Correlation of Simple Laboratory Result Parameters to CTP and Meld Scores, and The Diagnostic Role of Simple Laboratory Indexes to Cirrhosis Decompensation

Ni Nyoman Gita Kharisma Dewi, Ni Luh Putu Yunia Dewi*, Kadek Mercu Narapati Pamungkas*, Putu Itta Sandi Lesmana Dewi*, Dwijo Anargha Sindhughosa**, I Ketut Mariadi***

*Centre Research for Alimentary and Hepatobiliary System, Denpasar, Bali, Indonesia
**Division of Gastroenterology and Hepatology, Department of Internal Medicine, Udayana University/ Prof. Dr. IGNG Ngoerah General Hospital, Bali

Corresponding Author: I Ketut Mariadi, mariadi@unud.ac.id

ABSTRACT

Background *Liver cirrhosis represents the ultimate stage of any chronic liver ailment. Systemic inflammation plays a crucial role in fostering continuous liver damage. This study aims to evaluate the correlation of NLR, ABR, ALBI, APRI, ACR, LMR, and de ritis ratio to CTP, and MELD scores. Evaluated the diagnostic ability of NLR, ABR, ALBI, APRI, ACR, LMR, de ritis ratio, CTP, and MELD scores in predicting decompensated liver cirrhosis.*

Method *This cross-sectional study involves liver cirrhosis patients at RSUP Prof DR IGNG Ngoerah. Correlation tests employ either Pearson or Spearman, while diagnostic quality is assessed through the analysis of receiver operating characteristic (ROC) curves.*

Result *Of the 96 patients, this study found a significant moderate to very strong relationship between MELD score to ACR, APRI, ALBI, ABR, LMR, WBC, sodium, and albumin. NLR, ACR, De ritis, APRI, LMR, ALBI, ABR, sodium levels, and albumin have a moderate to very strong significant relationship to CTP score. ACR, de ritis, APRI, LMR, ALBI, ABR, WBC, sodium, and albumin levels with respective cut-offs ≤ 3.6; ≥ 1.5; ≥ 0.3; ≤ 2.8; ≥ 0.7; ≤ 1.6; ≥ 6.7, ≤ 136.50, and ≤ 3.0 can be used to predict decompensated liver cirrhosis.*

Conclusion *Using the CTP and MELD scores as predictive tools for assessing the severity of liver cirrhosis, information derived from laboratory test outcomes, specifically albumin, and ABR levels, can aid in establishing the diagnosis of decompensated cirrhosis.*

Keyword: *CTP score, decompensated liver cirrhosis, laboratory examination, MELD score*

ABSTRAK

Latar Belakang *Sirosis hati merupakan kondisi akhir dari semua penyakit hati kronis. Inflamasi sistemik memainkan peran penting dalam menyebabkan kerusakan hati yang progresif. Tujuan penelitian ini adalah menilai korelasi NLR, ABR, ALBI, APRI, ACR, LMR, rasio de ritis terhadap skor CTP dan MELD. Mengevaluasi kemampuan diagnostik NLR, ABR, ALBI, APRI, ACR, LMR, rasio de ritis, skor CTP, dan MELD dalam memprediksi sirosis hati dekompensasi.*

Metode *Studi potong lintang ini melibatkan pasien sirosis hati di RSUP Prof DR IGNG Ngoerah. Uji korelasi menggunakan uji Pearson atau Spearman, sementara kualitas diagnostik dinilai melalui analisis kurva receiver operating characteristic (ROC).*

Hasil *Dari 96 pasien, penelitian ini menemukan hubungan sedang hingga sangat kuat yang signifikan antara skor MELD dengan ACR, APRI, ALBI, ABR, LMR, leukosit, natrium, dan albumin. NLR, ACR, De ritis, APRI, LMR, ALBI, ABR, kadar natrium, dan albumin memiliki hubungan sedang hingga sangat kuat yang signifikan*

dengan skor CTP. ACR, De ritis, APRI, LMR, ALBI, ABR, leukosit, kadar natrium, dan albumin dengan cutoff masing-masing ≤ 3,6; ≥ 1,5; ≥ 0,3; ≤ 2,8; ≥ 0,7; ≤1,6; ≥ 6,7, ≤ 136,50, dan ≤ 3,0 dapat digunakan untuk memprediksi sirosis hati dekompensasi.

