IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 23, Issue 5 Ser. 10 (May. 2024), PP 39-46
www.iosrjournals.org

Risk Prediction-Scoring System For Acute Kidney Injury In Cirrhotic Patients: Using Renal, Liver, Inflammatory And Vascular Markers

Sudhir J Gupta,[A] Vineet L Gupta,[A] Sahil M Parmar[a]
[A] *Department Of Gastroenterology, Government Medical College And Super Specialty Hospital, Nagpur, India.*

Date of Submission: 18-05-2024 Date of Acceptance: 28-05-2024

I. Introduction

Around 20%-50% cirrhotic patients requiring hospitalization develops acute kidney injury (AKI) (1,2,3) and have bad prognosis with mortality rates up to 90% (4). Severity of liver disease is an important risk factor associated with AKI (5). The role of inflammation in AKI is increasingly recognized, and being reported as a prognostic factor (5). It has been reported that neutrophil-to-lymphocyte ratio (NLR) has a role in predicting acute kidney injury (6,7). It is observed that patients of liver cirrhosis have a combination of immune deficiency and systemic inflammation, which is referred as the cirrhosis-associated immune dysfunction (CAID) syndrome (8). The level of pro-inflammatory cytokines increases and induces vascular dysfunction, worsening renal vasoconstriction with systemic arterial vasodilation (9). Disturbance in renal arterial blood flow causes oxidative stress and renal tubule damage leading to acute kidney injury (9). Diuretic-induced diuresis, infections, gastrointestinal blood loss, nephrotoxic drugs, large volume paracentesis without adequate volume expansion and NSAIDs are some of the common factors precipitating acute kidney injury in patients of cirrhosis (1,10,11).

Monocyte chemotactic protein-1 (MCP-1) belonging to the CC chemokine subfamily of chemokines (12) is associated with severity of AKI in experimental models and is up regulated in both ischemic and nephrotoxic AKI (13,14,15). There is significant and progressive increase in MCP-1 over 24 hours following LVP (16). The MAP is inversely related to both angiotensin II and IL-6. MCP-1 levels increases in patients with more Δ MAP. MCP-1 plays a role in pathogenesis of post paracentesis circulatory dysfunction (16).

Renal function correlates with renal resistive index (RRI) in a variety of kidney disorders (17) and it increases in various clinical stages of cirrhotic renal dysfunction (18). Increase in RRI predict the occurrence of renal dysfunction and is also correlated with the intra-abdominal pressure (19). Intra abdominal pressure reduces the renal perfusion pressure leading to renal failure in cirrhotic patients. (20)

In decompensated cirrhotic patients, AKI have poor impact on survival in either the initial stage (21), or late stage (22,23). Multiple transient episodes of acute kidney injury have negative impact on mid-term survival (24). Repeated severe episodes of AKI increases risk of developing chronic kidney disease in patients of liver cirrhosis (25).

Hepatorenal syndrome (HRS) is also culmination of renal abnormality in decompensated cirrhotic. It's a condition found in patients of advanced hepatic failure, chronic liver disease, and portal hypertension due to arterial circulation abnormalities, impaired renal function and the activity of endogenous vasoactive systems. Cirrhotic patients have marked peripheral vasodilation leading to reduction of total systemic vascular resistance and arterial hypotension, however there is marked renal vasoconstriction, leading to decreased glomerular filtration rate (GFR) (26). Around 18% of Cirrhotic patients develop HRS after 1 year and 39% after 5 years. (27)

There are two types of HRS.
Type 1 HRS: In this there is rapid progressive decline in kidney function with increase of serum creatinine to a level ≥ 2.5 mg/dl, with a poor prognosis. (28)
Type II HRS: In this there is slow progressive increase in the serum creatinine level to >1.5 mg/dl and average survival of 4–6 months. (29)

In tense ascites large volume paracentesis (LVP) is optimum for the treatment. Various studies have been conducted comparing LVP with diuretics. These studies have shown that infusion of albumin along with LVP is more effective than diuretics. LVP combined with albumin is safe and is associated with less frequency

of renal impairment, hyponatremia and hepatic encephalopathy as compared with diuretics. LVP is generally a safe procedure with extremely low risk of local complications such as bowel perforation and hemorrhage. (30)

A scoring system combining values which can be easily calculated at the time of admission predicting the risk of AKI and could be a valuable tool to stratify patients for monitoring, early intervention, prevention, and to improve patient outcomes and care. Hence, we conducted a study with an aim, to evaluate factors predicting acute kidney injury in cirrhotic patients and to develop a scoring system to predict acute kidney injury in patients of liver cirrhosis that will help to predict risk of AKI.

Material and methods

Study population

This prospective cohort study was done at Government medical college and super specialty hospital a tertiary care of central India from March 2019 to February 2020. During this period total 461 cirrhotic patients were admitted in our hospital. Out of these 461 patients, 35 were having spontaneous bacterial peritonitis (SBP) with AKI, 20 were having only SBP, 116 were having AKI, 9 were having cellulitis with AKI, hepatocellular carcinoma in 15 and upper gastrointestinal bleed in 98. Hence, 293 patients were excluded from the study. A total of 168 patients of cirrhosis of liver with ascites between 18 to 68 years of age were enrolled in this study. Approval from ethics committee of the institution was taken. Ethics committee approval number was 175EC/Pharmac/GMC/NGP.

