A STUDY ON THE EFFECT OF SHORT-TERM IV HUMAN ALBUMIN INFUSION IN HOSPITALIZED PATIENTS WITH ACUTE DECOMPENSATION OR COMPLICATIONS OF CHRONIC LIVER DISEASE ON MORBIDITY AND MORTALITY IN HOSPITAL UNIVERSITY SAINS MALAYSIA.

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DISSERTATION SUBMITTED IN PARTIAL

FULFILMENT OF THE REQUIREMENT

FOR MASTER OF MEDICINE

(INTERNAL MEDICINE)

UNIVERSITI SAINS MALAYSIA

2022

ACKNOWLEDGEMENT

I would like to express my gratitude to Allah SWT for giving me the opportunity and endlessly guiding me in the completion of this thesis. The completion of this undertaking could also not have been possible without participation, cooperation, and assistance from so many parties whose names may not all be enumerated. Their contributions are sincerely appreciated and gratefully acknowledged. However, I would like to express my deep and utmost appreciation, particularly to the following people:

1. Dr. Amry Bin Rahim, my main supervisor, who had assisted and provided guidance in carrying out this study until its completion. This work would not have been possible without his support and encouragement.
2. Prof Madya Dr Najib Majdi Bin Yaacob, my co-supervisor, who had been supportive and provided invaluable advice during the progress of this study.
3. My colleagues, especially Dr Phong Qiu Shi and all the other staff in the Department of Internal Medicine, Hospital USM who constantly provided support and inspiration that enabled me to complete this research project.
4. My family, for their unconditional support and constant prayers that enabled me to complete my dissertation.

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LIST OF SYMBOLS, ABBREVIATIONS AND ACRONYMS

CLD	Chronic Liver Disease
SMT	Standard Medical Therapy
HA	Human Albumin
IV	Intravenous
HUSM	Hospital Universiti Sains Malaysia
RAAS	Renal Angiotensin Activating System
HRS	Hepatorenal syndrome
LVP	Large Volume Paracentesis
PICD	Paracentesis-induced circulatory dysfunction
SBP	Spontaneous Bacteria Peritonitis
GIB	Gastrointestinal Bleeding
NAFLD	Non-alcoholic Fatty Liver Disease
ATTIRE	Albumin To prevenT Infection in chronic liveR failurE
HCV	Hepatitis C Virus
AASLD	American Association for The Study Of Liver Disease
EASL	European Association for The Study of The Liver

ABSTRAK

Latar belakang: Albumin adalah konstituen utama tekanan onkotik plasma yang memodulasi pengedaran cecair di antara bahagian-bahagian badan. Pemahaman yang lebih baik tentang fungsi fisiologi albumin yang lain telah meluaskan penggunaannya melangkaui penyelenggaraan volum intravaskular. Dalam pesakit sirosis, albumin digunakan dalam usaha untuk mengurangkan pembentukan asites, untuk meningkatkan fungsi peredaran darah dan buah pinggang dan mengurangkan sindrom hepatorenal pada pesakit yang mengalami peritonitis bakteria spontan. Walau bagaimanapun, terdapat kontroversi sama ada mensasarkan albumin serum yang lebih tinggi akan memberi manfaat kepada pesakit sirosis kerana kekurangan ujian klinikal berskala besar . Oleh itu, kajian ini bertujuan untuk membandingkan sama ada infusi albumin dengan mensasarkan albumin serum yang lebih tinggi 30 g per liter atau lebih, berbanding dengan penjagaan perubatan standard, akan meningkatkan kelangsungan hidup jangka pendek dalam pesakit sirosis yang dirawat di hospital

Metod: Kajian kohort retrospektif telah dijalankan di Hospital Universiti Sains Malaysia dari tahun 2017 hingga 2022 ke atas 198 pesakit berumur antara 27 ke 86 tahun yang telah dimasukkan ke hospital akibat penyakit hati dekompensasi dengan tahap albumin serum kurang daripada 30 g seliter semasa kemasukan. Pesakit telah disaring sama ada menerima terapi perubatan standard bersama albumin manusia intravena selama 3 hari atau terapi perubatan standard sahaja. Titik akhir utama komposit ialah kadar kelangsungan hidup pada hari ke-14 selepas permulaan rawatan atau kemasukan ke hospital dengan terapi perubatan standard. Masa kelangsungan hidup dianalisis dengan

kaedah Kaplan Meier dan dibandingkan antara kumpulan melalui ujian Log-rank. Perubahan dalam parameter antara dua kumpulan dan dalam kumpulan telah diuji menggunakan ukuran berulang ANCOVA.

Keputusan: Hasil daripada kajian kami menunjukkan peningkatan yang ketara dalam masa kelangsungan hidup median di kalangan pesakit yang menerima albumin manusia berbanding terapi perubatan standard sahaja (*P* <0.001). Pengukuran berulang ANCOVA menunjukkan bahawa min albumin berbeza dengan ketara antara titik masa dalam kedua-dua terapi perubatan standard sahaja (F=37.18, *P*<0.001) dan kumpulan albumin manusia (F=9.833, *P*=0.002). Analisis perbandingan berbilang dengan pelarasan Bonferroni mendedahkan bahawa albumin meningkat secara signifikan dari pengukuran awal hingga akhir (adj MD: -1.47, 95% CI: -2.40 hingga -0.53) dalam kumpulan terapi perubatan standard bersama albumin manusia. Sebaliknya, min albumin secara statistik menurun dengan ketara daripada pengukuran awal hingga akhir (adj MD: 1.68, 95% CI: 1.13 hingga 2.23) dalam kumpulan terapi perubatan standard sahaja.