Kesimpulan *Skor CTP dan MELD dapat digunakan sebagai alat untuk memprediksi keparahan sirosis hati. Hasil pemeriksaan laboratorium berupa kadar albumin dan ABR dapat membantu menegakkan diagnosis sirosis dekompensasi.*

Kata kunci: *pemeriksaan laboratorium, sirosis hati dekompensasi, skor CTP dan MELD*

INTRODUCTION

Liver cirrhosis contributes to elevated mortality and morbidity rates among individuals suffering from chronic liver disease. Liver cirrhosis is defined by the presence of fibrosis and nodules within the liver, which develop as a consequence of prolonged liver injury. Some conditions can injure the liver, namely viral infections, toxins, or autoimmune processes. In developed nations, prevalent factors leading to liver cirrhosis include hepatitis C (HCV), alcoholic liver disease, and non-alcoholic steatohepatitis (NASH). Meanwhile, in developing countries, hepatitis B (HBV) and C (HCV) virus infections are common culprits for liver cirrhosis. The progression of liver cirrhosis may give rise to complications such as hepatocellular carcinoma (HCC) and hepatic decompensation, marked by conditions like ascites, hepatic encephalopathy, and variceal bleeding. These complications significantly contribute to an increased mortality rate among individuals with liver cirrhosis.[1-2]

Liver cirrhosis is the 11th and 15th cause of death for morbidity, causing 2.2% of deaths and 1.5% of morbidity in 2016. Based on world prevalence data for 2019, the mortality rate due to liver cirrhosis has reached 2.4%.[3-4] However, the exact prevalence of cirrhosis worldwide is not known with certainty. The occurrence of liver cirrhosis is approximately 0.15% and 0.27% in the United States, respectively. Data regarding the prevalence of liver cirrhosis in Indonesia is still lacking. However, some studies state that the average prevalence of liver cirrhosis in Indonesia reaches 3.5% in internal medicine units in public hospitals.[5]

The systemic inflammatory process plays an essential role in liver damage. Systemic inflammation contributes to exacerbating liver damage and poor outcome. Therefore, inflammatory markers, such as neutrophils and lymphocytes, can predict outcomes in viral hepatitis, HCC, liver transplantation, and non-alcoholic fatty liver disease.[6]

Application of a scoring system to predict outcome and severity of cirrhosis has been widely used.[7] Health workers commonly use the Child-Turcotte-Pugh (CTP) and model for end-stage liver disease (MELD) scoring systems. However, simple laboratory tests, such as neutrophil-lymphocyte ratio (NLR), can be an option in developing countries with limited resources. Apart from NLR, albumin-bilirubin score (ALBI), aspartate aminotransferase to platelet ratio (APRI), de raitis ratio, albumin-bilirubin ratio (ABR), albumin-creatinine ratio (ACR), and lymphocyte-monocyte ratio (LMR) are also stated to be used to help predict liver cirrhosis outcomes.[8-15] This study examines the relationship between NLR, APRI, ACR, LMR, de raitis ratio, and ABR on CTP and MELD scores. In addition, this study analyzes each parameter's cut-off and the sensitivity and specificity level of each parameter in diagnosing decompensated cirrhosis.

MATERIAL AND METHODS

Ethical Clearance

This research is a component of the investigation approved by the Research Committee of the Faculty of Medicine at Udayana University/Sanglah General Hospital under the ethical clearance number 997/ UN14.2.2.VII.14/LT/2021.

Population and study design

There were a total of 96 patients in this cross-sectional study. Twenty-three of them do not have data for calculating the MELD score. The MELD score was calculated only in patients with complete sodium, creatinine, bilirubin, and INR data. The inclusion criteria used in this study were patients with a diagnosis of liver cirrhosis, at least 18 years old, both male and female and willing to participate by signing an informed consent. The exclusion criteria in this study were patients with cirrhosis of the liver with chronic kidney failure stages 1 to 5, as well as

other malignancies other than primary malignancy in the liver. All patients in this study had complete blood count results in white blood cell count and complete liver profile, including liver enzymes, serum albumin, total bilirubin, direct and indirect bilirubin, and blood clotting factors.