Exclusion criteria

Patients with sepsis as spontaneous bacterial peritonitis or any other infection, hepatocellular carcinoma, cardiac, pulmonary or intrinsic renal failure, acute gastrointestinal bleeding one week before the study, patients with chronic kidney disease, patients with history of renal replacement therapy one week before admission were excluded from the study.

Detailed clinical history including demographic profile, drug history, duration of the disease, and other parameters were noted in proforma. The variables were analyzed including etiology of liver disease, reason for admission, comorbidities, various laboratory data including, hemoglobin, neutrophils, leukocytes, bilirubin, sodium and albumin, baseline serum creatinine, international normalized ratio (INR), mean arterial pressure (MAP), and renal resistive index (RRI) at admission. Cirrhosis was diagnosed by combination of biochemical, radiological and endoscopic findings. The severity of liver disease was assessed with the Child-Turcotte-Pugh (CTP) score and Model of End-stage Liver Disease [MELD] score.

AKI was defined as an increase in serum creatinine ≥0.3 mg/dL within 48 hours or percentage increase in serum creatinine ≥50% from baseline.

Renal resistive index (RRI) 4 hours fasting was required before the measurement of RRI. A convex transducer of 3.5-MHz was used for duplex Doppler ultrasound examination, (Hitachi EUB-8500 and Siemens Sonoline Elegra). RRI was measured on interlobar arteries three times in different regions of each kidney. A mean RI was calculated. (Mean of both kidneys).

The RRI was calculated as:

RRI = (peak systolic velocity – end diastolic velocity)/peak systolic velocity

Mean arterial pressure (MAP)

MAP = diastolic blood pressure + 1/3(systolic blood pressure - diastolic blood pressure)

Neutrophil lymphocyte ratio (NLR)

NLR was calculated using neutrophil and lymphocyte counts at baseline.

NLR = neutrophil count/lymphocyte count.

After baseline assessment of all patients they under went large volume paracentesis (LVP) of approximate 5 liters. Injection human albumin (20%) was administered simultaneously at a dose of 1 U (100 ml) for every 5 liters of ascites drained. MAP was calculated after 4 hours of LVP. The difference between post LVP MAP and pre LVP MAP was calculated. It was labeled as delta MAP (Δ MAP). Follow up was done at one, three and six months. Renal function test (serum creatinine and blood urea) was assessed on each follow up

Statistical analyses

Data was coded and analyzed in statistical software STATA, Version 12.1, 2011. Descriptive statistics like mean, standard deviation (SD) for continuous variables and frequency /percentages for categorical variables were calculated. Two-independent samples t-test to compare means and Chi-square test to compare proportions between AKI and Non-AKI patients were performed. Receiver Operating Characteristics (ROC) Curves were fitted to identify best cut-offs for individual clinical parameters and also for total score on devised scoring system for AKI. Binary multivariable logistic regression analysis was performed to obtain statistical weights from estimated beta (regression) coefficients after suitable mathematical transformations. Validity measures like Sensitivity (%), Specificity (%), Correctly classified (%), Area Under Curve of ROC (%) has also been

evaluated.

II. Results

Demographic and laboratory characteristics in cases of cirrhotic

Out of 168 cases of liver cirrhosis enrolled in study 142 (84.52%) were male and 26 (15.48%) were female with male to female ratio of 5.4. The mean age of cases were 44.73±10.68 years and mean BMI was 17.13 ±1.25 Kg/m2. Etiology of cirrhosis of liver in our study was alcohol in 112 (66.66%), others in 30 (17.85%) and hepatitis B related in 26 (15.47%) with mean CTP score of 8.39 ±1.65 and mean MELD score of 17.13 ±3.12. Liver function test as noted was mean total bilirubin of 3.28 ±2.11 mg/dl, mean serum albumin 3.32 ±0.47 g/l, mean AST and ALT of 53.65 ±40.86 IU and 54.77 ± 28.94 IU respectively with mean INR of 1.65 ± 0.18. The various other parameters assessed were mean NLR of 5.37 ± 1.33, mean Δ MAP of 5.4 ±1.32 mm of Hg and mean RRI was 0.69 ±0.44. Baseline mean serum creatinine and urea was 0.93 ±0.16 mg/dl and 22.97 ±4.96 mg/dl respectively. Follow up mean serum creatinine and urea at one month was 1.1 ± 0.16 mg/dl and 26.19 ± 5.70 mg/dl respectively, at three months 1.20 ±0.28 mg/dl and 29.26 ±7.39 mg/dl respectively and at six months 1.08 ±0.20 mg/dl and 29.09 ± 4.28 mg/dl respectively. (Table 1)(enclosed)

Comparison of baseline parameters in patients of liver cirrhosis developing AKI on follow-up with patients without AKI.