Kesimpulan: Infusi albumin manusia dalam sirosis hati dekompensasi akut adalah berfaedah dan ketara meningkatkan kelangsungan hidup jangka pendek. Walau bagaimanapun, terdapat keperluan untuk ujian yang teguh untuk menilai penggunaan albumin manusia dengan mensasarkan tahap albumin serum yang lebih tinggi dalam rawatan pesakit yang dirawat di hospital dengan komplikasi berkaitan sirosis.

Kata kunci: sirosis hati, Albumin Manusia, Terapi perubatan standard, Sirosis hati dekompensasi akut.

ABSTRACT

Background: Albumin is the main constituent of plasma oncotic pressure which modulates the distribution of fluid in between the body compartments. Better understanding of albumin's other physiologic functions has expanded its application beyond the maintenance of intravascular volume. In cirrhotic patients, albumin is used to reduce ascites formation, improve circulatory and renal functions, and prevent hepatorenal syndromes in those with spontaneous bacterial peritonitis. However, there is a controversy of whether targeting higher serum albumin would be beneficial in cirrhotic patient due to confirmatory large-scale clinical trials that are still lacking. Therefore, this study aimed at comparing whether an albumin infusion with aiming a higher serum albumin 30 g per litre or more, as compared with standard medical care, would improve short term survival of hospitalized cirrhotic patients.

Methods: A retrospective cohort study was conducted in Hospital Universiti Sains Malaysia year 2017 to 2022 on 198 patients between the ages of 27 to 81 years old who had been hospitalized due to decompensated liver disease with serum albumin level of less than 30 g per litre on admission. Patient were screened through either received standard medical therapy with 3 days intravenous human albumin or standard medical therapy alone. The primary composite end point was the survival rate at day 14 after the initiation of treatment or hospitalization with standard medical therapy. The survival time was analysed using Kaplan Meier method and compared between groups by means of the Log-rank test. The changes in parameters between two groups and within the group were tested using repeated measure ANCOVA.

Results: The outcome from our study denoted a significant improvement in the median survival time among patients who received human albumin as compared to standard medical therapy alone (***P***<0.001). Repeated measure ANCOVA indicate that mean albumin differed significantly between time points in both standard medical therapies alone (F=37.18, ***P***<0.001) and human albumin group (F=9.833, ***P***=0.002). Multiple comparison analyses with a Bonferroni adjustment revealed that there was a significant increase in mean albumin from initial to the final measurement (adj MD: -1.47, 95% CI: -2.40 to -0.53) for the standard medical therapy with human albumin group. In contrast, the was a significant decrease in mean albumin from initial to final measurement (adj MD: 1.68, 95% CI: 1.13 to 2.23) for the standard medical therapy alone group.

Conclusion: Human albumin infusion in an acute decompensated liver cirrhosis is beneficial and notably improved short-term survival of patients. Nevertheless, there is a need for a robust and randomized controlled trials to appraise the use of human albumin with aimed at higher serum albumin level in the treatment of hospitalized patients with cirrhosis-related complications.

Keywords: liver cirrhosis, Human Albumin, Standard medical therapy, Acute decompensated liver cirrhosis

CHAPTER 1: BACKGROUND

1.1 Introduction

Liver disease accounts for approximately 2 million deaths per year worldwide. According to the latest WHO data published in 2020, death caused by liver disease, accounted for 3.05% (5 125) of the country's total death. The age adjusted death rate is 17.91 per 100,000 of the population in Malaysia. Moreover, liver cirrhosis is the 14th most common cause of death, causing over a million death per year worldwide. Therefore, many studies have been published regarding the dismal prognosis of decompensated liver cirrhosis with an overall survival of 2-4 years (Carvalho and Machado, 2018).

The natural history of cirrhosis is characterised by an asymptomatic compensated phase followed by a decompensated phase, marked by the development of overt clinical signs. The most common are ascites, bleeding, encephalopathy, and jaundice (Guidelines, 2018). The most frequently seen liver decompensation sign is ascites and once it develops, about one-half of the patient will be succumb to death within 5 years (Planas et al., 2006).

Human albumin is crucial in maintaining fluid balance in the body by regulating the oncotic pressure between the intra- and extra-vascular spaces (Quinlan et al., n.d.). Its oncotic power, prolonged half-life, and ability to attract water from the interstitium to the intravascular compartment through indirect osmotic function make albumin a powerful plasma expander (Caraceni et al., n.d.). As the result, it is the most used to reduce abnormal fluid build-up by cirrhosis and preclinical studies support its anti-inflammatory role. Nevertheless, albumin is comparatively costly than other fluids, shortages in

production do occur, crucially, confirmatory large-scale clinical trials to support its use are still lacking (Fernández et al., 2019).