Demographic, clinical, and laboratory value of the study

The demographic characteristics contained in this study are age, gender, and nutritional category. Age in this study was divided into <65 years and ≥ 65 years. The nutrition category is divided into two, malnutrition and non-malnutrition based on body mass index (BMI). The clinical manifestations found in the patients in this study were ascites, haematemesis/melena, or esophageal varices. In this study, the etiology of liver cirrhosis is divided into infection and non-infection. The etiology for infection were hepatitis B and C viruses. If positive HbsAg was located, liver cirrhosis was established due to hepatitis B infection, while anti-HCV reactive was diagnosed as hepatitis C infection. A complete blood count of all patients was obtained from the medical record. Normal laboratory results count of WBC (4.1-11.0 x 10^3/mL), platelet (140-440 x 10^3/mL), hemoglobin (12-16 g/dL), albumin (3.40-4.80 g/dL), BUN (8.00-23.00 mg/dL), and natrium (136-145 mmol/L).

Liver cirrhosis-related indicator and laboratory ratio

We identified seven ratios based on the results of laboratory tests that have a relationship with liver cirrhosis. We also calculate ALBI based on laboratory test results. The seven laboratory ratios are neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), aspartate aminotransferase-platelet ratio (APRI), albumin-bilirubin ratio (ABR), lymphocyte-monocyte ratio (LMR), serum glutamic oxaloacetic transaminase to serum glutamic pyruvic transaminase (de ritis) ratio, and serum albumin to creatinine ratio (ACR) were obtained for all patients which we calculated using the assistance of Ms. Excel. The albumin to bilirubin index score (ALBI) was calculated using an online calculator.

The liver function indicator in this study uses the CTP and MELD scores. There are three classifications based on the results of calculating the CTP score, namely CTPA(total score 5-6), CTP B (total score 7-9), and CTP C (total score 10-15). The MELD score in this study was calculated using an application calculator and divided into two categories, namely ≥ 20 (high) and <20 (low). Patients are categorized into decompensated and compensated cirrhosis. Decompensated cirrhosis for patients with CTP scores B and C with clinical symptoms such as upper gastrointestinal bleeding, hepatic encephalopathy, or ascites.

Statistical Analysis of the Data

Data were collected into a computer and analyzed using IBM SPSS software package version 24.0 (Armonk, NY: IBM). Qualitative data are described using numbers and percentages. Quantitative data were tested for normality with the Kolmogorov-Smirnov test. The data is said to be normally distributed if the p-value> 0.05. Data with a normal distribution are presented as mean ± standard deviation, while data with non-normal distribution are shown as the median (minimum-maximum value). Categorical data were analyzed by the Chi-square or Fisher's exact test, which was said to be statistically significant when the p-value <0.05. A mean followed the data compare analysis using the Independent t-test for normally distributed data. In contrast, data not normally distributed were analyzed using the Mann-Whitney U-test. Correlation tests were performed on NLR, PLR, LMR, ABR, serum ACR, de ritis, APRI, ALBI, WBC, sodium, serum creatinine, and albumin levels against MELD and CTP scores using the Pearson test for normally distributed data and Spearman for non-normally distributed data. The results were declared significant if the value of p <0.005 had a moderate, strong, and solid relationship if r >0.4–<0.6, 0.6–<0.8, and 0.8–1.00, respectively. The quality of each variable in diagnosing decompensated liver cirrhosis is assessed by analysis of receiver operating characteristic (ROC) curves so that the value of the area under the curve, cut-off, sensitivity, and specificity of each variable will be obtained.

RESULT

Assessment of the Severity Level of Liver Cirrhosis Using Different Indices

The total number of patients included in this cross-sectional study was 96. The mean age of patients in the decompensated cirrhosis group was 54.52 ± 10.431, with 69.7% being male. Based on the results of the compare mean analysis, it was found that there were significant differences in the twelve variables between

the decompensated and compensated cirrhosis groups. The ten variables, namely NLR, serum ACR, de ritis, APRI, LMR, ALBI, ABR, albumin, CTP score, and MELD score, had a p-value <0.001. The other variables, WBC and sodium levels, had a p-value <0.005.

The correlation test results using the Pearson and Spearman tests found a negative correlation in four variables to the MELD score. The CTP score also found that five variables had a negative correlation. NLR, serum ACR, de ritis, APRI, LMR, ALBI, ABR, levels of WBC, sodium, and albumin significantly correlated with the MELD score with a p-value <0.005, and only PLR and serum creatinine which were not significantly associated with the CTP score.

