ORIGINAL ARTICLE

Prognostic value of a predictive score based on functional parameters for clinical outcome in patients with decompensated cirrhosis of the liver

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ABSTRACT

Aim To create a predictive score based on functional parameters of the liver and determine its prognostic value in survival of patients with decompensated cirrhosis.

Methods Retrospective observational study included 91 consecutive patients with decompensated cirrhosis. Functional parameters (bilirubin, AST – aspartate aminotransferase, ALT – alanine aminotransferase, ALP – alkaline phosphatase, GGT – gamma-glutamyltranferase, albumin, prothrombin time, platelet count, haematocrit and creatinine), Child-Pugh (CP) and Model of End-Stage Liver Disease (MELD) scores have been measured at first hospitalization and at every exacerbation episode over follow-up period of 24 months.

Results Using Cox regression analysis, we found that age (OR=1.206; p=0.03; 95% CI=1.019-1.428), serum bilirubin (OR=1.017; p=0.003; 95% CI=1.006-1.029), INR (International normalized ratio) (OR=6.262; p=0.002; 95% CI=1.924-20.378) and serum creatinine (OR=1.019; p=0.005; 95% CI=1.006-1.032) had statistically strong association with the incidence of a six-month mortality. Age (OR=1.120; p=0.006; 95% CI=1.033-1.214), serum bilirubin (OR=1.021; p=0.0001; 95% CI=1.010-1.032), GGT (OR=1.007; p=0.023; 95% CI=1.001-1.014), INR (OR=9.571; p=0.001; 95% CI=2.610-35.098), haematocrit (OR=0.695; p=0.001; 95% CI=0.559-0.864) and serum creatinine (OR=1.023; p=0.0001; 95% CI=1.011-1.035) showed an increased the risk for a 24-month lethal outcome. Predictive score derived from liver functional parameters, CP and MELD scores, each independently has shown a high degree of death prediction after 6 or 24 months in patients with end-stage liver disease.

Conclusion Predictive score derived from liver functional parameters had a better prognostic value for short-term and long-term mortality comparing to MELD and Child-Pugh score.

Key words: end-stage liver disease, survival rate, transplantation, waiting list

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INTRODUCTION

Nowadays, the liver transplantation is a gold standard for the treatment of the End Stage Liver Disease (ESLD). Decompensated cirrhosis is one of the most common causes of ESLD.

All patients with decompensated cirrhosis are candidates for liver transplantation. They should be put in the waiting list in proper time, neither too early nor too late (1). Liver transplantation performed in proper time is associated with good prognosis (2). Many different risk factors and clinical characteristics of the patient may impact either short-term or long-term mortality; obese patients have significantly increased morbidity and a higher risk for 1-year mortality (3). To determine urgency for liver transplantation different functional parameters of the liver function and clinical scores such as Child-Pugh (CP) (4), Model of End-Stage Liver Disease (MELD) (5), and other scores (6,7) are used for evaluation of short-term and long-term mortality rate.

Liver functional parameters, bilirubin, aspartate-amino transferase (AST), alanine-amino transferase (ALT), alkaline phospahatase (ALP), gamma-glutamyltransferase (GGT), albumin, prothrombin time, international normalized ratio (INR), platelet count, haematocrit, creatinine and haemoglobin are used as independent prognostic factors for survival rate in patients with decompensated cirrhosis, or some of them are included in clinical prognostic scores such as CP and MELD scores (8, 9, 10). Among liver functional parameters, serum bilirubin, INR, creatinine, lactate, albumin and CRP are good independent prognostic factors for short-term and long-term survival rate in patients with decompensated cirrhosis (11,12). In decompensated cirrhosis ALT and AST have no prognostic value for mortality rate (13).

Child-Turcotte-Pugh (CTP) score, or its modification Child-Pugh (CP) score is the most applied prognostic score in patients with decompensated cirrhosis, due to its simplicity in every day clinical practice (14). It is based on grading of five parameters: albumin, bilirubin, prolonged prothrombin time, ascites and encephalopathy. According to Child-Pugh scoring system patients are classified into three classes: A (5-6 points), B (7-9 points) and C (>9 points) (15). Several studies have shown good prognostic value of CP score in the patients with decompensated cirrhosis for long-term survival rate (8,16). CP score has no predictive value for short-term mortality rate (9).

