಿಂಡ್ರೋಮ್ ಆಗಿದ್ದು, ಇದು ಮೊದಲೇ ದೀರ್ಘಕಾಲದ ಪಿತ್ತಜನಕಾಂಗದ ಕಾಯಿಲೆಯ ರೋಗಿಗಳಲ್ಲಿ ಕಂಡುಬರುತ್ತದೆ ಮತ್ತು ಒಂದು ಅಥವಾ ಹೆಚ್ಚಿನ ಬಾಹ್ಯ ಅಂಗಾಂಗ ವೈಫಲ್ಯಗಳು ಮತ್ತು ಹೆಚ್ಚಿದ ಮರಣಕ್ಕೆ ಸಂಬಂಧಿಸಿದೆ. ಆದ್ದರಿಂದ ಆರಂಭಿಕ ಹಸ್ತಕ್ಷೇಪ ಅತ್ಯಗತ್ಯ. ನಿರ್ಧಾರ ತೆಗೆದುಕೊಳ್ಳುವಲ್ಲಿ ಮುನ್ನರಿವಿನ ಅಂಕಗಳು ಸಹಾಯ ಮಾಡುತ್ತವೆ. ಈ ಮುನ್ನರಿವಿನ ಅಂಕಗಳ ತುಲನೆ ಮಾಡುವುದು ಈ ಅಧ್ಯಯನದ ಉದ್ದೇಶವಾಗಿದೆ.

ಅಧ್ಯಯನದ ಉದ್ದೇಶವನ್ನು ನಮಗೆ ವಿವರವಾಗಿ ವಿವರಿಸಲಾಗಿದೆ ಮತ್ತು ಸಂಗ್ರಹಿಸಿದ ಎಲ್ಲಾ ಮಾಹಿತಿಯು ಅಧ್ಯಯನದ ಉದ್ದೇಶಕ್ಕಾಗಿ ಮಾತ್ರ. ಸಂಗ್ರಹಿಸಿದ ಡೇಟಾವನ್ನು ಸಾಮಾನ್ಯ ವೈದ್ಯಕೀಯ ಇಲಾಖೆ, ಎಸ್‌ಡಿಯುಎಂಸಿ, ಕೋಲಾರ್ ಸಲ್ಲಿಸಲಾಗುತ್ತದೆ ಮತ್ತು ಗೌಪ್ಯತೆಯನ್ನು ಖಾತ್ರಿಪಡಿಸಲಾಗುತ್ತದೆ. ಅಧ್ಯಯನದ ಅರ್ಹತೆಗಳು ಮತ್ತು ದೋಷಗಳನ್ನು ನಮಗೆ ವಿವರಿಸಲಾಗಿದೆ.

ದೀರ್ಘಕಾಲದ ಯಕೃತ್ತಿನ ವೈಫಲ್ಯದ ಮೇಲೆ ತೀವ್ರ ರೋಗನಿರ್ಣಯ ಮಾಡಿದ ಎಲ್ಲಾ ರೋಗಿಗಳನ್ನು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಸೇರಿಸಲಾಗುವುದು. ಈ ಅಧ್ಯಯನದ ರೋಗಿಗಳಿಗೆ ಸಿಬಿಸಿ, ಎಲ್‌ಎಫ್‌ಟಿ, ಆರ್‌ಎಫ್‌ಟಿ, ಸೀರಮ್ ವಿದ್ಯುದ್ವಿಚ್ ಪರೀಕ್ಷೆಗಳನ್ನು ಮಾಡಲಾಗುತ್ತದೆ. ಮುನ್ನರಿವಿನ ಅಂಕಗಳನ್ನು ಲೆಕ್ಕಹಾಕಲಾಗುತ್ತದೆ.

ಫಲಿತಾಂಶದ ಕೇಂದ್ರೀಕರಣ ಮತ್ತು ಕ್ಲಿನಿಕಲ್ ಅಂಶಗಳನ್ನು ಮಾಡಲಾಗುತ್ತದೆ. ಆರೈಕೆಯ ಗುಣಮಟ್ಟವನ್ನು ಅಧ್ಯಯನದ ಉದ್ದಕ್ಕೂ ನಿರ್ವಹಿಸಲಾಗುವುದು.

ದಯವಿಟ್ಟು ಈ ಕೆಳಗಿನ ಮಾಹಿತಿಯನ್ನು ಓದಿ ಮತ್ತು ನಿಮ್ಮ ಕುಟುಂಬ ಸದಸ್ಯರೊಂದಿಗೆ ಚರ್ಚಿಸಿ. ಅಧ್ಯಯನಕ್ಕೆ ಸಂಬಂಧಿಸಿದಂತೆ ನೀವು ಯಾವುದೇ ಪ್ರಶ್ನೆಯನ್ನು ಕೇಳಬಹುದು. ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನೀವು ಒಪ್ಪಿದರೆ, ನಿಮ್ಮಿಂದ

ಅಥವಾ ನಿಮ್ಮ ಇಬ್ಬರ ಜವಾಬ್ದಾರಿಯುತ ವ್ಯಕ್ತಿಯಿಂದ ನಾವು ಮಾಹಿತಿಯನ್ನು (ಪ್ರೊಫಾರ್ಮಾದ ಪ್ರಕಾರ) ಸಂಗ್ರಹಿಸುತ್ತೇವೆ. ಸಂಬಂಧಿತ ಇತಿಹಾಸವನ್ನು ತೆಗೆದುಕೊಳ್ಳಲಾಗುವುದು. ಸಂಗ್ರಹಿಸಿದ ಈ ಮಾಹಿತಿಯನ್ನು ಪ್ರಬಂಧ ಮತ್ತು ಪ್ರಕಟಣೆಗೆ ಮಾತ್ರ ಬಳಸಲಾಗುತ್ತದೆ.