Table 1. Demographic Characteristics of Study Population

Characteristic	Decompensated	Compensated	P value
Demograghic			
Age, years	54.52 ± 10.431	52.20 ± 9.734	0.307*
Gender			
Male	46 (69.7%)	20 (30.3%)	0.537#
Female	19 (63.3%)	11 (36.7%)	
Nutritional category		0:31	
Malnourished	32 (100%)	0 (0.0%)	**<0.001#**
Non malnourished	33 (51.6%)	31 (48.4%)	
Blood Examination Result			
WBC	8.35 (1.59-34.37)	6.29 (2.01-21.05)	**0.014****
Serum Creatinin	0.89 (0.57-1.25)	0.94 ± 0.215	0.962**
Na	131.22 ± 8.024	138.00 (103.00-145.00)	**0.018****
Albumin	2.465 ± 0.58	3.54 ± 0.558	**<0.001***
Laboratory Ratio			
NLR	4.725 (0.55 – 43.91)	3.816 ± 2.163	**<0.001****
ACR	2.741 ± 0.852	3.923 ± 0.881	**<0.001***
De Ritis	1.88 (0.47-11.71)	1.44 (0.66-5.13)	**<0.001****
APRI	0.52 (0.03-68.10)	0.27 (0.14-2.96)	**<0.001****
PLR	97.48 (0.69-712.31)	103.639 ± 67.185	0.395**
LMR	1.81 (0.32-6.10)	2.673 ± 1.394	**<0.001****
ALBI	0.94 ± 0.32	0.55 ± 0.21	**<0.001***
ABR	0.75 (0.07-5.07)	2.78 (0.68-10.48	**<0.001****
Liver Function Indicator			
MELD Score	20.345 ± 7.964	10.00 (7.00-24.00)	**<0.001****
CTP Score	9.5 (7.00-14.00)	6.00 (5.00-7.00)	**<0.001****

WBC: white blood cell; NLR: neutrophile-lymphocyte ratio; ACR: albumin creatinine ratio; APRI: albumin platelet ratio index; PLR: platelet lymphocyte ratio; LMR: lymphocyte monocyte ratio; ALBI: albumin bilirubin; ABR: albumin bilirubine ratio. Data analyzed by independent samples t-test, data analyzed by Mann-Whitney, #data analyzed by chi-square

Table 2. Correlation between laboratory ratio to MELD and CTP Score.

Parameter	MELD Score		CTP Score	
	r	P	r	p
NLR	0.379	0.001*	0.457	<0.001*
ACR	-0.518	<0.001*	-0.684	<0.001*
De Ritis	0.283	0.015*	0.459	<0.001*
APRI	0.575	<0.001*	0.585	<0.001*
PLR	0.074	0.534	0.038	0.712
LMR	-0.483	<0.001*	-0.496	<0.001*
ALBI	0.864	<0.001*	0.806	<0.001*
ABR	-0.839	<0.001*	-0.850	<0.001*
WBC	0.405	<0.001*	0.295	0.003*
Serum Creatinin	0.046	0.697	-0.002	0.985
Na	-0.824	<0.001*	-0.485	<0.001*
Albumin	-0.652	<0.001*	-0.809	<0.001*

r = spearman or pearson coefficient, *statistically significant at p < 0.05

Table 3. Validity (AUC, Sensitivity, and Specificity)

Parameter	AUC	p	95%CI	Cut-off	Sensitivity	Specificity
NLR	0.633	0.115	0.474-0.792			
ACR	0.884	<0.001*	0.814-0.955	≤ 3.6	80.6%	83%
De ritis	0.717	0.010*	0.578-0.856	≥ 1.5	69%	80%
APRI	0.685	0.028*	0.522-0.848	≥ 0.3	79.3%	66.7%
PLR	0.551	0.548	0.389-0.712			
LMR	0.779	<0.001*	0.682-0.877	≤ 2.8	67.7%	78.5%
ALBI	0.843	<0.001*	0.741-0.944	≥ 0.7	79.3%	80%
ABR	0.909	<0.001*	0.851-0.967	≤ 1.6	96.8%	75.4%
WBC	0.656	0.014*	0.546-0.766	≥ 6.7	63.1%	65%
Serum Creatinin	0.497	0.963				
Na	0.699	0.018*	0.546-0.852	≤ 136.50	66.7%	72%
Albumin	0.956	<0.001*	0.921-0.991	≤ 3.0	93.5%	81.5%
MELD	0.833	<0.001*	0.717-0.948	≥ 10.5	86.2%	73%
CTP	0.995	<0.001*	0.982-100	≥ 6.5	100%	93%