MELD is an objective score and it is used as the main component of some transplant programs (17). MELD is a good score for stratification and ranking of urgency for liver transplantation (15,18). It is based on three simple objective parameters: serum level of creatinine, bilirubin and INR. MELD is a good prognostic marker for short-term survival for patients who are waiting for liver transplantation (19,20).

Some studies have shown that MELD and CP scores had a similar good prognostic value for short-term survival in patients with decompensated cirrhosis, but MELD score was found to be a better prognostic factor for long-term survival than CP score; albumin-bilirubin (ALBI) score was a better prognostic factor than both of them (8,10,21,22).

There are many scores used for prediction of clinical outcome in patients with severe liver disease, but besides having no good prognostic value, they also have some disadvantages and limitations (6,8,9,13,22). Current studies are looking for a score which will be simpler and with a better prognostic value (23-26).

The aim of this study was to create a predictive score based on functional parameters of the liver and compare its prognostic value with CP and MELD scores in survival of patients with decompensated cirrhosis.

PATIENTS AND METHODS

Patients and study design

This retrospective observational cohort study included 91 patients with decompensated cirrhosis who were admitted to the Department of Gastroenterology, Internal Medicine Clinic, University Clinical Centre Tuzla, Bosnia and Herzegovina, and analysed in the period between 1 January 2020 and 30 April 2022. Functional parameters of the liver function, Model for End-Stage Liver Diseases (MELD) score (27) and clinical Child-Pugh score (28) were measured at first hospitalization and at every rehospitalization over a follow-up period. All patients with decompensated cirrhosis underwent a follow-up for 24 months after admission to assess clinical outcome

and mortality rate. Clinical follow-up was performed by telephone or through a patient's examination. After 6 and 24 months clinical outcome and mortality rate (death due to liver insufficiency or due to other diseases) were determined.

The inclusion criteria were decompensated cirrhosis and age >18 years. The exclusion criteria were any other liver disease, malignant diseases, neuromuscular disorders, renal dysfunction, and haematological diseases.

Methods

Laboratory tests. Whole blood samples were immediately collected in a tube containing EDTA, centrifuged at 2000xg for 15 minutes at room temperature. Plasma concentrations of functional parameters (bilirubin, AST, ALT, GGT, prothrombin time, INR, albumin, creatinine, haemoglobin, haematocrit and platelets count) were measured using routine standard methods within 30 minutes using the Analyzer SYSMEX XN 100 (SYSMEX Corporation1-5-1 Wakinohama-Kaigandori, Chuo-Ku, Kobe 651-0073, Japan).

Clinical scores for severity of liver disease. Model for End-Stage Liver Disease - MELD score (29) is a numerical scale from 6 to 40 indicating a level of severity of a disease for patients who are candidates for liver transplantation (age >12 years). The higher score corresponds to the more severe stage of disease. Formula for calculation of MELD score is 0.957 x *log*e (creatinine mg/dL) + 0.378 x *log*e (bilirubin mg/dL) + 1.12 x *log*e (INR) + 0.643 (29).

Child-Pugh score (15) includes 5 parameters: albumin, bilirubin, prolongated prothrombin time, ascites and encephalopathy. Each parameter is pointed by 0, 1 or 2. Albumin >35 g/L=0 point, 28-35 g/L=1 point, and <28 g/L=2 points; bilirubin <34 μmol/ L=0 point, 34-51 μmol/ L=1 point, and >51 μmol/ L=2 points; prolongated prothrombin time 4 s=0 point, 4-6 s=1 point, and >6 s=2 points; none ascites=0 point, controlled ascites=1 point and uncontrolled ascites=2 points; none encephalopathy=0 point, controlled encephalopathy=1 point and uncontrolled encephalopathy=2 points). According to Child-Pugh score points patients are divided into three groups: A (5-6), B (7-9) and C (>9).

According to modification of Child-Pugh score, Child-Turcotte-Pugh score (CTP) (22), class A of the patients has a good prognosis if complications (such as uncontrolled bleeding) do not occur, CTP class B may be or may not be a candidate for liver transplantation depending on his clinical conditions, CTP class C is a candidate for the liver transplantation and it is a good predictor for short-term survival and positively correlates with neutrophil to lymphocyte ratio (NLR) (30).