Albumin is a major prognostic factor in liver cirrhosis. It is significant predictor of death. A low serum albumin level has been associated with an increased risk of death among hospitalized patients who have decompensated liver disease and infections and albumin infusions that increase serum level more than 30g/L have reduced systemic inflammation among patients with decompensated cirrhosis (Fernández et al. 2019). As the result, albumin treatment has been widely used due to its oncotic properties, enabling it to abrogate the cardiocirculatory changes associated with portal hypertension.

At the present, there are three approved indications for administration on human albumin in liver cirrhosis which include after large volume paracentesis to prevent paracentesis-induced circulatory dysfunction, spontaneous bacterial peritonitis and hepatorenal syndrome. Other proposed indications for albumin use are still controversial. A randomized trial of albumin infusions in hospitalized patients showed that an increase in the albumin level to a target of 30 g/L or more was not more beneficial than the current standard of care in the United Kingdom (China et al., 2021). Thus, in this study, we aim to review the benefits of short-term IV human albumin in hospitalized patient with acute decompensation or complication of chronic liver disease.

1.2 Objectives

1.2.1 General Objective:

To compare the effect of short-term IV human albumin treatment in comparison with standard medical treatment among patients with acute decompensation or worsening complications of CLD.

1.2.2 Specific Objectives:

1. To compare the 14-days survival between patients who receive short-term IV human albumin and those receiving standard medical therapy
2. To compare changes in clinical parameters (Child- Pugh score, total bilirubin, albumin level and INR) between patients who receive short-term IV human albumin and standard medical treatment.

1.3 Hypothesis

1. Administration of short-term IV human albumin in hospitalized CLD patients improve patient's short-term survival compared to those receiving standard medical therapy alone.
2. There will be improvement in clinical parameters (Child- Pugh score, total bilirubin, albumin level and INR) in patients who receive short-term IV human albumin compared to those receiving standard medical therapy alone.

1.4 Research Question

1. Does the use of short-term IV human albumin in hospitalized CLD patients improve 14 days survival as compared to those who received standard medical therapy alone?
2. Are there any changes in clinical parameters between patients who receive short-term IV human albumin and standard medical therapy alone?

CHAPTER 2: LITERATURE REVIEW

2.1 The effect of long-term albumin administration on mortality in decompensated liver cirrhosis.

The ANSWER (human albumin for the treatment of ascites in patients with hepatic cirrhosis) trial, published in 2018, was the first prospective study of long- term albumin administration in cirrhosis patients. Albumin in combination with standard medical therapy has shown to act as a disease-modifying treatment and prolonged overall survival, with a 38% reduction in the mortality hazard ratio compared with SMT alone. It also improved patient's quality of life, and is cost effective (Caraceni et al., 2018).

On the contrary, the main findings of the ANSWER study, namely improved survival, and reduced incidences of complications, were not confirmed by the MACHT study, a prospective, randomized placebo-controlled study that enrolled patients with decompensated cirrhosis who were waiting for liver transplant. In this trial, patients included in the active arm of the study received long- term midodrine plus albumin (40 g every 15 days; a median duration of 80 days), while the control group received SMT plus placebos. There were no significant differences between the groups in the cirrhosis complications or survival rates (Solà et al., 2018)

2.2 The effect of albumin infusions on mortality in hospitalized liver cirrhosis patient.

China et al found albumin infusions in hospitalized cirrhosis patients with an albumin level that was increased to a target of 30 g/L or more, had similar results as the current standard care in the United Kingdom. The trial involved 777 hospitalized patients with decompensated cirrhosis who had a serum albumin level of less than 30 g/L randomly assigned to receive either targeted 20% human albumin solution for up to 14 days or until discharge, whichever came first, or standard care. According to study, there were no significant differences between the groups with the respect of death or time to death, development of complications, and hospitalization duration. (China et al., 2021).

2.3 Indication of albumin treatment in liver cirrhosis.

In liver cirrhosis, albumin synthesis is reduced because of liver dysfunction and abnormal blood flow distribution (Garcia-Martinez et al., 2013). The reduction in albumin level causes a decrease in intravascular blood volume that leads to compensatory activation of the renin-angiotensin system and sympathetic nervous system, and to an increased release of antidiuretic hormone, which culminated in salt and water retention, as well as renal perfusion reduction (Arroyo et al., 2000). Hence, human albumin was first introduced in the management of cirrhotic patients who had hypoalbuminemia and ascites in the 1950s, due to its oncotic properties (Garcia-Martinez et al., 2013) . The current recommendations of human albumin infusion in patients with liver cirrhosis is spontaneous bacterial peritonitis (SBP), Hepatorenal syndrome (HRS), and after large volume paracentesis (LVP) to prevent paracentesis-induced circulatory dysfunction (Guidelines,

2018)(Runyon, 2013). Other indication of albumin infusion such as volume expansion is still controversial (Sharma et al., 2017)Thévenot et al., 2014).

2.4 Albumin for spontaneous bacterial peritonitis.

The first randomized study assessing the beneficial of albumin infusion performed in 1999 showed that patients with cirrhosis and SBP receiving cefotaxime plus had a reduced mortality rate as compared to patients receiving cefotaxime alone (Of et al., 1999). Another study analysed 200 high risk cirrhotic patients with SBP who randomly received

only albumin, terlipressin alone, low dose albumin plus terlipressin or midodrine (Salman et al., 2016). Using terlipressin in combination with low-dose albumin lead to a low incidence of renal impairment and reduce inpatient's mortality rate (Salman et al., 2016).