Out of 168 cases on follow up 60 (35.71%) cases developed AKI and 108 (64.28%) cases were without AKI. Patients of liver cirrhosis developing AKI on follow up were having statistically raised NLR (5.85 ±0.27 vs. 5.14 ± 0.16, p=0.0140), raised Δ MAP (6.46 ± 0.22 vs. 4.81 ±0.13, p=0.0001), high MELD score (19.1 ±0.52 vs. 16.03 ±0.37, p=0.0001) and increased RRI (0.70± 0.007 vs. 0.67 ±0.005, 0.0031) at baseline compared with patients of cirrhosis of liver who did not developed AKI on follow up. There was no difference in serum creatinine level between the groups. (Table 2) (enclosed)

Cut-off for each clinical parameter

The best cut-offs for the above five clinical parameters by fitting Receiver Operator Characteristics (ROC) Curve to our own data were used. These cut-offs formed a basis for a devising a risk scoring system that will help us in predicting AKI in our study population with more accuracy and reliability. (Table 3) (enclosed)

Cut-off of ≥ 6 mm of Hg for Δ MAP was considered with AUC of 0.8410, with sensitivity of 80% and specificity of 79.63%. Similarly cut-off of ≥ 5.7 was considered for NLR with AUC 0.6716 with sensitivity of 70% and specificity of 68.52%. Cut-off of ≥ 0.7 was considered for RRI with AUC of 0.6951 and sensitivity of 76.67% and specificity of 79.63%. Cut-off of ≥ 18 was considered for MELD with AUC of 0.7679 and sensitivity of 60% and specificity of 68.52%. Cut-off of ≥ 1 mg/dl was considered for serum creatinine with AUC of 0.4500 and sensitivity of 56.67%and specificity of 42.59%. (Table 3) (enclosed)

Devising a Risk prediction scoring system

Different parameters would contribute in different magnitude to the proposed risk scoring system. In order to find their relative importance jointly, a multivariable analysis model was fitted using the best cut-offs from ROC. Unconditional Multiple Logistic Regression (MLR) analysis was performed for predicting a binary outcome (AKI yes/no). Beta (β) regression coefficients (weights) from the fitted model were transformed in to integer scores by doing suitable mathematical adjustment [score = mod |(beta coeffcient)| rounded to nearest integer]. Such transformation was necessary to make the scoring system easy for understanding and interpretation in actual clinical practice. Thus score for NLR 1.5 is rounded to respective weight of 2 and similarly for Δ MAP 2.98 to 3, for serum creatinine 0.17 to 1, for MELD 1.52 to 2 and for RRI 1.21 to 2. (Table 4) (enclosed) Finally, the aggregate of the weighted scores resulted in to a 10-point scoring system. (Table 5) (enclosed)

Thus, any individual patient measured on the above scoring system may get a minimum score of Zero (0) and a maximum score of ten (10). (Table 5) (enclosed) Again a ROC Curve was fitted to the devised 10-point scoring system (Figure 1) to identify the best cut-off.

ROC analysis suggested a total score ≥ 4 is an optimum cut off for a ten-point scoring using MLR analysis. This cut-off will enable a clinician to predict AKI in 66.67% of the suspected cases, with statistical significance (p=0.023). (Table 6) (enclosed)

Therefore, a total score more than or equal to 4 on this 10-point scoring system yield a reasonably good sensitivity of approximatley 67%, specificity of approximatley 78%, positive lilkelihood ratio (LR+) of 3 and 73% correctly classified, With a predictive accuracy (AUC) = 81% the devised scoring system can be considered for early identification and better management of AKI cases in cirrhosis of liver.

III. Discussion

Renal failure is not uncommon complication in liver cirrhosis patients. It is associated with high morbidity and mortality (31). Renal dysfunction occurs in 20–50% of hospitalized patients (23). Renal failure is serious complication of decompensated cirrhosis, rapidly leading towards death and liver transplantation. Hepatorenal syndrome (HRS) is a type of acute kidney injury with frequent and life threatening complication in decompensated cirrhosis (32). The pathophysiology of HRS is related to renal arterial vasoconstriction with hypo perfusion secondary to splanchnic vasodilatation. Recent studies suggested that, circulating proinflammatory cytokines levels are increased in patients of cirrhosis with renal failure. The patients of liver cirrhosis are characterized by changes in systemic hemodynamics (33). The clinical course of this disease is frequently complicated by renal dysfunction. The intrarenal resistance can be measured by Doppler ultrasound, which measures renal blood flow and correlates with portal venous pressure (34,35). Many studies have observed that intrarenal RIs are significantly lower in healthy controls as compared to cirrhotic patients. Decompensated patients of liver cirrhosis with normal serum creatinine may have elevated RRIs (36,37,38,39,40).

NLR is a recognized predictor of survival in patients of cirrhosis of liver with hepatitis B virus (HBV) infection, hepatocellular carcinoma and in patients awaiting transplantation (41,42,43) Moreover, some studies have shown that in uncomplicated cirrhosis, raised NLR could predict mortality independent of the MELD and CTP scores (44).