Statistical analysis

Continuous variables are expressed as the mean±SD. They were analysed by Student's t test and ANOVA. Categorical variables are presented as frequencies (%) and were analysed with the $\chi 2$ test with Yates correction. Odds ratio with 95% confidence interval (CI) was calculated. The Kaplan–Meier test was used to estimate the survival rate. Cox regression analysis was used to determine the prognostic value of the variables. Differences between analysed parameters were considered significant at $p<0.05$.

RESULTS

This retrospective observational study included 91 patients with decompensated cirrhosis (mean age 64.3±11.0 years). There were 60 (65.9%) males and 31 (34.1%) females.

Kaplan–Meier analysis showed survival rate in patients with decompensated cirrhosis of 92.3% after 6 months and 85.7% after 24 months.

The INR, serum bilirubin and creatinine were significantly higher, but serum albumin, haematocrit and platelet counts were significantly lower in patients who died compared with patients who survived over the period of follow-up (Table 1). Patients

Table 1. Functional parameters of the liver in patients with decompensated cirrhosis who survived and died over 24 months of follow-up

Parameter	Mean±SD		p
	Survived	Died	
Age (years)	64.04±11.25	66.00±9.85	0.56
Total bilirubin (μmol/L)	40.48±32.78	129.12±112.23	0.02
AST (IU/L)	97.62±89.79	141.92±132.01	0.26
ALT (IU/L)	56.69±36.66	60.31±34.04	0.73
ALP (IU/L)	139.81±112.65	121.62±128.11	0.64
GGT (IU/L)	133.22±14.84	124.23±163.22	0.84
Albumin (g/L)	27.26±6.71	22.43±4.88	0.005
INR	1.51±0.39	2.23±0.82	0.008
Platelet ($x10^9$/l)	122.82±88.42	81.92±51.14	0.03
Haematocrit (%)	32.59±7.62	26.31±7.80	0.02
Creatinine (mmol/L)	98.23±52.55	198.08±119.61	0.01
Haemoglobin (g/dL)	6.42±1.60	5.49±1.67	0.08

AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; GGT, gamma-glutamyltranferase; INR, international normalized ratio

with fatal outcome had a higher CP and MELD scores than patients with non-fatal outcome.

Age (OR=1.206; p=0.03; 95% CI=1.019-1,428), serum bilirubin (OR=1.017; p=0.003; 95% CI=1.006-1,029), INR (OR=6.262; p=0.002; 95% CI=1.924-20.378) and serum creatinine (OR=1.019; p=0.005; 95% CI=1.006-1.032) showed a statistically strong association with the incidence of six-month mortality (Table 2).

Table 2. Relative risk of functional parameters of the liver for six-month mortality rate in patients with decompensated cirrhosis

Variable	p	OR (95% CI)
Age	0.03	1.206 (1.019-1.428)
Total bilirubin	0.003	1.017 (1.006-1.029)
INR	0.002	6.262 (1.924-20.378)
Creatinine	0.005	1.019 (1.006-1.032)

INR, international normalized ratio; OR, odds ratio; CI, Confidence interval

Age (OR=1.120; p=0.006; 95% CI=1.033-1,214), serum bilirubin (OR=1.021; p=0.0001; 95% CI=1.010-1.032), GGT (OR=1.007; p=0.023; 95% CI=1.001-1.014), INR (OR=9.571; p=0.001; 95% CI=2.610-35,098), haematocrit (OR=0.695; p=0.001; 95% CI=0.559-0,864) and serum creatinine (OR=1.023; p=0.0001; 95% CI=1.011-1,035) showed an increased risk for a 24-month lethal outcome (Table 3).

Table 3. Relative risk of functional parameters of the liver for 24-month mortality rate in patients with decompensated cirrhosis

Variable	p	OR (95% CI)
Age	0.006	1.120 (1.033-1.214)
Total bilirubin	0.0001	1.021 (1.010-1.032)
GGT	0.023	1.007 (1.001-1.014)
INR	0.001	9.571 (2.610-35.098)
Haematocrit	0.001	0.695 (0.559-0.864)
Creatinine	0.0001	1.023 (1.011-1.035)

GGT, gamma-glutamyltransferase; INR, international normalized ratio; OR, odds ratio; CI, Confidence interval