2.5 Albumin in the treatment of hepatorenal syndrome.

Albumin plus terlipressin were more effective in improving renal function than the combination of albumin, midodrine and octreotide providing a survival advantage in responder patients (Cavallin et al., 2015). The administration of terlipressin or noradrenaline in combination with albumin is effective at reversing HRS, and responding patients had a greater survival rate than non- responders, potentially extending the time to liver transplant (Saif et al., 2018).

2.6 Albumin in abdominal paracentesis

After large volume paracentesis, intraabdominal pressure drops abruptly, which increases venous return to right arterial pressure leads to increase in cardiac input and stroke volume According to AASLD and EASL guidelines, LVP should be performed together with the administration of albumin to prevent paracentesis-induced circulatory dysfunction (Guidelines, 2018)(Runyon, 2013).

2.7 Conceptual framework

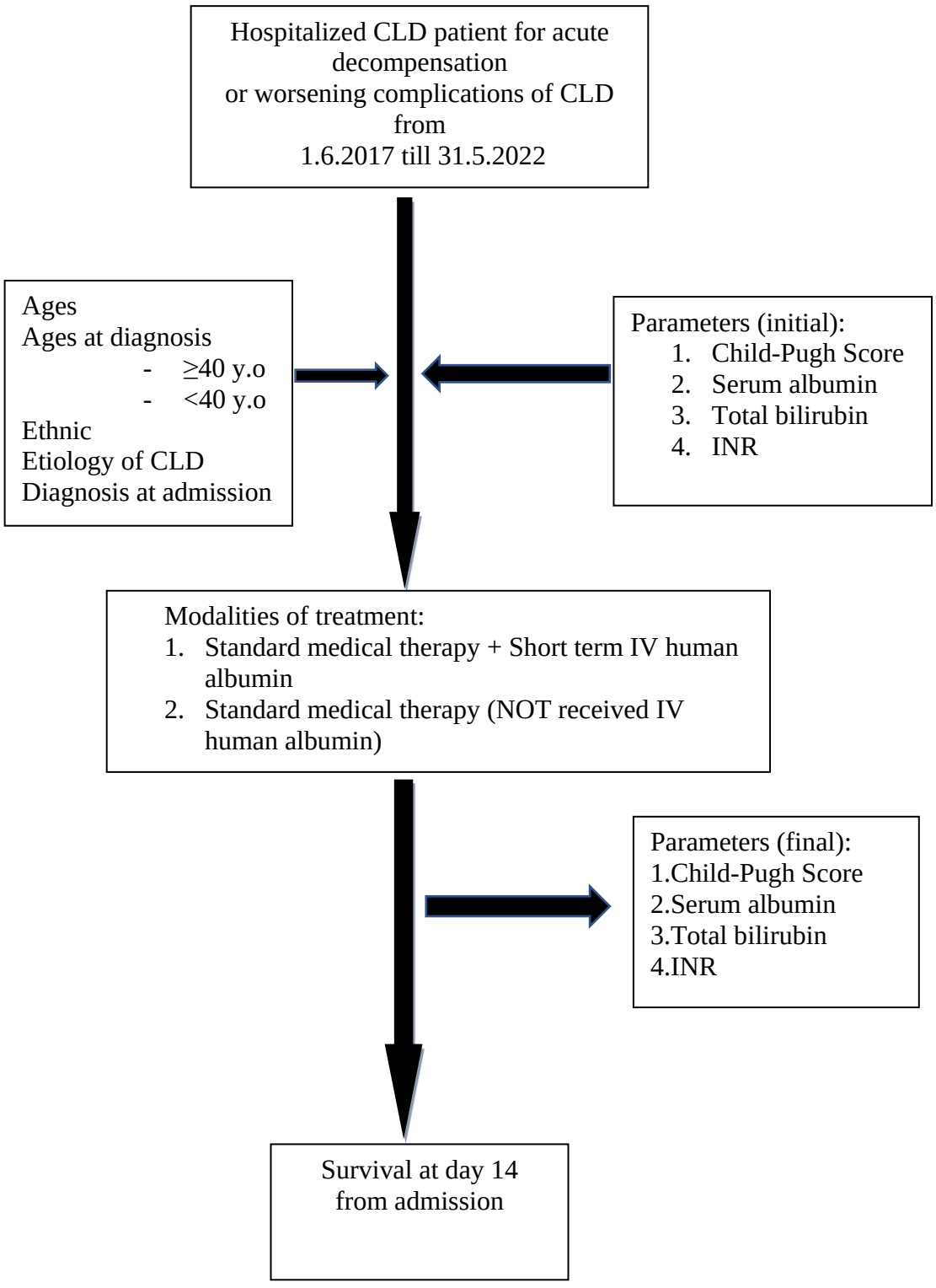


Figure 1: Conceptual framework

2.8 Rationale of Study

This study was conducted to ascertain whether the use of short-term IV human albumin justifies the management of hospitalized CLD patients with acute decompensation or worsening complication of CLD. Reduced serum albumin concentration is a well-established indicator of a poorer outcome for cirrhotic patients. The management of decompensated cirrhosis creates a heavy burden for the healthcare system, and effective treatment can prevent serious complications and improve patient's quality of life and survival.