Mean arterial pressure (MAP) is a good reliable index of circulatory dysfunction in patients with liver cirrhosis ascites. Low MAP has shown association with advancement of hepatorenal syndrome (45), hyper dynamic circulation (46,47,48), indicating that MAP may be an important factor to indicate the prognosis of patients with cirrhosis of liver. MAP lower than 50–60 mmHg have a positive correlation with increased morbidity in cases of kidney dysfunction (45).

In our study patients of liver cirrhosis developing AKI on follow up were having statistically raised NLR, high Δ MAP, high MELD score and increased RRI at baseline compared with patients of liver cirrhosis who did not developed AKI on follow up.

Salman TA et al found that patients of liver cirrhosis with deranged renal function had significant decrease in MAP after LVP compared to patients of liver cirrhosis with normal renal function. They also found that RRI decreased in both the group post LVP but it was still higher in the cases of cirrhosis of liver with deranged renal function (49). Lai *et al* found a significant decrease in the MAP during the first 2 h of LVP (50). Phillip *et al* also found a decrease in the MAP immediately, 2 h after and 6 h after LVP (51).

Maroto et al. found that group of cirrhotic patients with renal failure have high RRIs and on follow-up they found RRI as a marker of poor survival in the univariate analysis (52). Similarly Platt et al. measured RRI in 180 patients of liver cirrhosis without kidney dysfunction and on follow-up, the HRS developed in 26% of patients with an initial RRI >0.7, and only 1% in those with normal RRIs (53).

Joana Gameiro et al found that high NLR is independently associated with AKI (p=0.028) (54). Mohsen Abu Alfeilat et al found that mean NLR was significantly higher in AKI compare to non-AKI patients (55).

MELD score is a prognostic marker in a wide variety of causes of liver cirrhosis and severity and, incorporating an assessment of renal function (56).

In this study, we devised a cost effective and easily calculable risk score that predicts acute kidney injury in liver cirrhotic patients. This scoring system, which can be calculated easily from a biochemistry panel, complete hemogram, Doppler of renal artery and blood pressure reported at the time of hospital admission, reliably predicting AKI in cirrhotic patients with AUROC of 0.8136.

The variables used, as risk factors for the prediction of AKI in this score are serum creatinine, RRI, NLR, MELD score and Δ MAP which are already proved predictors of kidney dysfunction in previous literature. The scoring system has minimum zero and maximum 10 score with cut-off of ≥ 4. Thus a total score more than or equal to 4 on this 10-point scoring system had reasonably good sensitivity of approximately 67%, specificity of approximately 78%, positive likelihood ratio (LR+) of 3 and 73% correctly classified, with a predictive accuracy (AUC) of 81%.

Some limitations were noted. It was a single-center prospective cohort study that limits the generalization of our results, hence a multicenter large cohort studies are further required. Finally, we used serum creatinine at admission as a baseline, which tends to underestimate the incidence of AKI, but the other serum creatinine based glomerular filtration rate (GFR) formulas like the modification of diet in renal disease (MDRD) in cirrhosis of liver overestimates GFR.

However, our study suggests, to our knowledge, that this may be the first risk prediction scoring system for predicting AKI in patients of liver cirrhosis that includes inflammation, liver, renal and vascular system function assessment. The predictive value of our AUROC curve is strong, suggesting the potential confirmation of this scoring system in other population.

IV. Conclusion

Development of AKI in Patients of cirrhosis can be predicted by a scoring system which combines neutrophil-lymphocyte ratio, mean arterial pressure, MELD score and increased renal resistive index at baseline. The development of acute kidney injury in cirrhosis of liver is multi-factorial. The advantage of this novel scoring system is that it involves dynamic and static parameter like markers of inflammation, liver, renal and vascular system. It is simple, cost effective, reproducible, reliable and easily calculated scoring system. However large scale studies are required to know the long term prognosis and further validation.

Statement of Ethics

This study was conducted in accordance with the World Medical Association Declaration of Helsinki. Institutional ethics committee approval was taken prior to starting of study. Informed consent was obtained from the study population.

Disclosure Statement

The authors have no conflicts of interest.

Funding Sources

Grants and financial support: nil.