*significant statistically at $p < 0.05$

DIAGNOSTIC PERFORMANCE OF LABORATORY RATIO

Serum albumin to creatinine ratio ≥3.6 can help in establishing the condition of decompensated liver cirrhosis with a sensitivity level of 80.6% and a specificity of 83%. There are several other variables with cut-off and sensitivity, as well as specificity of each, namely de ritis (cut off ≥ 1.5, sensitivity 69%, specificity 80%), APRI (cut off ≥ 0.35, sensitivity 79.3%, specificity 66.7%), LMR (cut off ≥ 2.8, sensitivity 67.7%, specificity 78.5%), ALBI (cut off ≥ 0.68, sensitivity 79.3%, specificity 80%), ABR (cut off 1.65, sensitivity 96.8%, specificity 75.4%), WBC level (cut off ≥ 6.76, sensitivity 63.1%, specificity 65%), sodium level (cut off ≥ 136.50, sensitivity 66.7%, specificity 72%), and albumin level (cut off ≥3, sensitivity 93.5%, specificity (81.5) to enforcement diagnosis of DLC. This study found that the CTP score is superior to the MELD score in differentiating decompensated and compensated liver cirrhosis. The MELD score had a cut-off≥ 10.5, a sensitivity of 86.2%, and a specificity of 73%, while the CTP score had a cut-off of ≥ 6.5, a sensitivity of 100%, and a specificity of 93%.

DISCUSSION

Liver cirrhosis is a condition that is generally known as an end-stage process. Liver cirrhosis is characterized by the formation of fibrosis and nodules in the liver due to chronic liver injury. The most common causes of liver cirrhosis are alcohol use disorders, non-alcoholic fatty liver disease, and hepatitis B and C infections.[1-3] Liver cirrhosis can cause *hepatocellular carcinoma*.[17] Therefore, cirrhosis of the liver can lead to increased mortality and morbidity. Establishing a good diagnosis will help in reducing mortality due to liver cirrhosis.

In areas with limited resources, supporting examinations in the form of a biopsy could be hard, thus making it difficult to predict the severity of liver cirrhosis and determine which patients should be referred for liver transplantation. Using simple laboratory results, apart from clinical ones, will greatly help predict the severity of liver cirrhosis. It is hoped that the laboratory examination results will assist in developing a scoring system that can be used by medical personnel in predicting the severity of liver cirrhosis.

In the pathophysiology of the cirrhotic liver, it is stated that there is a role of excessive inflammatory response. The liver comprises of hepatocytes, parenchyma cells, and other cells collectively referred to as nonparenchymal cells. Three types of nonparenchymal cells—endothelial cells, liver sinusoidal endothelial cells (LSECs), Kupffer cells (KCs), and hepatic stellate cells (HSCs)—line the walls of the liver sinusoids. Both parenchymal and nonparenchymal cells play crucial roles in the onset and progression of liver fibrosis and cirrhosis. The primary mechanism for initiating fibrosis involves the activation of hepatic stellate cells, occurring in two phases. The initial phase, known as the initiation or pre-inflammatory phase, is triggered by factors such as cellular apoptosis, oxidative stress, stimuli from Kupffer cells, hepatocytes, platelets, and the endothelium. The subsequent perpetuation phase involves cell proliferation, fibrogenesis, and a significant inflammatory response.[18-19]

Neutrophil to lymphocyte ratio and PLR are inflammatory markers that are simple and affordable to examine. NLR and PLR can categorize liver cirrhosis based on its severity. Apart from NLR and PLR, other markers such as ABR, ALBI, and ACR are also

stated to help assess the severity of liver cirrhosis by relating it to the MELD score or CTP score. De ritis and APRI obtained from calculating SGOT, SGPT, and platelets were also stated to have a relationship with liver cirrhosis. This study found that those with a moderate to strong positive relationship with CTP score were NLR, de ritis, APRI, ALBI, sodium levels, and albumin.

In contrast, ACR, LMR, ABR, sodium levels, and albumin had a moderate to strong negative correlation direction. The MELD score found a moderate to strong positive significant relationship were NLR, APRI, ALBI, and WBC levels. In contrast, ACR, LMR, ABR, sodium, and albumin levels had a moderate to strong negative correlation.