According to predictive values of functional parameters of the liver determined by logistic regression analysis, predictive score was created with the formula:

$$\pi = \frac{1}{1+e^{-z}};$$

$z = 1{,}572 - 0{,}414\ x\ HCT + 0{,}024\ x\ CREA + 0{,}061\ x\ TBIL$

Π-probability of outcome (from 0 to 1), HCT-haematocrit, CREA-creatinine, TBIL-total serum bilirubin

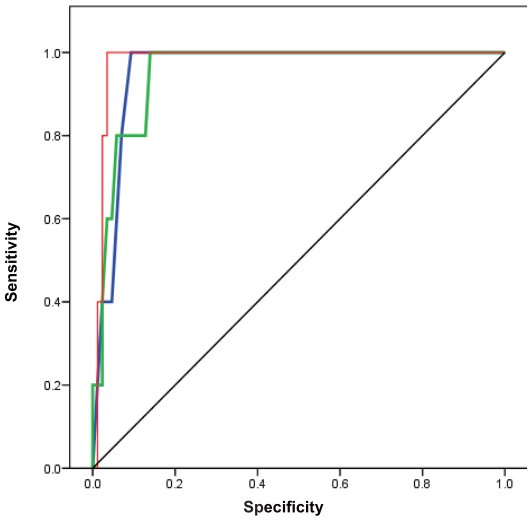

Figure 1. Predictive score based on functional parameters, Child-Pugh (CP) and Model for End-Stage Liver Disease (MELD) scores for short-term mortality in patients with decompensated cirrhosis;
blue line - CP score; green line - MELD score; red line - predictive score based on functional parameters of the liver; black line - referent line;

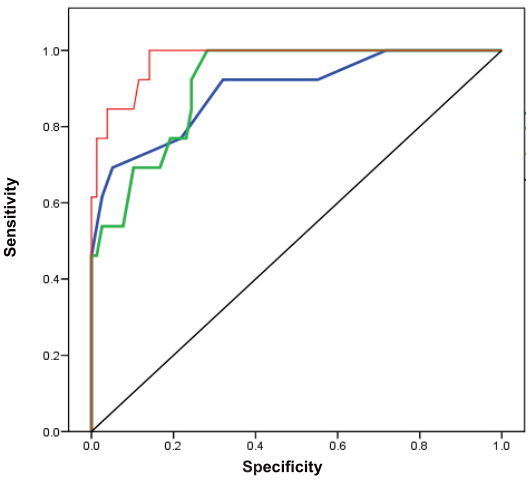

Figure 2. Predictive score based on functional parameters, Child-Pugh (CP) and Model for End-Stage Liver Disease (MELD) scores for long-term mortality in patients with decompensated cirrhosis;
blue line - CP score; green line - MELD score; red line - predictive score based on functional parameters of the liver; black line - referent line;

Receiver operating characteristics analysis was performed in order to test prognostic value of the predictive score based on functional parameters of the liver for mortality rate after six and 24 months. Its prognostic value was compared with CP and MELD scores. Each score independently had a significant level of prediction for short-term (Figure 1) and long-term mortality rate (Figure 2).

DISCUSSION

Predictive score based on functional parameters of the liver was created in this study. It had a better prognostic value for short-term and long-term mortality comparing to MELD and Child-Pugh score in the patients with decompensated cirrhosis. Functional parameters of the liver function, serum bilirubin, international normalized ratio (INR) and serum creatinine showed statistically strong predictive value for short-term and long-term mortality. The GGT and haematocrit had a good prognostic value only for long-term mortality in patients with decompensated cirrhosis. Serum aminotransferase AST and ALT levels and platelet count had no predictive value.

Several studies showed similar results (11-13). Jeong et al. (11) using univariate regression analyses identified that MELD score, lactate, platelet, INR, bilirubin, creatinine, albumin, and C-reactive protein (CRP) predicted in-hospital mortality; multivariate regression analysis showed that MELD score, lactate, albumin, and CRP were significantly associated with in-hospital mortality. In the cohort of 78 patients with decompensated cirrhosis Sullivan et al. (13) found that 70 patients had a normal ALT and 12 had a normal AST with no correlation between complications or death and aminotransferase levels.

In this study, liver functional parameters had almost equally good prognostic value compared with MELD and CP scores for short-term survival. However, MELD score had a better prognostic value than the CP score and liver functional parameters for long-term survival in patients with decompensated cirrhosis. These results are similar and consistent with findings in the studies by Chen et al. (7), Fragaki et al. (10), Jeong et al. (11) and Wu et al. (22).