Figure 1 ROC graph for total score

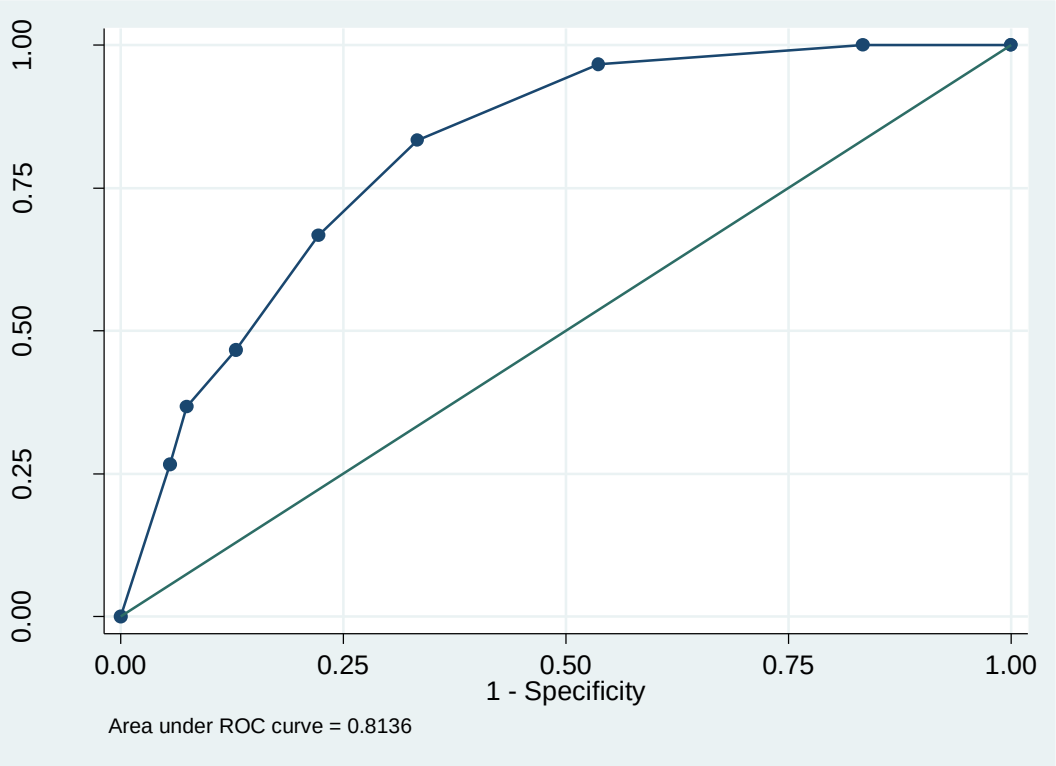

Table 1 Demographic details, clinical and laboratory parameters of patients.

Variables	Cases (n=168) Mean ± SD
Age (years)	44.73±10.68
Male: Female	5.4:1
BMI (kg/m2)	17.13 ±1.25
Etiology	Alcohol =112 (66.66%) Others =30 (17.85%) HBV= 26 (15.47%)
Child-Turcotte-Pugh (CTP) score	8.39 ±1.65
MELD score	17.13 ±3.12
Hemoglobin (g/L)	9.62 ± 0.97
NLR	5.37 ± 1.33
Total Bilirubin (mg/dl)	3.28 ±2.11
Serum Albumin (g/dL)	3.32 ±0.47

AST (U/L)	53.65 ±40.86
ALT (U/L)	54.77 ± 28.94
INR	1.65 ± 0.18
Delta (Δ) MAP (mm of Hg) (baseline)	5.4 ±1.32
RRI (baseline)	0.69 ±0.44
Urea (mg/dl) (baseline)	22.97 ±4.96
Creatinine (mg/dl) (baseline)	0.93 ±0.16
Urea (mg/dl) (first month)	26.19 ± 5.70
Creatinine (mg/dl) (first month)	1.1 ± 0.16
Urea (mg/dl) (third month)	29.26 ±7.39
Creatinine (mg/dl) (third month)	1.20 ±0.28
Urea (mg/dl) (sixth month)	29.09 ± 4.28
Creatinine (mg/dl) (sixth month)	1.08 ±0.20

BMI = body mass index, MELD = Model of End-stage Liver Disease, NLR= Neutrophil lymphocyte ratio, AST= aspartate transaminase, ALT= alanine aminotransferase, INR= International normalized ratio, RRI= Renal resistive index, MAP= Mean arterial pressure, SD= standard deviation

Table 2 Table of comparison of baseline parameters between patients developing AKI on follow up with those patients not developing AKI.

Parameters	Non AKI (n=108) Mean ± SD	With AKI (60) Mean ± SD	P value
NLR	5.14 ± 0.16	5.85 ±0.27	0.0140
Δ MAP (mm of Hg)	4.81 ±0.13	6.46 ±0.22	0.0001
MELD score	16.03 ±0.37	19.1 ±0.52	0.0001
RRI	0.67 ±0.005	0.70± 0.007	0.0031
Serum creatinine (mg/dl)	0.94 ±0.02	0.92 ±0.31	0.5562

MELD = Model of End-stage Liver Disease, NLR= Neutrophil lymphocyte ratio, RRI= Renal resistive index, Δ MAP= Delta Mean arterial pressure, AKI= acute kidney injury. SD= standard deviation

Table 3 Table of best cut- off for each clinical parameter was identified using ROC curve

Parameters	Sensitivity	Specificity	Percentage correctly classified	Likelihood ratio + (LR+)	Likelihood ratio– (LR-)	Area under curve (AUC)
Δ MAP ≥ 6 mm of Hg	80%	79.63%	79.76%	3.92	0.25	0.8410
NLR ≥ 5.7	70%	68.52%	69.05%	2.22	0.43	0.6716
RRI ≥ 0.7	76.67%	79.63%	78.57%	3.76	0.29	0.6951
MELD ≥ 18	60%	68.52%	65.48%	1.90	0.58	0.7679
Serum creatinine ≥ 1 mg/dl	56.67%	42.59%	47.62%	0.98	1.01	0.4500

MELD = Model of End-stage Liver Disease, NLR= Neutrophil lymphocyte ratio, RRI= Renal resistive index, Δ MAP= Delta Mean arterial pressure, AKI= acute kidney injury.