This study found that significant prognostic markers of decompensated cirrhosis were ACR (cut off ≤ 3.6, sensitivity 80.6%, specificity 83%), de ritis (cut off ≥1.5, sensitivity 69%, specificity 80%), APRI (cut off ≥ 0.3, sensitivity 79.3%, specificity 66.7%), LMR (cut off ≤ 2.8, sensitivity 67.7%, specificity 78.5%), ALBI (cut off ≥ 0.7, sensitivity 79.3%, specificity 80%), ABR (cut off ≤ 1.6, sensitivity 96.8%, specificity 75.4%), WBC level (cut off ≥ 6.7, sensitivity 63.1, specificity 65%) and sodium level (cut off ≤ 136.50, sensitivity 66.7%, specificity 72%), and albumin (cut off ≤ 3.0, sensitivity 93.5, specificity 81%). The results of this study are in line with several other studies which state that ACR, de ritis, APRI, LMR, ALBI, ABR, WBC, Sodium, and Albumin have a relationship with liver disease conditions, one of which is liver cirrhosis. [8-15,20-23] The MELD score has a cut-off of ≥ 10.5, a sensitivity of 86.2%, and a specificity of 73, while the CTP score cut-off of ≥ 6.5, with a sensitivity of 100% and a specificity of 93%. The results of this study indicate that the CTP score is superior to the MELD score.

This study succeeded in assessing the correlation of several markers based on laboratory results on MELD and CTP scores and the diagnostic performance of laboratory ratios, MELD, and CTP scores in establishing decompensated cirrhosis conditions. There have been previous studies addressing topics like this. However, that study only assessed NLR, PLR, ALBI, and ABR. This study has the advantage of assessing the correlation and diagnostic performance of other markers, namely WBC, sodium level, albumin level, serum creatinine, ACR, de ritis, APRI, and LMR. The results of this study will be useful for future studies in determining a scoring system for diagnostic or prognostic enforcement related to liver cirrhosis.

There are several areas for improvement in this study. First, this study was a small sample based on only one center data. Second, this study has not attempted to assess the diagnostic ability of these markers for spontaneous bacterial peritonitis (SBP), acute-on-chronic liver failure (ACLF), and hepatocellular carcinoma (HCC).

CONCLUSION

Based on the study results, it can be concluded that ALBI, ABR, and sodium levels strongly correlate with the MELD score. ALBI, ABR, and albumin levels strongly correlate with the CTP score. The quality of the diagnostic performance for decompensated cirrhosis from ALBI and ABR has good results. The sensitivity and specificity of ABR were 96.8% and 75.4% with a cut-off of 1.6, while albumin levels were 93.5% and 81.5% with a cut of 3.0. Based on these results, the results of laboratory tests can be used as a marker to help diagnose decompensated cirrhosis.

REFERENCES

1. Sharma B, John S. Hepatic Cirrhosis. 2023. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. [Cited 19 September 2023]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482419/.
2. Tapper EB, Parikh ND. 2023. Diagnosis and Management of Cirrhosis and Its Complications: A Review. *JAMA.* 329(18):1589–1602. doi:10.1001/jama.2023.5997
3. Ginès P, Krag A, Abraldes JG, Solà E, Fabrellas N, Kamath PS. 2021. Liver cirrhosis. Lancet. 398(10308):1359-1376. doi: 10.1016/S0140-6736(21)01374-X.
4. Huang, D.Q., Terrault, N.A., Tacke, F. *et al.* 2023. Global epidemiology of cirrhosis — etiology, trends, and predictions. *Nat Rev Gastroenterol Hepatol* 20, 388–398. https://doi.org/10.1038/s41575-023-00759-2
5. Hasan I, Putra RP, Yunihastuti E, Kurniawan J. 2022. The Validity and Reliability of the Indonesian Version of the Chronic Liver Disease Questionnaire (CLDQ) in Measuring Quality of Life in Patients with Liver Cirrhosis. Acta Med Indones. 54(1):10-18. PMID: 35398821.
6. Sungkar T, Rozi MF, Dairi LB, Zain LH. 2019.The neutrophil-to-lymphocyte ratio (NLR) and its correlation with severity of decompensated liver cirrhosis based on Child-Turcotte Pugh (CTP) score. Journal of Clinical and Diagnostic Research. 2019 Feb, Vol-13(2): OC29-OC31. DOI: 10.7860/JCDR/2019/39895.12618.
7. Peng Y, Qi X, Guo X. 2016. Child-Pugh Versus MELD Score for Evaluating Prognosis in Liver Cirrhosis: A Systematic Review and Meta-Analysis of Observational Studies. Medicine (Baltimore). 95(8):e2877. doi 10.1097/MD.0000000000002877.
8. Metawea MI, Moteleub HNAE. 2022. Diagnostic role of simple indices in HCV-related liver cirrhosis outcomes: a prospective cross-sectional study. Clin Exp Hepatol. (1):29-35. doi 10.5114/ceh.2022.114169.