ನಿಮ್ಮಿಂದ ಸಂಗ್ರಹಿಸಲಾದ ಎಲ್ಲಾ ಮಾಹಿತಿಯನ್ನು ಗೌಪ್ಯವಾಗಿಡಲಾಗುತ್ತದೆ ಮತ್ತು ಯಾವುದೇ ಹೊರಗಿನವರಿಗೆ ಬಹಿರಂಗಪಡಿಸುವುದಿಲ್ಲ. ನಿಮ್ಮ ಗುರುತು ಬಹಿರಂಗಗೊಳ್ಳುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನವನ್ನು ಸಾಂಸ್ಥಿಕ ನೈತಿಕ ಸಮಿತಿಯು ಪರಿಶೀಲಿಸಿದೆ ಮತ್ತು ನೀವು ಸಾಂಸ್ಥಿಕ ನೈತಿಕ ಸಮಿತಿಯ ಸದಸ್ಯರನ್ನು ಸಂಪರ್ಕಿಸಬಹುದು . ಈ ಅಧ್ಯಯನವನ್ನು ಒಪ್ಪಿಕೊಳ್ಳಲು ಯಾವುದೇ ಬಲವಂತವಿಲ್ಲ. ನೀವು ಬಯಸದಿದ್ದರೆ ನೀವು ಪಡೆಯುವ ಕಾಳಜಿ ಬದಲಾಗುವುದಿಲ್ಲ

ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನೀವು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಒಪ್ಪಿಕೊಂಡರೆ ಮಾತ್ರ ನೀವು ಹೆಬ್ಬೆರಳು ಅನಿಸಿಕೆಗೆ ಸಹಿ / ಒದಗಿಸುವ ಅಗತ್ಯವಿದೆ

ರೋಗಿಯ ಎಡ ಹೆಬ್ಬೆರಳು ಅನಿಸಿಕೆ / ಸಹಿ ಸಾಕ್ಷಿಯ ಎಡ ಹೆಬ್ಬೆರಳು ಅನಿಸಿಕೆ / ಸಹಿ

ಹೆಚ್ಚಿನ ಮಾಹಿತಿಗಾಗಿ ಸಂಪರ್ಕಿಸಿ:

ಡಾ. ಮಾನಸ ದೀಕ್ಷಿತ್ ಸಿ

ಜನರಲ್ ಮೆಡಿಸ್ಥನ್,

ಶ್ರೀ ದೇವರಾಜ್ ಉರ್ಸ್ ವೈದ್ಯಕೀಯ ಕಾಲೇಜು

ದೂರವಾಣಿ ಸಂಖ್ಯೆ: 9902011512

ಒಪ್ಪಿಗೆ ಪತ್ರ

ಶೀರ್ಷಿಕೆ: - ಲಾಫಾಸ್ನ (ಲ್ಯಾಕ್ಟೇಟ್ ಉಚಿತ ಎ.ಪಿ.ಎ.ಎಸ್.ಎಲ್-ಎ ಸಿ ಎಲ್ ಎಫ್ ಸಂಶೋಧನಾ ಕನ್ಸೋರ್ಟಿಯಂ - ಕ್ರೋನಿಕ್ ಯಕೃತ್ತು ವೈಫಲ್ಯದ ಸ್ಕೋರ) ವಿರುದ್ಧ ಕ್ರೋನಿಕ್ ಯಕೃತ್ತು ವೈಫಲ್ಯದ ಮೇಲೆ ಪ್ರಮಾಣಿತ ಪ್ರೊಗ್ನೋಸ್ಟಿಕ್ ಸ್ಕೋರ್ಗಳ ತುಲನಾತ್ಮಕ ಅಧ್ಯಯನ

ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ: ಡಾ. ಮಾನಸ ದೀಕ್ಷಿತ್ ಸಿ

ನಾನು, ಶ್ರೀ/ ಶ್ರೀಮತಿ/ ಕುಮಾರಿ . ..., ಆರ್.ಎಲ್. ಜಲಪ್ಪ ಆಸ್ಪತ್ರೆಯಲ್ಲಿ " ಲಾಫಾಸ್ನ ತುಲನಾತ್ಮಕ ಅಧ್ಯಯನ (ಲ್ಯಾಕ್ಟೇಟ್ ಉಚಿತ ಎ ಪಿ ಎ ಎಸ್ ಎಲ್-ಎ ಸಿ ಎಲ್ ಎಫ್ ಸಂಶೋಧನಾ ಕನ್ಸೋರ್ಟಿಯಂ – ಕ್ರೋನಿಕ್ ಯಕೃತ್ತು ವೈಫಲ್ಯದ ಸ್ಕೋರ್ನಲ್ಲಿ ಕಾರ್ಯಗತಗೊಳಿಸಿ) ವಿ. ಎಸ್. ಕ್ರೋನಿಕ್ ಯಕೃತ್ತು ವೈಫಲ್ಯದ ಮೇಲೆ ಪ್ರಮಾಣಿತ ಪ್ರೊಗ್ನೋಸ್ಟಿಕ್ ಸ್ಕೋರ್ಗಳು" ನನ್ನನ್ನು ಅಧ್ಯಯನಕ್ಕೆ ಸೇರಿಸಲಾಗುವುದು.

ನನ್ನ ಕ್ಲಿನಿಕಲ್ ಪರೀಕ್ಷಾ , ತನಿಖೆಗಳು, ಮೌಲ್ಯಮಾಪನ ಅಧ್ಯಯನದ ಉದ್ದೇಶಕ್ಕಾಗಿ ದಾಖಲಿಸಲಾಗುತ್ತದೆ ಎಂದು ನನಗೆ ನನ್ನ ಸ್ವಂತ ಅರ್ಥವಾಗುವ ಭಾಷೆಯಲ್ಲಿ ವಿವರಿಸಲಾಗಿದೆ.

ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನನ್ನ ಭಾಗವಹಿಸುವಿಕೆ ಸಂಪೂರ್ಣವಾಗಿ ಸ್ವಯಂಪ್ರೇರಿತವಾಗಿದೆ ಮತ್ತು ನಾನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಅಧ್ಯಯನದಿಂದ ಹಿಂದೆ ಸರಿಯಬಹುದು ಮತ್ತು ಇದು ನನ್ನ ವೈದ್ಯರೊಂದಿಗಿನ ನನ್ನ ಸಂಬಂಧ ಅಥವಾ ನನ್ನ ಕಾಯಿಲೆಗೆ ಚಿಕಿತ್ಸೆಯ ಮೇಲೆ ಪರಿಣಾಮ ಬೀರುವುದಿಲ್ಲ ಎಂದು ನನಗೆ ವಿವರಿಸಲಾಗಿದೆ.

ಅಧ್ಯಯನದ ಅಪಾಯ / ಲಾಭದ ಬಗ್ಗೆ ನನಗೆ ವಿವರಿಸಲಾಗಿದೆ.

ಈ ಅಧ್ಯಯನದಿಂದ ಉತ್ಪತ್ತಿಯಾಗುವ ವೈದ್ಯಕೀಯ ಮಾಹಿತಿಯು ಸಾಂಸ್ಥಿಕ ದಾಖಲೆಗಳ ಭಾಗವಾಗಲಿದೆ ಮತ್ತು ನಾನು ಹೇಳಿದ್ದನ್ನು ಸಂಸ್ಥೆಯು ಗೌಪ್ಯವಾಗಿಡುತ್ತದೆ ಎಂದು ನಾನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ.

ಈ ಅಧ್ಯಯನವು ಉದ್ಭವಿಸುವ ಯಾವುದೇ ಡೇಟಾ ಅಥವಾ ಫಲಿತಾಂಶದ ಬಳಕೆಯನ್ನು ನಿರ್ಬಂಧಿಸದಿರಲು ನಾನು ಒಪ್ಪುತ್ತೇನೆ, ಅಂತಹ ಬಳಕೆಯು ವೈಜ್ಞಾನಿಕ ಉದ್ದೇಶಕ್ಕಾಗಿ ಮಾತ್ರ.

ವಿಚಾರಣೆಗಾಗಿ ನನ್ನ ಬಳಿ ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ ಮೊಬೈಲ್ ಸಂಖ್ಯೆ ಇದೆ.

ಚಿಕಿತ್ಸೆಯ ಅವಧಿಯುದ್ದಕ್ಕೂ ಗುಣಮಟ್ಟದ ಆರೈಕೆಯನ್ನು ನಿರ್ವಹಿಸಲಾಗುವುದು ಎಂದು ನನಗೆ ತಿಳಿಸಲಾಗಿದೆ.

ನಾನು, ನನ್ನ ಉತ್ತಮ ಮನಸ್ಸಿನಲ್ಲಿ, ಈ ಅಧ್ಯಯನದ ಭಾಗದಲ್ಲಿ ಸೇರಿಸಲು ಸಂಪೂರ್ಣ ಒಪ್ಪಿಗೆ ನೀಡುತ್ತೇನೆ.

ತನಿಖಾಧಿಕಾರಿ: ಡಾ. ಮಾನಸ ದೀಕ್ಷಿತ್ ಸಿ

ದೂರವಾಣಿ ಸಂಖ್ಯೆ: 9902011512

ಭಾಗವಹಿಸುವವರ ಸಹಿ / ಹೆಬ್ಬೆರಳು ಅನಿಸಿಕೆ

ಹೆಸರು:

ಸಾಕ್ಷಿಯ ಸಹಿ / ಹೆಬ್ಬೆರಳು ಅನಿಸಿಕೆ: ದಿನಾಂಕ:

ಹೆಸರು: ರೋಗಿಗೆ ಸಂಬಂಧ

MASTERCHART

S.no.	Age (years)	Gender	UHID	Admission	Discharge/death	Hospital stays	outcome (leaving hospital)	outcome @28 days
1	57	M	889411	1/14/2021	1/26/2021	12	discharge	alive
2	43	M	928283	6/28/2021	6/30/2021	2	discharge	alive
3	55	F	887875	1/6/2021	1/23/2021	17	discharge	alive
4	45	M	932544	7/18/2021	8/14/2021	27	death	dead
5	44	M	884345	12/21/2020	12/25/2020	4	death	dead
6	70	M	935565	7/7/2021	7/15/2021	8	discharged	alive
7	44	M	887465	6/24/2021	6/28/2021	4	death	dead
8	40	M	74555	4/8/2022	26-04-2022	18	discharge	alive
9	42	M	76275	4/15/2022	28-04-2022	13	discharge	alive
10	40	M	76495	4/16/2022	24-04-2022	8	death	dead
11	33	M	14037	1/22/2022	1/30/2022	8	death	dead
12	40	M	57337	12/1/22	30/1//22	18	discharge	alive
13	42	M	63913	16-02-2022	28-02-2022	12	death	dead
14	32	M	67007	5/3/22	31-03-2022	26	discharge	alive
15	50	M	71415	26-03-2022	27-03-2022	1	death	dead
16	55	M	70719	2/4/22	6/4/22	4	death	dead
17	50	M	66248	1/3/22	9/3/22	8	discharge at request	alive
18	40	M	62697	9/2/22	18-02-2022	9	discharge	alive
19	32	M	61829	5/2/22	22-02-2022	17	discharge	alive
20	38	M	69697	18-03-2022	26-03-2022	8	discharge	alive
21	30	M	70575	21-03-2022	22-03-2022	1	death	dead
22	77	M	58270	17-01-2022	31-01-2022	14	death	dead
23	72	M	14035	7/4/22	12/4/22	5	death	dead
24	74	M	70803	23-03-2022	31-03-2022	8	death	dead
25	40	M	68322	11/3/22	28-03-2022	17	discharge	alive
26	46	M	70021	19-03-2022	10/4/22	22	discharge	alive
27	46	M	65259	9/2/22	18-02-2022	9	discharge	alive
28	45	M	947499	18-09-2021	30-09-2021	12	discharge	alive
29	74	M	66714	4/3/22	16-03-2022	12	death	dead
30	37	M	71946	28-03-2022	15-04-2022	18	discharge	alive
31	49	M	60343	28-01-2022	8/2/22	11	discharge	alive
32	40	M	59513	15-02-2022	24-02-2022	9	discharge	alive
33	46	M	61004	1/2/22	9/2/22	8	discharge	alive
34	48	M	62209	8/2/22	21-02-2022	13	discharge	alive
35	70	M	83592	16-05-2022	23-05-2022	7	Death	dead
36	30	M	67946	10/3/22	10/3/22	0	Death	dead
37	40	f	66358	2/3/22	4/3/22	2	discharge at request	alive
38	65	M	935137	29-07-2021	2/8/21	4	discharge	alive
39	35	M	944689	6/9/22	17-09-2022	11	referral	dead (22/9/22)
40	60	M	39121	18-10-2021	20-10-2021	2	discharge	alive
41	43	M	50826	9/12/22	15-12-2022	6	discharge	alive
42	46	M	50015	6/12/21	16-12-2021	10	discharge	alive
43	55	M	51528	13-12-2021	25-12-2021	12	discharge	alive
44	60	M	52879	19-12-2021	30-12-2021	11	discharge	alive
45	42	f	54538	28-12-2021	30-12-2021	2	discharge	alive
46	52	M	64266	17-02-2022	22-02-2022	5	discharge	alive
47	48	M	39029	15-08-2022	26-08-2022	11	death	dead
48	50	M	169806	24.11.22	25.11.22	1	death	dead
49	42	M	179331	23.11.22	29.11.22	6	DAMA	dead
50	44	M	920826	10/6/2021	24-06-2021	14	discharge	alive
51	48	M	925883	18-06-2021	21-06-2021	3	death	death
52	58	M	925916	18-06-2021	28-06-2021	10	discharge	alive
53	46	M	923988	17-06-2021	30-06-2021	13	discharge	alive
54	54	M	929192	4/7/2021	24-07-2021	20	discharge	alive

55	44	M	932577	18-07-2021	25-07-2021	7	death	dead
56	38	M	928828	19-07-2021	9/8/2021	21	discharge	alive
57	60	M	942795	30-08-2021	28-09-2021	29	death	dead
58	35	M	949127	25-09-2021	8/10/2021	13	discharge	alive
59	48	M	942703	28-09-2021	15-10-2021	17	discharge	alive
60	60	M	937889	9/8/2021	15-08-2021	6	discharge at request	dead
61	40	M	45766	16-11-2021	26-11-2021	10	discharge	alive
62	42	M	57992	15-01-2022	27-01-2022	12	discharge	alive
63	49	M	53890	24-12-2021	1/2/22	39	discharge	alive
64	50	m	938449	11/8/2021	17-08-2021	6	death	dead
65	52	m	935949	31-07-2021	7/7/2021	7	discharge	alive
66	56	m	940863	21-08-2021	28-08-2021	7	discharge	alive
67	36	m	941002	22-08-2021	3/9/2021	12	discharge	alive
68	52	m	936013	31-07-2021	17-08-2021	17	discharge	alive
69	54	m	950007	29-09-2021	7/10/2021	8	discharge	alive
70	43	m	950105	29-09-2021	14-10-2021	15	discharge	alive
71	55	m	41835	30-10-2021	12/11/2021	13	discharge	alive
72	44	m	42681	10/11/21	15-11-2021	5	discharge at request	alive
73	60	m	46661	19-11-2021	27-11-2021	8	discharge	alive

S.no.	complaints	previous decompensation	hepatitis B / hepatitis C	alcohol history (IN YEARS)	last drink (days)	other comorbidities
1	abdominal pain / abdominal distension/ fever	yes	negative	10	14	
2	abdominal distension/ pain abdomen	no	negative	8	15	
3	fever / cough/dark stools	no	N/A	5	60	
4	abdominal distension / yellowish discolouration of eyes	yes	negative	15	14	
5	yellowish discolouration of eyes/altered sensorium	yes	negative	10	4	
6	abdominal distension /lower limb swelling/decreased responsiveness	no	n/a	4	10	Type 2 Diabetes mellitus
7	generalised swelling /fever/breathlessness/abdominal pain	yes	negative	15	21	
8	GTCS / fever / jaundice/ abdominal pain	no	negative	15	2	
9	jaundice/edema/abdominal distension	no	negative	nil	nil	T2DM
10	edema/breathlessness/vomiting	no	n/a	5	4	t2dm
11	abdominal pain / distension / jaundice	yes	n/a	10	30	
12	ABDOMINAL DISTENSION / abdominal pain	yes	negative	10	7	
13	abdominal distension jaundice	yes	negative	15	15	
14	abdominal distension jaundice swelling of limbs	no	negative	10	5	
15	fever/abdominal pain	yes	negative	12	6	
16	fever / abdominal distension / jaundice	no	negative	12	5	