Based on the level of prognostic value of each liver functional parameter, we created a predictive score derived from liver functional parameters, and compared its predictive value with CP and MELD scores. Each of them independently has shown a great degree of death prediction after 6 or 24 months in patients with end-stage liver disease. Our study has also shown that predictive score derived from liver functional parameters had a better predictive value trend than MELD and CP scores, and MELD score had a better predictive value than CP score.

Our study has two limitations: a relatively small number of patients was enrolled in the study, and it was conducted in a single centre.

In conclusion, to our knowledge and as a result of this study, a new predictive score derived from liver functional parameters was created. It is based on three simple functional parameters: haematocrit, serum creatinine and total bilirubin, which are determined usually in all patients with decompensated cirrhosis. This predictive score has a better prognostic value than MELD and CP scores for short-term and long-term survival rate in patients with decompensated cirrhosis, and it might be used for patient selection for liver transplantation. It is simpler to determine than other used scores. More studies need to be done to prove its validity.

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TRANSPARENCY DECLARATION

Competing interests: None to declare.

REFERENCES

1. Ravaioli F, De Maria N, Di Marco L, Pivetti A, Casciola R, Ceraso C. From listing to recovery: a review of nutritional status assessment and management in liver transplant patients. Nutrients 2023; 15:2778-82.
2. Kulkarni AV, Reddy R, Sharma M, Iyengar S, Rambhatla A, Gv P. Healthcare utilization and outcomes of living donor liver transplantation for patients with APASL-defined acute-on-chronic liver failure. Hepatol Int 2023; 5:1-8.
3. Tejedor-Tejada J, Garcia-Pajares F, Safadi R, Muriz-Barreiro V, Molina E, Juan-Casamayor L. The impact of obesity on postoperative complications and short-term survival after liver transplantation. Eur J Gastroenterol Hepatol 2023; 35:782-9.
4. Haj M, Rockey DC. Predictors of clinical outcomes in cirrhosis patients. Curr Opin Gastroenterol 2018; 34:266-71.
5. Stine JG, Stukenborg GJ, Wang J, Adkins A, Niccum B, Zimmet A. Liver transplant candidates have impaired quality of life across health domains as assessed by computerized testing. Ann Hepatol 2020; 19:62-8.
6. Buechter M, Sarah Kersting S, Gerken G, Kahraman A. Enzymatic liver function measured by LiMAx - a reliable diagnostic and prognostic tool in chronic liver disease. Sci Rep 2019; 9:13577.