9. Bhandari S, Gulati S, Sharma N, Kumar A, Singh A. 2021. Evaluation of Neutrophil to Lymphocyte ratio (NLR) and its utility as a prognostic marker in COVID-19 patients. Authorea Preprints. 35(8):2349-2562. DOI: 10.18410/jebmh/2021/616
10. Loaeza-del-Castillo A, Paz-Pineda F, Oviedo-Cárdenas E, Sánchez-Avila F, Vargas-Voráckova F. 2008. AST to platelet ratio index (APRI) for the noninvasive evaluation of liver fibrosis. Ann Hepatol. 7(4):350-7. PMID: 19034235.
11. Kurniawan WD, Widodo B, Agustina B. AST to Platelet Ratio Index (APRI) and Degree of Severity based on Child-Pugh Classification among Cirrhosis Patients at Internal Medicine Ward in a Tertiary Hospital. 2(32):46-51. Available from: *https://e-journal.unair.ac.id/MBIO/*
12. Anju R, Shah K. 2017. Significance of SGOT & SGPT ratio (De Ritis Ratio) & GGT levels in patients of liver cirrhosis with and without a history of alcoholism. Int J Research Med. 6(2):1-3.
13. Abdelghani, A., Ibrahim, M.H.ED., Mohamed, O.M. *et al.* 2021. Urinary albumin-to-creatinine ratio in decompensated liver cirrhosis among elderly Egyptian patients: a single-center experience. *Egypt J Intern Med* **33**, 32. Available from: https://doi.org/10.1186/s43162-021-00062-z
14. Zhang J, Feng G, Zhao Y, Zhang J, Feng L, Yang J. 2015. Association between lymphocyte-to-monocyte ratio (LMR) and the mortality of HBV-related liver cirrhosis: a retrospective cohort study. BMJ Open. 5(8):e008033. doi: 10.1136/bmjopen-2015-008033.
15. Emenena I, Emenena B, Kweki AG, Aiwuyo HO, Osarenkhoe JO, Iloeje UN, Ilerhunmwuwa N, Torere BE, Akinti O, Akere A, Casimir OE. 2023. Model for End-Stage Liver Disease (MELD) Score: A Tool for Prognosis and Prediction of Mortality in Patients With Decompensated Liver Cirrhosis. Cureus. 15(5). DOI: 10.7759/cureus.39267
16. Llovet, J.M., Kelley, R.K., Villanueva, A. *et al.* 2021. Hepatocellular carcinoma. *Nat Rev Dis Primers* **7**, 6. Available from: https://doi.org/10.1038/s41572-020-00240-3
17. Zhou WC, Zhang QB, Qiao L. 2014. Pathogenesis of liver cirrhosis. World J Gastroenterol. 20(23):7312-24. doi: 10.3748/wjg.v20.i23.7312. PMID: 24966602; PMCID: PMC4064077.
18. Geong GY, Kang SH, Lee CM. 2019. An updated review on the epidemiology, pathophysiology, etiology, and diagnosis of liver cirrhosis.ResearchGate. [Cited 19 September 2023]. Available from: https://www.researchgate.net/publication/331752269
19. Kim WR, Biggins SW, Kremers WK, Wiesner RH, Kamath PS, Benson JT, Edwards E, Therneau TM. 2008. Hyponatremia and mortality among patients on the liver-transplant waiting list. N Engl J Med. 359(10):1018-26. doi: 10.1056/NEJMoa0801209.
20. Vyas, D. 2021. Study The Relation Between Serum Sodium And The Model For End-Stage Liver Disease Score In Patients With Liver Cirrhosis. *International Journal of Medical and Biomedical Studies*, *5*(3). https://doi.org/10.32553/ijmbs.v5i3.1830
21. Bernardi M, Angeli P, Claria J, Moreau R, Gines P, Jalan R, Caraceni P, Fernandez J, Gerbes AL, O'Brien AJ, Trebicka J.2020. Albumin in decompensated cirrhosis: new concepts and perspectives. Gut. 69(6):1127-38. DOI: 10.1136/gutjnl-2019-318843
22.