17	abdominal distension	no	negative	10	14	
18	abdominal distension	no	negative	8	5	
19	abdominal pain	no	negative	10	4	
20	abdominal distension / edema/	no	negative	8	15	
21	abdominal pain / distension / jaundice	yes	negative	12	5	
22	abdominal distension / lower limb swelling	no	negative	15	7	
23	abdominal distension /jaundice /fever	no	negative	12	30	
24	abdominal distension / edema/	yes	negative	30	30	t2dm/htn
25	abdominal distension / jaundice	no	negative	12	3	
26	fever / abdominal distension / jaundice	no	negative	6	6	
27	abdominal pain abdominal distension	no	negative	8	3	
28	fever / pain abdomen / altered sensorium	no	negative	20	7	
29	abdominal distension / jaundice	no	negative	20	3	
30	abdominal distension / altered sensorium	no	negative	8	6	
31	Abdominal distension / generalised weakness	No	Negative	10	2	
32	Abdominal distension	No	Negative	6	5	
33	Abdominal distension / abdominal pain / fever	Yes	Negative	5	7	
34	jaundice / fever / abdominal distension	no	Negative	6	15	
35	Generalised weakness / nausea / vomiting	No	Negative	-	-	T2DM / HTN / IHD
36	Jaundice / fever	No	Negative	5	3	Native medication
37	Jaundice / nausea / abdominal pain	Yes	HbSAg	-	-	-
38	abdominal distension / pain abdomen	no	negative	20	6	
39	abdominal pain / malena	yes	negative	15	14	
40	swelling of limbs / easy fatiguability / appetite loss	no	negative	10	30	t2dm
41	abdominal pain	yes	negative	10	30	htn
42	lower limb swelling / generalised weakness	no	negative	8	1	
43	abdominal distension / loss of appetite	no	HbSAg	10	30	
44	abdominal distension / generalised weakness / jaundice	no	negative	7	12	
45	abdominal pain / generalised weakness	no	negative	6	5	
46	abdominal distension / loss of appetite	yes	negative	8	12	htn / copd
47	abdominal distension / fever / abdominal pain	yes	negative	12	8	
48	abdominal pain / altered sensorium, haemtemesis	yes	negative	15	14	
49	altered sensorium / fever / jaundice	no	negative	15	12	

50	**abdominal pain / jaundice**	**yes**	**negative**	**10**	**7**	
51	**altered sensorium / fever / jaundice**	**yes**	**negative**	**12**	**14**	
52	**abdominal distension / jaundice**	**yes**	**negative**	**15**	**7**	
53	**altered sensorium**	**no**	**negative**	**10**	**14**	
54	**abdominal distension / loss of appetite**	**yes**	**negative**	**14**	**6**	
55	**Altered sensorium / abdominal distension / jaundice**	**Yes**	**Negative**	**10**	**7**	
56	**abdominal distension / jaundice**	**no**	**negative**	**8**	**21**	
57	**altered sensorium / jaundice / abdominal distension**	**yes**	**negative**	**12**	**50**	**t2dm / htn**
58	**jaundice/ abdominal distension**	**yes**	**negative**	**7**	**6**	
59	**altered sensorium**	**no**	**negative**	**6**	**15**	**t2dm**
60	**altered sensorium**	**yes**	**negative**	**15**	**10**	**t2dm/htn**
61	**jaundice / abdominal distension**	**no**	**negative**	**8**	**12**	
62	**abdominal distension / jaundice / loss of appetite**	**no**	**negative**	**10**	**15**	
63	**altered sensorium**	**no**	**negative**	**12**	**5**	
64	**altered sensorium / jaundice / abdominal distension**	**yes**	**negative**	**15**	**14**	**t2dm**
65	**fever / abdominal distension / jaundice**	**no**	**negative**	**12**	**3**	
66	**loss of appetite limb swelling**	**no**	**negative**	**20**	**3**	
67	**lower limb swelling / generalised weakness**	**no**	**negative**	**10**	**15**	
68	**abdominal distension / jaundice / generalised weakness**	**yes**	**NA**	**8**	**10**	
69	**abdominal distension / loss of appetite**	**no**	**negative**	**6**	**30**	
70	**abdominal distension / vomiitng / generalised weakness**	**no**	**negative**	**7**	**5**	
71	**cough / fever / jaundice / abdominal distension**	**no**	**negative**	**10**	**15**	
72	**abdominal distension / jaundice / generalised weakness**	**no**	**negative**	**8**	**7**	
73	**abdominal distension / abdominal discomfort / loss of appetite**	**yes**	**negative**	**15**	**4**	