Table 4 Binary multiple logistic regression (MLR) model to predict AKI using best cut-offs of 5 variables

Parameters	β Coefficient	Odd ratio	95% confidence interval	P value	Respective weight
NLR	-1.582	0.20	0.03-1.15	0.073	2
Δ MAP	2.98	19.84	4.27-92.17	0.000	3
Serum creatinine	-0.17	0.84	0.19-3.61	0.817	1
MELD	1.52	4.60	0.97-21.66	0.053	2
RRI	1.21	3.38	0.84-13.58	0.086	2

MELD = Model of End-stage Liver Disease, NLR= Neutrophil lymphocyte ratio, RRI= Renal resistive index, Δ MAP= Delta Mean arterial pressure, AKI= acute kidney injury.

Table 5 Risk prediction score system

Parameters	Score	Min	Max
Δ MAP ≥ 6 mm of Hg	3	0	3
NLR ≥ 5.7	2	0	2
RRI ≥ 0.7	2	0	2
MELD ≥ 18	2	0	2
Serum creatinine ≥ 1 mg/dl	1	0	1
Total score	10	0	10

MELD = Model of End-stage Liver Disease, NLR= Neutrophil lymphocyte ratio, RRI= Renal resistive index, Δ MAP= Delta Mean arterial pressure, AKI= acute kidney injury.

Table 6 Frequency distribution of AKI and Non AKI subjects by total scores

Total score	Non AKI (n=108)	AKI (n=60)
< 4	64 (59.26%)	20 (33.33%)
≥ 4	44 (40.74%)	40 (66.67%)
P =0.023		

AKI= Acute kidney injury

References:

[1] Garcia-Tsao G, Parikh Cr, Viola A. Acute Kidney Injury In Cirrhosis. Hepatology. 2008;48(6):2064–2077.
[2] Tandon P, James Mt, Abraldes Jg, Et Al. Relevance Of New Definitions To Incidence And Prognosis Of Acute Kidney Injury In Hospitalized Patients With Cirrhosis: A Retrospective Population- Based Cohort Study. Sands Jm, Ed. Plos One. 2016;11(8):E0160394.
[3] Davenport A, Sheikh Mf, Lamb E, Et Al. Acute Kidney Injury In Acute-On-Chronic Liver Failure: Where Does Hepatorenal Syn- Drome Fit? Kidney Int. 2017;92(5):1058–1070.
[4] Fede G, D'amico G, Arvaniti V, Et Al. Renal Failure And Cirrho- Sis: A Systematic Review Of Mortality And Prognosis. J Hepatol. 2012;56(4):810–818.
[5] Thabut D, Massard J, Gangloff A, Et Al. Model For End-Stage Liver Disease Score And Systemic Inflammatory Response Are Major Prognostic Factors In Patients With Cirrhosis And Acute Functional Renal Failure. Hepatology. 2007;46:1872–1882.
[6] Abu Alfeilat M, Slotki I, Shavit L. Single Emergency Room Measurement Of Neutrophil/Lymphocyte Ratio For Early Detection Of Acute Kidney Injury (Aki). Intern Emerg Med. Epub 2017, Jul 29.
[7] Yilmaz H, Cakmak M, Inan O, Et Al. Can Neutrophil- Lymphocyte Ratio Be Independent Risk Factor For Predicting Acute Kidney Injury In Patients With Severe Sepsis? Ren Fail. 2015;37(2): 225–229.
[8] Bucsics T, Mandorfer M, Schwabl P, Et Al. Impact Of Acute Kidney Injury On Prognosis Of Patients With Liver Cirrhosis And Ascites: A Retrospective Cohort Study. J Gastroenterol Hepatol. 2015;30(11):1657–1665.
[9] Giron-Gonzalez Ja, Martinez-Sierra C, Rodriguez-Ramos C, Et Al. Implication Of Inflammation-Related Cytokines In The Natural History Of Liver Cirrhosis. Liver Int. 2004;24(5):437–445.
[10] Ginès P, Schrier Rw. Renal Failure In Cirrhosis. N Engl J Med 2009;361:1279–1290.
[11] Fasolato S, Angeli P, Dallagnese L, Et Al. Renal Failure And Bacterial Infections In Patients With Cirrhosis: Epidemiology And Clinical Features. Hepatology 2007;45:223–229.
[12] Egashira K. Molecular Mechanisms Mediating Inflammation In Vascular Disease: Special Reference To Monocyte Chemoattractant Protein-1. Hypertension 2003; 41: 834–41.
[13] Munshi R, Johnson A, Siew Ed, Et Al. Mcp-1 Gene Activation Marks Acute Kidney Injury. J Am Soc Nephrol 2011; 22: 165–75.
[14] Murali Ns, Ackerman Aw, Croatt Aj, Et Al. Renal Upregulation Of Ho-1 Reduces Albumin-Driven Mcp-1 Production: Implications For Chronic Kidney Disease. Am J Physiol Renal Physiol 2007; 292: F837–44.
[15] Rice Jc, Spence Js, Yetman Dl, Et Al. Monocyte Chemoattractant Protein-1 Expression Correlates With Monocyte Infiltration In The Post-Ischemic Kidney. Ren Fail 2002; 24: 703–23.
[16] Carl De, Ghosh S, Cheng J, Et Al. Post-Paracentesis Circulatory Derangements Are Related To Monocyte Activation. Liver Int. 2014;34(7):1001-1007.
[17] Tublin Me, Bude Ro, Platt Jf. The Resistive Index In Renal Doppler Sonography: Where Do We Stand? Am J Roentgenol 2003; 180:885–892.
[18] Rivolta R, Maggi A, Cazzaniga M, Et Al. Reduction Of Renal Cortical Blood Flow Assessed By Doppler In Cirrhotic Patients With Refractory Ascites. Hepatology 1998; 28:1235–1240.
[19] Kirkpatrick Aw, Colistro R, Laupland Kb, Et Al. Renal Arterial Resistive Index Response To Intraabdominal Hypertension In A Porcine Model. Crit Care Med 2007; 35:207–213.
[20] Malbrain Ml. Abdominal Pressure In The Critically Ill: Measurement And Clinical Relevance. Intensive Care Med 1999; 25:1453–1458.
[21] Piano S, Rosi S, Maresio G, Et Al. Evaluation Of The Acute Kidney Injury Network Criteria In Hospitalized Patients With Cirrhosis And Ascites. J Hepatol 2013;59:482–489.
[22] Fagundes C, Barreto R, Guevara M, Et Al. A Modified Acute Kidney Injury Classification For Diagnosis And Risk Stratification Of Impairment Of Kidney Function In Cirrhosis. J Hepatol 2013;59:474–481.
[23] Huelin P, Piano S, Solà E, Et Al. Validation Of A Staging System For Acute Kidney Injury In Patients With Cirrhosis And Association With Acute-On-Chronic Liver Failure. Clin Gastroenterol Hepatol 2017;15:438–445.
[24] Tsien Cd, Rabie R, Wong F. Acute Kidney Injury In Decompensated Cirrhosis. Gut 2013;62:131–137.
[25] Chawla Ls, Eggers Pw, Star Ra, Et Al. Acute Kidney Injury And Chronic Kidney Disease As Interconnected Syndromes. N Engl J Med 2014;371:58–66.
[26] Salerno F, Gerbes A, Ginès P, Wong F, Arroyo V. Diagnosis, Prevention And Treatment Of Hepatorenal Syndrome In Cirrhosis. Gut 2007; 56:1310–1318.
[27] Schuppan D, Afdhal Nh. Liver Cirrhosis. Lancet 2008; 371:838–851.
[28] Arroyo V, Guevara M, Ginès P. Hepatorenal Syndrome In Cirrhosis: Pathogenesis And Treatment. Gastroenterology 2002; 122:1658–1676.
[29] Ginès P, Guevara M, Arroyo V, Et Al. Hepatorenal Syndrome In Cirrhosis. Lancet 2003; 362:1819–1827.
[30] Pache I, Bilodeau M. Severe Haemorrhage Following Abdominal Paracentesis For Ascites In Patients With Liver Failure. Aliment Pharmacol Ther 2005; 21:525–529.
[31] Garcia-Tsao G, Parikh Cr, Viola A: Acute Kidney Injury In Cirrhosis. Hepatology 2008;48:2064–2077.
[32] Martín-Llahí M, Guevara M, Torre A, Et Al: Prognostic Importance Of The Cause Of Renal Failure In Patients With Cirrhosis. Gastroenterology 2011;140:488–496.
[33] Angeli P, Gines P, Wong F, Et Al: Diagnosis And Man- 21 Agement Of Acute Kidney Injury In Patients With Cirrho- Sis: Revised Consensus Recommendations Of The Inter- National Club Of Ascites. Gut 2015;64:531–537
[34] Zeller T, Bonvini Rf, Sixt S: Color-Coded Duplex Ultrasound For Diagnosis Of Renal Artery Stenosis And As Follow-Up Examination After Revascularization. Catheter Cardiovasc Interv 2008;71:995–999.
[35] Chudek J, Kolonko A, Krol R, Et Al. The Intrarenal Vascular Resistance Parameters Measured By Duplex Doppler Ultrasound Shortly After Kidney Transplantation In Patients With Immediate, Slow, And Delayed Graft Function. Transplant Proc