As for our current practice, hospitalised CLD patients will be given human albumin for a short-term duration if serum albumin concentration is less than 30 gram per litre. However, there was a group of patients who did not receive human albumin despite having low serum albumin due to various causes, which includes, the avaibility of human albumin, absence of oedema and other causes. If the result of this study is able to prove that the use of short-term human albumin is beneficial to hospitalised CLD patients, we may propose that all CLD patients with acute decompensation or worsening complication of CLD should be given human albumin.

CHAPTER 3: METHODOLOGY

3.1 Study Design:

This is a retrospective cohort study which was conducted in USM Hospital, Kubang Kerian, Kelantan, Malaysia for a period of one and a half years from May 2020 to May 2022. Data collected were from June 2017 to May 2022.

3.2 Sample Area:

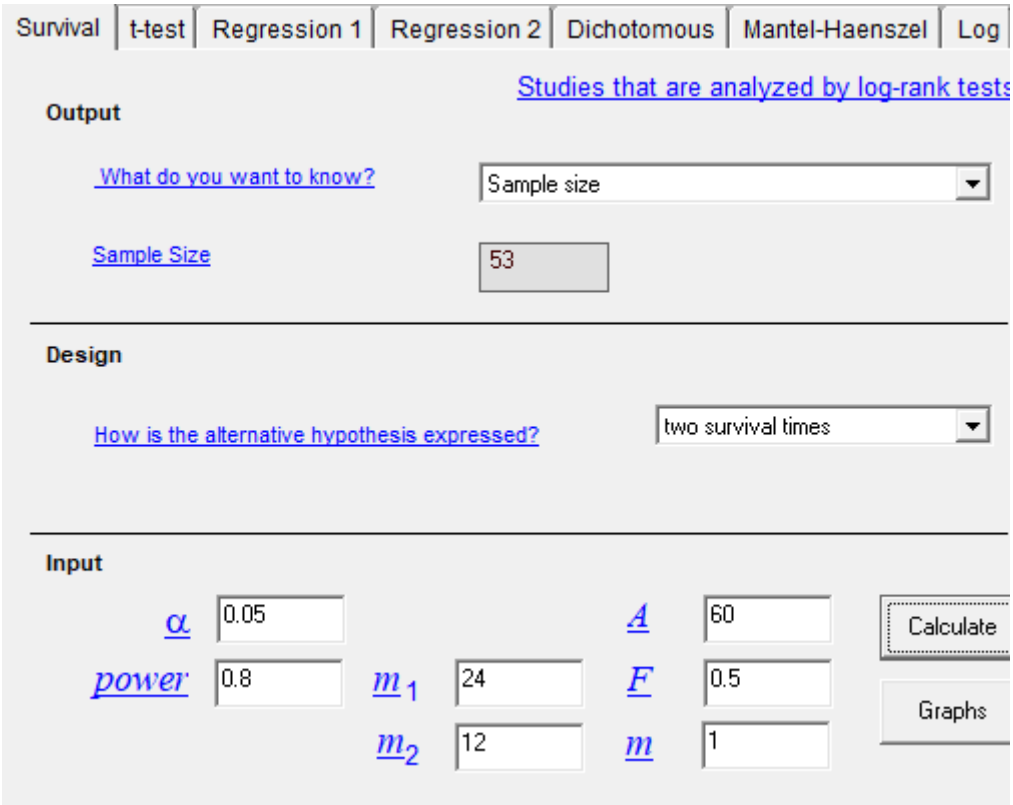
The study included medical wards, the high dependency and intensive care units in HUSM.

3.3 Study population:

I. Reference population - Patients with confirmed case of chronic liver disease in Kelantan.
II. Source population - Patients with confirmed case of chronic liver disease who were admitted for acute decompensation or worsening complication of CLD from 2017 onwards.
III. Sampling frame - Patients with confirmed case of chronic liver disease who were admitted for acute decompensation or worsening complication of CLD from 2017 onwards based on inclusion and exclusion criteria.

3.4 Sample Size Estimation:

1. For objective 1: To compare the 14-days survival between patients receiving short-term IV human albumin and those receiving standard medical therapy.Sample size calculated using Power & Sample Size calculator version 3.1.2 and using the following parameters.
    - $\alpha = 0.05$
    - Power: 80%
    - m 1: the median time among the standard medical therapy plus human albumin group (by literature)
    - m2: the median time among the standard medical therapy group (from the population)
    - m: ratio of prognostic to standard medical therapy group (from the population)
    - Accrual time (A): 60 months
    - Additional follow up (F): 14 days (~0.5 month)