S.no.	CVS	CNS	Hepatic encephalopathy grade	Haemoglobin (gm%)	packed cell volume (%)	platelets (thousand/mm^3)	white blood cells count (thousand / mm^3)	urea	creat
1	Normal	Normal	0	11.1	31.4	128	17.56	18	0.7
2	Normal	Normal	0	11	38	108	12	48	1.3
3	Normal	Normal	0	11.4	30.8	122	19.7	43	1.3
4	Normal	Abnormal	3	11	30	108	11	52	2.4
5	Normal	Abnormal	4	10	29.1	85	9.03	33	2.6
6	Normal	Abnormal	3	11.5	31.2	119	8.1	36	1
7	Normal	Abnormal	3	10	32	95	12	104	3.9
8	Normal	Abnormal	2	12.2	32.8	138	17	26	0.8
9	Normal	Abnormal	2	7.2	21.9	50	9.2	25	0.9
10	Normal	Abnormal	2	7.7	21.4	134	9.05	33	0.6
11	Normal	Abnormal	1	8.8	27.6	66	15.63	107	1.6
12	Normal	Abnormal	1	12.34	43	178	35.34	105	1.7
13	Normal	Abnormal	2	12.5	35.6	168	16.15	52	0.9
14	Normal	Abnormal	2	12.8	35.2	30	10.96	257	5.6
15	Normal	Abnormal	1	12.7	34.7	170	11.28	30	1.2
16	Normal	Normal	0	9.3	27	96	17.5	72	1.7
17	Normal	Abnormal	1	5.8	16.9	120	10.16	43	0.9
18	Normal	Abnormal	2	12	37.2	216	14.39	55	0.9
19	Normal	Abnormal	3	7.2	20.8	271	31.86	21	0.7
20	Normal	Abnormal	2	12.5	40	420	22.68	60	0.7
21	Normal	Abnormal	2	8	24	78	12	24	0.4
22	Normal	Normal	0	9.4	28	72	10.2	68	1.1
23	Normal	Abnormal	1	7.1	21.6	352	7.6	132	4.4
24	Normal	Abnormal	2	11	30.3	333	8.56	74	1.5
25	Normal	Abnormal	1	11.5	34.6	30	4.23	12	0.6
26	Normal	Normal	0	9	28.6	103	13.2	34	0.7
27	Normal	Normal	0	11.2	36.1	108	12.4	29	0.7
28	Normal	Abnormal	3	11.5	35	58	31.2	64	1
29	Normal	Normal	0	12.1	33.5	415	10.46	60	1.5
30	Normal	Abnormal	3	9.8	28.6	180	15.87	21	0.5
31	Normal	Normal	0	16.2	47	109	9.48	27	1.1
32	Normal	Normal	0	12.5	35.3	171	6.17	26	1.2
33	Normal	Normal	0	11.4	37.1	107	12.2	66	1.3
34	Normal	Normal	0	12.4	40.1	112	14.2	10	0.5
35	Normal	Abnormal	3	9.7	27.9	104	17.03	124	4.8
36	Normal	Abnormal	3	12.4	38.8	53	16.52	71	2
37	Normal	Normal	0	10.7	31.9	167	5.89	48	1.2
38	Normal	Normal	0	12.7	35.7	139	8.94	19	0.9
39	Normal	Abnormal	3	10.6	29.4	38	4.53	55	1.3
40	Normal	Normal	0	12.1	42	122	6.54	20	1.1
41	Normal	Normal	0	11.8	30.6	59	6.71	14	0.6
42	Normal	Abnormal	2	6.3	17.5	80	5.99	13	0.7
43	Normal	Normal	0	12.6	39.2	304	6.13	25	0.7
44	Normal	Normal	0	12.6	37.6	131	9.18	25	1
45	Normal	Normal	0	12.4	35.5	76	4.38	22	1.2
46	Normal	Normal	0	15	45.5	199	10.5	36	1.1
47	Normal	Abnormal	3	8.6	24.2	78	12.2	108	2.9

48	Normal	Abnormal	4	10.8	29.8	102	15.42	166	5.2
49	Normal	Abnormal	3	10.1	32	50	4.12	57	2.1
50	Normal	Abnormal	1	12.6	38	77	8.4	54	1.1
51	Normal	Abnormal	3	11	32	74	9.6	74	1.7
52	Normal	Normal	0	12	34	112	8.8	55	1.3
53	Normal	Normal	0	13	37	105	7.6	64	1.1
54	Normal	Abnormal	1	10.4	28	112	4.8	26	0.7
55	Normal	Abnormal	3	9.4	30	78	6.9	128	1.9
56	Normal	Normal	0	12	30	94	6.8	56	0.9
57	Normal	Abnormal	3	10	28	65	11.2	66	2.1
58	Normal	Normal	0	12	34	128	6.5	74	0.9
59	Normal	Abnormal	1	13	35	177	4.9	44	1.1
60	Normal	Abnormal	3	9.8	30	134	8.5	76	1.2
61	Normal	Abnormal	1	10.4	26	122	6.1	44	0.8
62	Normal	Abnormal	1	12	34	203	6.5	45	1
63	Normal	Abnormal	3	11	33	133	7.8	64	1.1
64	Normal	Abnormal	3	10	32	74	6.1	90	2.6
65	Normal	Normal	0	12	34	112	7.4	40	0.7
66	Normal	Normal	0	11.6	32	108	6.5	52	0.9
67	Normal	Abnormal	1	12.4	33	78	7.9	66	1
68	Normal	Normal	0	9.7	26	112	8.3	70	0.6
69	Normal	Abnormal	1	8.4	25	68	8.9	66	1.1
70	Normal	Normal	0	10.5	31	144	7.1	38	0.8
71	Normal	Abnormal	1	11.2	31	98	11.6	77	1.1
72	Normal	Normal	0	10.8	33	122	6.8	94	0.9
73	Normal	Abnormal	1	11.7	32	178	7.4	76	0.9

S.no.	sodium	potassium	total billirubin	direct billirubin	Aspartate Transaminase	alanine transaminase	Alkaline Phosphatase	total protein	albumin	globulin
1	137	4.8	9	5.2	68	25	108	8.1	3	5.1
2	128	4.2	6.7	4	170	28	133	5	1.5	2.5
3	133	3.9	5.8	3.9	167	72	104	6.5	2.4	4.1
4	133	4.2	5.8	3.3	27	19	138	4	1.1	2.9
5	134	4.8	26.3	21.6	340	330	205	6.9	2.5	4.4
6	129	4.7	7	4.9	277	45	5.5	2.5	2.5	3
7	130	4.2	12	3	146	50	153	5.5	1.5	2.5
8	133	3.1	20.8	8.6	78	56	192	6.9	3.2	3.6
9	134	4.2	8	5.6	104	66	136	6	2.5	3.5
10	128	2.7	14.7	12.5	284	36	266	7	2.9	4.1
11	135	5.2	9.8	8.6	42	16	122	7.2	2.2	5
12	119	6.1	6.4	5	150	91	134	5.8	2.9	2.9
13	150	4.6	20.1	17.2	25	126	258	2.8	2.8	5
14	131	3.6	15.7	14.2	82	46	275	6	2.5	3.5
15	137	4	19.5	17.3	201	69	307	8.1	2.6	5.5
16	129	5.8	7.9	5.4	73	27	262	5.6	1.6	4
17	128	3.9	8.8	4.7	67	120	179	5.8	2	3.8
18	141	2.9	6.2	4.8	95	65	147	6.6	3.6	3
19	129	4.5	19.6	17.2	94	19	181	6.3	2.3	3.9
20	135	5.5	5	3.3	55	22	158	5.8	2.3	3.5
21	135	2.7	17.6	15	161	22	201	6.4	2.6	3.8
22	132	4.8	12.2	11.4	112	64	45	6	2.1	3.9