7. Chen PC , Chen BH, Huang CH, Jeng WJ, Hsieh YC, Teng W. Integrated model for end-stage liver disease may be superior to some other model for end-stage liver disease-based systems in addition to Child-Turcotte-Pugh and albumin-bilirubin scores in patients with hepatitis B virus-related liver cirrhosis and spontaneous bacterial peritonitis. Eur J Gastroenterol Hepatol 2019; 31:1256-63.
8. Oikonomou T, Goulis L, Doumtsis P, Tzoumari T, Akriviadis E, Cholongitas E. ALBI and PALBI grades are associated with the outcome of patients with stable decompensated cirrhosis. Ann Hepatol 2019; 18:126-36.
9. Xavier SA, Vilas-Boas R, Carvalho PB, Magalhães JT, Marinho CM, Cotter JB. Assessment of prognostic performance of Albumin-Bilirubin, Child-Pugh, and Model for End-stage Liver Disease scores in patients with liver cirrhosis complicated with acute upper gastrointestinal bleeding. Eur J Gastroenterol Hepatol 2018; 30:652-8.
10. Fragaki M, Sifaki-Pistolla D, Orfanoudaki E, Kouroumalis E. Comparative evaluation of ALBI, MELD, and Child-Pugh scores in prognosis of cirrhosis: is ALBI the new alternative? Ann Gastroenterol 2019; 32:626-32.
11. Jeong JH, Lee SB, Sung A, Shin H, Kim DH. Factors predicting mortality in patients with alcoholic liver cirrhosis visiting the emergency department. Medicine (Baltimore) 2023; 102:3307-14.
12. Yuan Nie, Lin-Xiang Liu, Tao Chen, Yue Zhang, Xuan Zhu. Serum lactate level predicts 6-months mortality in patients with hepatitis B virus-related decompensated cirrhosis: a retrospective study. Epidemiol Infect 2021; 149:26-9.
13. Sullivan MK, Daher HB, Rockey DC. Normal or near normal aminotransferase levels in patients with alcoholic cirrhosis. Am J Med Sci 2022; 363:484-9.
14. Reuben A. Child comes of age. Hepatology 2002;35:244-5.
15. Botta F, Giannini E, Romangoli P. MELD scoring system is useful for predicting prognosis in patients with liver cirrhosis and is correlated with residual liver function: a European study. Gut 2003; 52:134-9.
16. Wang J, Zhang Z, Yan X, Li M, Xia J, Liu Y. Albumin-Bilirubin (ALBI) as an accurate and simple prognostic score for chronic hepatitis B-related liver cirrhosis Dig Liver Dis 2019; 51:1172-8.
17. Brunson HO, McDonald MF, Godfrey E, Keeling SS, Cholankeril G, Kanwal F. Is liver transplant justified at any MELD score? 2023; 107:680-92.
18. Wiesner R, Edwards E, Freeman R. Model for end-stage liver disease (MELD) and allocation of donor livers. Gastroenterology 2003; 124: 91-6.
19. Zhang T, Ye B, Shen JJ. Prognostic value of albumin-related ratios in HBV-associated decompensated cirrhosis. J Clin Lab Anal 2022; 36:e24338.
20. Zhang W, Aryan M, Chen Z, Khan W, Thompson B Kwenda E. Prognostic value of neutrophil-to-lymphocyte ratio in cirrhosis patients undergoing transjugular intrahepatic portosystemic shunt. Eur J Gastroenterol Hepatol 2022; 34:435-42.
21. Granados VV, Salazar-Quiñones M, Cheng-Zárate L, Malpica-Castillo A, Mercado JH, Ticse R. Comparison of the prognostic value of mortality Child Pugh Score and forecasting models of chronic liver disease in patients with decompensated cirrhosis of the Hospital Nacional Cayetano Heredia, Lima-Peru. Rev Gastroenterol Peru 2015; 35:307-12.
22. Wu SH, Zheng YX, Tian ZW, Chen MS, Hong-Zhuan Tan HZ. Scoring systems for prediction of mortality in decompensated liver cirrhosis: a meta-analysis of test accuracy. World J Clin Cases 2018; 6:995-1006.
23. Zhou J, Li X, Wang M, Gu C, Liu J. Platelet-to-monocyte ratio as a novel promising agent for the prognosis of hepatitis B virus-associated decompensated cirrhosis. Can J Gastroenterol Hepatol 2023; 2023:6646156.
24. Semmler G, Yang Z, Fritz L, Köck F, Hofer BS, Balcar L. Dynamics in liver stiffness measurements predict outcomes in advanced chronic liver disease. Gastroenterology 2023; S0016-5085(23)04768-6.
25. Xu MM, Wu Y, Li SS, Geng N, W Lu W, Duan BW. Application of different prognostic scores in liver transplantation decision-making for acute-on-chronic liver failure. Zhonghua Gan Zang Bing Za Zhi 2023;31: 574-581.
26. Oikonomou T, Chrysavgis L, Kiapidou S, Adamantou M, Parastatidou D, Papatheodoridis GV. Aspartate aminotransferase-to-platelet ratio index can predict the outcome in patients with stable decompensated cirrhosis. Ann Gastroenterol 2023; 36:442-8.
27. Yousfi MM, Douglas DD,Harrison E. Model for end-stage liver disease (MELD). Dynamic changes in MELD score is important in predicting mortality for patients awaiting liver transplantation (LTX). Hepatology 2001; 34:254A.
28. Papatheodoridis GV, Cholongitas E, Dimitriadou E. MELD vs Child-Pugh and creatinine-modified Child-Pugh score for predicting survival in patients with decompensated cirrhosis. World J Gastroenterol 2005; 11:3099-104.
29. Sumskiene J, Kupcinskas L, Pundzius J, Sumskas L. Prognostic factors for short and long-term survival in patients selected for liver transplantation. Medicina (Kaunas) 2005; 41:39-46.
30. Sahani S, Das D. Neutrophil to lymphocyte ratio (NLR) and its correlation with Child Turcotte Pugh (CTP) Score in predicting severity of decompensated liver cirrhosis. J Assoc Physicians India 2022; 70:11-12.