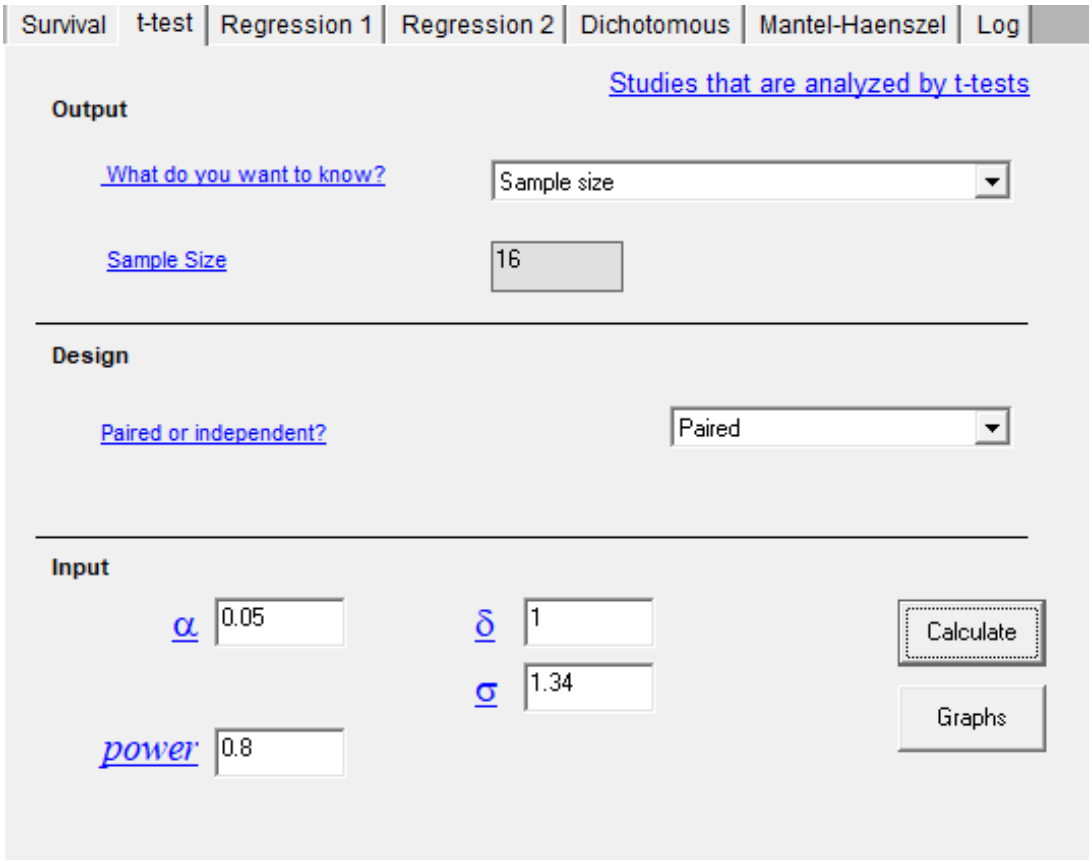


Based on expert opinion the median survival time for CLD patients with standard medical therapy and human albumin is, 24 month and the median survival time in CLD without IV human albumin is 12 months.

Total subjects for sample size were 106 (53 in the control group and 53 in interventional group). In the event, 50% of sample size is not achieved, the total sample size needs to be divided with 0.5, thus total subjects for sample size will be 212 (106 in control group and 106 in interventional group).

2. For objective 2: To compare changes in clinical parameters (Child- Pugh score, total bilirubin, albumin level and INR) between patients who are receiving short term IV human albumin and standard medical treatment. Sample size is calculated using Power & Sample Size calculator version 3.1.2 with the following parameters

- $\alpha = 0.05$
- Power: 80%
- **δ:** A difference in population means
- **σ:** A difference in the response of matched pairs



Based on a study by (Gentilini et al., 1999), the difference in response to albumin is 1.34, while difference in the mean response is 1. Total subjects for sample size will be 32 (16 in the control and 16 in interventional group).

The highest sample size required for objective 1 is 106. Thus, the final sample size required for my study is 212 divided into 106 patients in each group.

3.5 Sampling Method

Convenience sampling method was applied. All CLD patients were above 18 years old and admitted for acute decompensation or worsening complication of CLD were screened using the inclusion and exclusion criteria. All eligible patients were included in the study.

3.6 Subject criteria

Inclusion criteria:

1. Subjects are adult CLD patients who were diagnosed based on histopathology or radiology imaging.
2. All patients admitted to hospital with acute decompensation or worsening of complications of chronic liver disease
3. Subjects are above 18 years old.
4. Serum albumin <30g/dl at the time of admission

Exclusion criteria:

1. Subjects with severe comorbidities include ESRF, heart failure with reduce EF and terminal stage cancer.
2. Advanced hepatocellular carcinoma with life expectancy of less than 12 weeks.
3. Known or suspected severe cardiac dysfunction.

3.7 Research Tools and Variables

1. Serum albumin (g/L), total bilirubin (mmol/L), international normalized ratio were obtained from LIS RESULT® application version 6.6.
2. Child Pugh Score was calculated using MD online calculator from the web https://www.mdcalc.com/calc/340/child-pugh-score-cirrhosis-mortality. Other parameters required were a presence of ascites and grade of hepatic encephalopathy that were obtained from patient's medical records.
3. Statistical Product and Service Solutions (SPSS) for Windows, SPSS Inc.© (Version 26, SPSS Inc., Chicago, IL, USA) was used for data analysis.