23	137	5	5.8	3.2	48	32	152	6.7	2.1	4.5
24	128	4.3	7.4	5.9	187	70	48.9	6	2.7	3.3
25	137	3.2	7.1	3.7	207	34	227	7.1	3.5	3.5
26	136	4.7	5.7	3.6	100	42	129	6.5	2.6	3.9
27	144	4	5.1	4.5	118	62	92	8	3.8	4.2
28	137	5	5.4	4.6	136	40	582	5.4	2.2	3.2
29	129	6.2	5.9	5	146	94	366	7.3	3.3	3.9
30	130	3.1	6.5	5.1	103	45	220	5.3	2.5	2.8
31	139	4.2	6.9	5.5	75	40	315	8.4	3.4	5
32	130	4.5	5.5	4	43	20	131	9	4.5	4.5
33	133	4.8	6.4	5.2	60	22	110	5.3	2.5	2.8
34	127	3.8	5.2	4.4	87	53	63	6.3	2.5	3.8
35	123	4.5	5.5	4.5	86	47	193	5.8	2.1	3.7
36	139	4.7	8.8	8.1	245	52	236	5	2.5	2.6
37	139	3.6	8.2	6.5	129	147	112	6.2	2.9	3.3
38	141	4	5.5	3.2	130	39	131	7.4	3.5	3.9
39	146	4.2	15.1	12.2	236	77	62	5.2	2.6	2.7
40	132	3.8	6.5	4.1	62	55	146	6.9	2.8	4.3
41	111	4.4	6.8	5.4	101	47	81	7.7	3	4.6
42	107	3.6	9.5	6.8	201	34	177	5	2.3	2.7
43	137	4	5.7	5.1	76	34	161	7.1	3	4.1
44	138	3.9	6.1	4.4	250	66	95	7.4	3	4.5
45	127	3.6	6.2	4.7	194	51	84	6.9	3.2	3.7
46	136	4.2	5.3	3.4	40	17	107	7.7	3.3	3.5
47	127	3.8	15.7	12.4	132	64	118	7.4	3.4	4
48	129	4.2	21.8	16.08	145	51	148	6.3	2.8	3.5
49	135	3.2	6.2	5.7	108	40	754	6.1	2	4.1
50	136	3.8	7.4	6.5	104	46	106	5.8	2.5	3.3
51	128	4.8	18.4	14.6	146	62	104	7.2	3.1	4.1
52	126	3.9	7.8	6.9	132	50	112	6.9	3.2	3.7
53	118	3.9	6.4	5.1	104	42	107	6	2.5	3.5
54	127	3.8	7	6.1	70	42	78	6.2	3	3.2
55	130	3.7	18	15.4	167	56	134	6	2.9	3.1
56	135	4	5	3.7	112	40	112	7.1	3.1	4
57	127	3.6	12	9.8	104	33	164	6	2.5	3.5
58	136	3.7	6	3.5	101	56	74	7.2	3.4	3.8
59	128	3.9	7	5.7	78	37	64	6	2.5	3.5
60	134	5.1	7.4	5.6	90	46	88	6.4	3	3.4
61	133	4.6	5.4	3.6	88	34	118	7.2	3.2	4
62	138	4.2	5.1	4.2	102	65	78	6.8	3.3	3.5
63	133	4.7	6.1	3.8	104	70	56	6.1	2.8	3.3
64	128	3.9	9.4	6.3	134	68	147	6.4	2.7	3.7
65	133	3.6	6.2	4.1	94	44	112	7	3.2	3.8
66	134	4.8	7	6.2	112	56	146	6.5	3.2	3.3
67	137	3.8	6.1	5.2	104	51	136	6.8	3.4	3.4
68	136	3.1	5.1	3.6	78	44	122	6.7	3.5	3.2
69	134	3.6	5.3	3	88	34	104	6.7	3.3	3.4
70	135	3.8	5.8	4.1	76	34	94	6.8	3.2	3.6
71	124	3.7	5.4	4.2	78	33	98	6	2.5	3.5
72	133	3.6	5.6	3.9	136	63	173	6.4	2.9	3.5
73	129	4.1	6.7	4.2	176	58	112	6.4	3.1	3.3