2006;38:42–45.
[36] Wang Y, Liu L-P, Wen S-B, Et Al. Renal Haemodynamics In Patients With Liver Cirrhosis Assessed By Colour Ultrasonography. J Int Med Res 2011; 39:249–255.
[37] Götzberger M, Kaiser C, Landauer N, Et Al. Intrarenal Resistance Index For The Assessment Of Early Renal Function Impairment In Patients With Liver Cirrhosis. Eur J Med Res 2008;13: 383–387.
[38] Sacerdoti A, Bolognesi M, Merkel C, Et Al. Renal Vasoconstriction In Cirrhosis Evaluated By Duplex Doppler Ultrasonography. Hepatology 1993; 17: 219–224
[39] Colli A, Cocciolo M, Riva C, Et Al. Abnormal Renovascular Impedance In Patients With Hepatic Cirrhosis: Detection With Duplex Us. Radiologie1993;187:561–563.
[40] Celebi H, Dönder E, Celiker H: Renal Blood Flow Detection With Doppler Ultrasonography In Patients With Hepatic Cirrhosis. Arch Intern Med 1997;157:564–567.
[41] Gao F, Li X, Geng M, Et Al. Pretreatment Neutrophil-Lymphocyte Ratio: An Independent Predictor Of Survival In Patients With Hepatocellular Carcinoma. Medicine (Baltimore) 94(11):E639, 2015.
[42] Chen L, Lou Y, Chen Y, Et Al. Prognostic Value Of The Neutrophil-To- Lymphocyte Ratio In Patients With Acute-On-Chronic Liver Failure. Int J Clin Pract 68(8):1034 – 1040, 2014.
[43] Leithead Ja, Rajoriya N, Gunson Bk, Et Al. Neutrophil-To-Lymphocyte Ratio Predicts Mortality In Patients Listed For Liver Transplantation. Liver Int 35(2):502 – 509, 2015.
[44] Biyikm, Ucarr, Solaky, Et Al.: Blood Neutrophil-To-Lymphocyte Ratio Independently Predicts Survival In Patients With Liver Cirrhosis. Eur J Gastroenterol Hepatol 25(4):435 – 441, 2013.
[45] Thooft A, Favory R, Salgado Dr, Et Al. Effects Of Changes In Arterial Pressure On Organ Perfusion During Septic Shock. Crit Care 2011; 15: R222.
[46] Llach J, Gines P, Arroyo V, Et Al. Prognostic Value Of Arterial Pressure, Endogenous Vasoactive Systems, And Renal Function In Cirrhotic Patients Admitted To The Hospital For The Treatment Of Ascites. Gastroenterology 1988; 94: 482-7.
[47] Xu Jy, Ma Sq, Pan C, Et Al. A High Mean Arterial Pressure Target Is Associated With Improved Microcirculation In Septic Shock Patients With Previous Hypertension: A Prospective Open Label Study. Crit Care 2015; 19: 130.
[48] Gomez Ev, Rodriguez Ys, Bertot Lc, Et Al. The Natural History Of Compensated Hcv-Related Cirrhosis: A Prospective Longterm Study. J Hepatol 2013; 58: 434-44.
[49] Salman Ta, Zaghla He, Attallah Km, Et Al. The Impact Of Large-Volume Paracentesis On Renal Haemodynamics In Cirrhotic Patients With Ascites. Egypt J Intern Med 2014;26:170-5.
[50] Lai Kn, Li P, Law E, Swaminathan R, Et Al. Large-Volume Paracentesis Versus Dialytic Ultrafiltration In The Treatment Of Cirrhotic Ascites. Q J Med 1991; 78:33–41.
[51] Phillip V, Saugel B, Ernesti C, Et Al. Effeects Of Paracentesis On Hemodynamic Parameters And Respiratory Function In Critically Ill Patients. Bmc Gastroenterol 2014; 14:18.
[52] Maroto A, Ginès A, Salo J, Et Al. Diagnosis On Functional Kidney Failure Of Cirrhosis With Doppler Sonography: Prognostic Value Of Resistive Index. Hepatology 1994;20:839–844.
[53] Platt J, Ellis J, Rubin J, Et Al. Renal Duplex Doppler Ultrasonography: A Noninvasive Predictor Of Kidney Dysfunction And Hepatorenal Failure In Liver Disease. Hepatology 1994;20:362–369.
[54] Gameiro J, Agapito Fonseca J, Monteiro Dias J, Et Al. Prediction Of Acute Kidney Injury In Cirrhotic Patients: A New Score Combining Renal, Liver And Inflammatory Markers. Int J Nephrol Renovasc Dis. 2018;11:149-154.
[55] Abu Alfeilat M, Slotki I, Shavit L. Single Emergency Room Measurement Of Neutrophil/Lymphocyte Ratio For Early Detection Of Acute Kidney Injury (Aki). Intern Emerg Med. Epub 2017, Jul 29.
[56] Kamath Ps, Kim Wr, Advanced Liver Disease Study Group. The Model For End-Stage Liver Disease (Meld). Hepatology. 2007;45 (3): 797–805.