3.8 Operational Definition

1. Chronic liver disease (CLD) is defined as a progressive destruction of the liver parenchyma over a period greater than 6 months leading to fibrosis and cirrhosis.
2. Acute decompensation of CLD is defined as patients who have developed complications of cirrhosis, such as variceal haemorrhage, ascites, spontaneous bacterial peritonitis, hepatocellular carcinoma, hepatorenal syndrome, or hepatopulmonary syndrome.
3. Complications of CLD is defined as patients who have developed complications of cirrhosis, such as variceal haemorrhage, ascites, spontaneous bacterial peritonitis, hepatocellular carcinoma, hepatorenal syndrome, or hepatopulmonary syndrome
4. Short term IV human albumin is defined as 20 % Iv human albumin 12.5 g – 25 g daily for 3 to 5 days.

5. Standard medical therapy (SMT) is defined as management of CLD that was aligned with the current practice guidelines, i.e., Diuretics and anti-aldosterone drug.
6. Child-Pugh score: classification of the severity of liver disease, according to the degree of ascites, the serum concentrations of bilirubin and albumin, the INR, and the degree of encephalopathy.

   -class A (well-compensated disease): 5-6

   -class B (significant functional compromise): 7-9

   -class C (decompensated disease): 10 -15

3.9 Data Collection

This is a retrospective cohort study that was conducted in HUSM, Kubang Kerian, Kelantan, Malaysia from April 2022 to June 2022. Data collected were from June 2017 to May 2022. This study had obtained approval from the Human Research Ethics Committee of USM (USM/JEPeM/22010058). Sample size was calculated usingPower & sample size calculator version 3.1.2 and a convenience sampling method was applied. A total of 455 patients were diagnosed with chronic liver disease (radiological proven) and admitted to Medical Unit Hospital Universiti Sains Malaysia. However, 257 patients were excluded due to underlying severe comorbidities includes ESRF, heart failure with reduce EF, and advanced hepatocellular carcinoma with life expectancy of less than 12 weeks. Hence, a total of 198 patients were enrolled in this study. The decision whether the patients received a short course of human albumin or standard medical therapy alone was decided by the admission and record office.

The data considered are age, sex, race, comorbid, etiology of chronic liver disease and the diagnosis. The initial (on admission) and final parameters (day 5 from the date of admission) of total bilirubin, serum albumin and international nationalized ratio (INR) for both groups were retrieved from LIS RESULT® application version 6.6 and Child-Pugh score was calculated using MD online calculator. Other parameters such as presence of ascites and grade of hepatic encephalopathy were obtained from patient's medical records.

The patient's survival at day 14 were identified if the patient stays more than 14 days or if the patient turns up again for follow-up 14 days after admission. The total duration stay was recorded. If the patient did not turn up after being discharge, the date of death was retrieved from Jabatan Pendaftaran Negara to know if patient survived at day 14 of admission. All the data was recorded in the data collection sheet.

3.10 Statistical Analysis

All data were analysed using Statistical Product and Service Solutions (SPSS) for Windows, SPSS Inc.© (Version 26, SPSS Inc., Chicago, IL, USA). Descriptive statistics were used to summarise the socio-demographic and clinical characteristics of the patients. Categorical data were presented as frequency (n) and percentage (%). Numerical data were expressed as mean (SD) based on their normality distribution. The survival time was analyzed by the Kaplan-Meier method and compared between groups by using the Log-rank test. We applied repeated measure ANCOVA analysis to look at the changes in parameters between the two groups and within the group. $P < 0.005$ was considered as statistically significant.

3.11 Confidentiality and Privacy

The subjects were identified using a unique serial number. No identifiable data was shared publicly. Upon completion of the study, all data were stored in CDs, and the database in the computer was erased. The data were retained by researchers for knowledge purposes only. Neither the patient's name nor any other information will be used in any publication or presentation as a result of this study.

3.12 Ethical Consideration

The study had obtained approval from the Human Research Ethics Committee of Universiti Sains Malaysia (USM/JEPeM/22010058).