S.no.	A/G ratio	Gamma Glutamyl Transferase	Prothrombin time	Activated Plasma Thromboplastin time	international normalised ratio	CLIF C ACLF	MELD	MELDNa	LaFAAS	Child-Pugh	Child - Pugh Class
1	0.6	60	24	59	1.9	44	23	14	6	11	C
2	0.7	137	24	64.2	1.82	36	29	28	6	12	C
3	0.6	393	24.5	63.4	2.15	47	28	27	6	13	C
4	0.7	163	21.3	66.3	1.82	43	31	30	9	14	C
5	0.6	134	33	112.8	3.08	54	42	40	12	15	C
6	0.7	140	24.3	58.4	1.8	51	25	26	8	14	C
7	0.6	154	43	78.3	3.8	59	43	43	10	15	C
8	0.8	469	22.7	40	1.98	44	27	28	8	12	C
9	0.7	135	19	34	1.6	37	23	23	6	12	C
10	0.7	166	28.6	48.4	2.07	43	28	29	6	12	C
11	0.4	34	31.5	45.2	2.92	47	33	33	9	14	C
12	1	300	24	32.9	2.09	48	32	32	8	12	C
13	0.6	106	26.5	27.1	2.37	47	29	27	8	13	C
14	0.7	344	16.9	30.9	1.8	44	37	37	9	13	C
15	0.5	163	38.1	40.5	3.65	52	35	34	9	14	C
16	0.4	57	33.7	36.1	3.16	50	36	34	8	13	C
17	0.5	86	27.3	35.9	2.46	44	30	29	7	14	C
18	1.2	365	24.3	33	2.08	42	21	22	7	11	C
19	0.59	139	24.7	49.9	2.17	51	30	30	9	14	C
20	0.7	33	22.6	36	1.94	41	22	22	7	13	C
21	0.7	572	44.1	128	4.35	47	34	35	8	14	C
22	0.5	112	27	40.8	2.4	55	30	29	6	13	C
23	0.47	52	22.5	32.6	1.94	55	32	34	8	13	C
24	0.8	556	21	53.5	1.8	49	29	29	7	13	C
25	1	806	28.4	40.3	2.56	38	23	26	7	13	C
26	0.7	172	24.9	31.6	2.2	38	23	24	6	12	C
27	0.9	421	15	30	1.9	34	19	20	6	10	C
28	0.7	427	27.4	41.7	2.3	53	24	23	8	15	C
29	0.9	565	22.7	41.7	1.8	47	27	28	6	11	C
30	0.9	153	20	38	1.6	45	23	24	6	13	C
31	0.6	133	22.6	31.6	1.9	37	22	22	6	11	C
32	1	257	19.7	31.1	1.65	27	23	25	5	9	B
33	0.9	118	20	32	1.68	37	25	25	5	11	C
34	0.6	61	22.5	32.6	1.95	36	26	27	5	12	C
35	0.6	126	19.4	41.5	1.63	59	35	35	8	13	C
36	1	163	19.4	30.3	1.6	46	28	27	8	13	C
37	0.9	65	20.5	31	1.7	30	25	23	5	11	C
38	0.9	630	19	29.8	1.56	40	19	18	5	10	C
39	0.9	65	20.6	33.7	1.74	49	28	25	8	14	C
40	0.6	18	18.6	30.2	1.5	39	22	23	5	10	C
41	0.6	80	24	33	1.9	32	26	28	4	11	C
42	0.9	721	23.5	36	2.05	43	28	29	7	14	C
43	0.7	58	19	33	1.6	33	19	20	5	10	C
44	0.6	98	12.8	25.8	1.75	41	20	21	5	11	C
45	0.8	104	15.8	27	1.6	29	26	27	5	10	C
46	0.9	305	19.3	30	1.62	35	20	21	5	10	C
47	0.8	164	45	66	4.4	61	45	42	11	14	C

48	**0.8**	**120**	**38**	**60**	**4.2**	**67**	**46**	**45**	**11**	**14**	**C**
49	**0.5**	**186**	**24.9**	**59.2**	**2.2**	**42**	**31**	**31**	**9**	**14**	**C**
50	**0.7**	**94**	**18.6**	**28**	**1.64**	**37**	**23**	**22**	**6**	**12**	**C**
51	**0.7**	**106**	**34**	**64**	**3.8**	**50**	**39**	**38**	**11**	**14**	**C**
52	**0.8**	**256**	**18**	**26**	**1.7**	**40**	**27**	**29**	**5**	**11**	**C**
53	**0.7**	**93**	**17.6**	**24.8**	**1.54**	**34**	**26**	**27**	**5**	**11**	**C**
54	**1**	**412**	**18**	**27**	**1.6**	**38**	**24**	**26**	**6**	**11**	**C**
55	**1**	**356**	**27**	**64**	**6**	**53**	**44**	**43**	**11**	**14**	**C**
56	**0.7**	**119**	**16**	**28**	**1.56**	**27**	**19**	**20**	**5**	**10**	**C**
57	**0.7**	**64**	**21**	**41.7**	**2.4**	**62**	**36**	**35**	**9**	**15**	**C**
58	**0.9**	**104**	**19**	**35**	**1.7**	**29**	**20**	**21**	**5**	**11**	**C**
59	**0.7**	**84**	**17**	**35**	**1.6**	**36**	**25**	**26**	**6**	**12**	**C**
60	**0.8**	**133**	**20**	**35**	**1.7**	**47**	**24**	**24**	**7**	**13**	**C**
61	**0.8**	**213**	**18**	**38**	**1.6**	**30**	**20**	**22**	**6**	**11**	**C**
62	**1**	**122**	**19**	**28**	**1.6**	**32**	**18**	**19**	**6**	**11**	**C**
63	**0.8**	**218**	**17**	**32**	**1.5**	**42**	**22**	**22**	**7**	**12**	**C**
64	**0.7**	**111**	**32**	**54**	**3.1**	**54**	**40**	**38**	**10**	**15**	**C**
65	**0.8**	**264**	**18**	**34**	**1.6**	**37**	**21**	**22**	**5**	**10**	**C**
66	**1**	**178**	**19**	**37**	**1.6**	**37**	**21**	**22**	**5**	**10**	**C**
67	**1**	**83**	**21**	**32**	**1.7**	**34**	**19**	**21**	**6**	**12**	**C**
68	**1.1**	**112**	**17**	**28**	**1.6**	**34**	**18**	**20**	**4**	**10**	**C**
69	**1**	**62**	**18**	**32**	**1.5**	**38**	**20**	**21**	**6**	**11**	**C**
70	**0.8**	**178**	**20**	**34**	**1.8**	**29**	**21**	**22**	**6**	**11**	**C**
71	**0.7**	**144**	**21**	**42**	**2.1**	**47**	**28**	**29**	**7**	**13**	**C**
72	**0.8**	**86**	**24**	**45**	**2.4**	**33**	**25**	**26**	**6**	**12**	**C**
73	**1**	**214**	**26**	**44**	**2.5**	**46**	**27**	**28**	**7**	**13**	**C**