3.13 Study Flow Chart

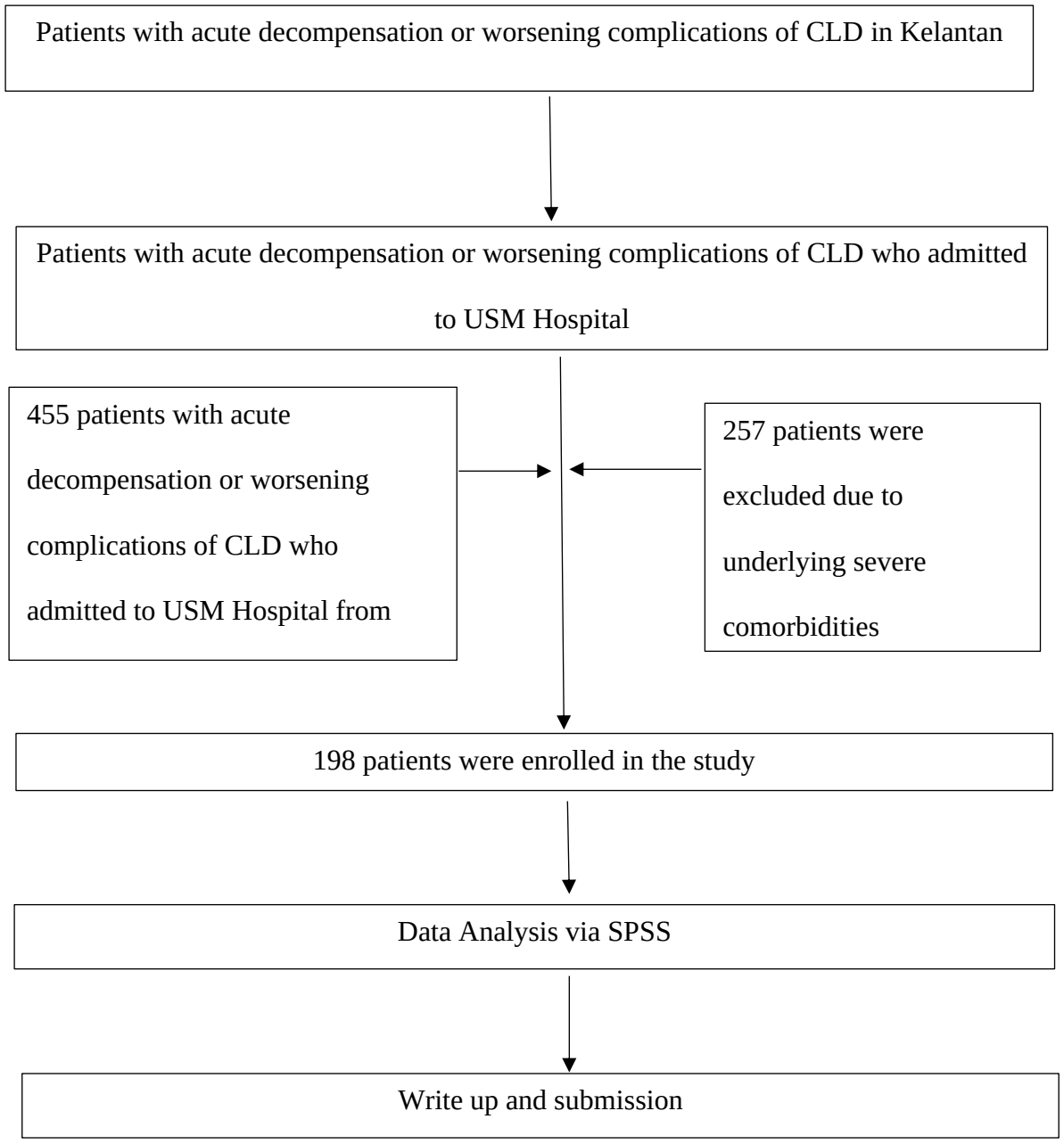


Figure 2: Study Flow Chart

CHAPTER 4: MANUSCRIPT

EFFECT OF SHORT-TERM IV HUMAN ALBUMIN INFUSION IN HOSPITALIZED PATIENT WITH ACUTE DECOMPENSATION OR COMPLICATIONS OF CHRONIC LIVER DISEASE ON MORBIDITY AND MORTALITY IN HUSM

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ABSTRACT

Background: Albumin is the main constituent of plasma oncotic pressure which modulates the distribution of fluid in between the different parts of the body. Better understanding of albumin's other physiologic functions has expanded its application beyond the maintenance of intravascular volume. In cirrhotic patient, albumin is used to reduce ascites formation, improve circulatory and renal functions, and prevent hepatorenal syndromes in those with spontaneous bacterial peritonitis. However, opinion are divided on whether targeting higher serum albumin would be beneficial for cirrhotic patients due to the fact that confirmatory large-scale clinical trials are still lacking. Therefore, this study aimed at comparing whether albumin infusion with aiming a higher serum albumin 30 g per litre or more, as compared with standard medical care, would improve short term survival in hospitalized cirrhotic patients.

Methods: A retrospective cohort study was conducted in Hospital Universiti Sains Malaysia from 2017 to 2022 with 198 patients between the ages of 27 to 81 years old who had been hospitalized due to decompensated liver disease and serum albumin level of less than 30 g per litre on admission. Patients either received standard medical therapy with 3 days intravenous human albumin or standard medical therapy alone. The composite

primary end point was the survival rate at day 14 after the initiation of treatment or hospitalization with standard medical therapy. The survival time was analysed using the Kaplan Meier method and compared between the groups using the Log-rank test. The changes in parameters between two groups and within the group were identified using repeated measure ANCOVA.

Results: The outcome from our study denoted a significant improvement in the median survival time among patients who had received human albumin as compared to standard medical therapy alone (***P***<0.001). Repeated measure ANCOVA indicate that mean albumin differed significantly between time points in both standard medical therapies alone (F=37.18, ***P***<0.001) and the human albumin group (F=9.833, ***P***=0.002). Multiple comparison analysis with a Bonferroni adjustment revealed that there was a significant increase in serum albumin from initial to final measurement (adj MD: -1.47, 95% CI: -2.40 to -0.53) in standard medical therapy with human albumin group. In contrast, the was a significant decrease in the mean albumin from initial to final measurement (adj MD: 1.68, 95% CI: 1.13 to 2.23) in the standard medical therapy alone group.

Conclusion: Human albumin infusion in an acute decompensated liver cirrhosis is beneficial and notably improved patient's short-term survival. Nevertheless, there is a need for a robust and randomized controlled trials to appraise the use of human albumin with aimed at a higher serum albumin level in treating hospitalized patients with cirrhosis-related complications.