Original Article

Hematological and Biochemical Alterations in Chronic Liver Disease and Their Correlation with MELD-Na Score and Short-Term Mortality - A Longitudinal Prospective Study

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Abstract

Background: Chronic liver disease (CLD) is a progressive deterioration of liver functions for more than six months. India contributed to 18.3% of the two million global liver disease–related deaths in 2015. The aim of this study is to assess the changes in hematological and biochemical parameters among CLD patients, their correlation with Model for End- stage Liver Disease – Sodium (MELD Na) Score and predict 28day mortality. This longitudinal prospective study included 205 CLD patients (>14 years age, disease >6 months) at a tertiary center in central India. Patients with Hepatitis A/E, anemia treatment, or bone marrow-suppressing drugs were excluded. **Material and Methods:** Hematological (TLC, platelet count, hemoglobin, PWR, NLR) and biochemical (bilirubin, AST, ALT) parameters were analyzed across MELD-Na groups and survival status. Statistical analysis of data was presented as median/IQR and analyzed using Kruskal-Wallis, Mann-Whitney, multivariate analysis, and ROC curves. **Results:** Mortality increased with rising MELD Na scores. Higher MELD Na groups showed increased TLC, NLR , serum bilirubin, ALT, and AST, with decreased platelet count and PWR. Non-survivors had significantly higher TLC, bilirubin, AST, ALT, and lower PWR. Serum bilirubin was the only independent predictor of mortality. ROC analysis showed good predictive accuracy for bilirubin (AUC 0.756; cut-off 3.2 mg/dL, sensitivity 77.3%, specificity 67.6%) and AST (AUC 0.701; cut-off 59.65 U/L, sensitivity 71.2%, specificity 52.5%). **Conclusion:** Alterations in hematological and biochemical parameters can serve as early indicators of high-risk patients, enabling timely interventions to minimize morbidity and mortality.

Keywords: CLD, Hematological Changes, Biochemical Changes.

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Introduction

Chronic liver disease (CLD) is a progressive deterioration of liver functions for more than six months.[1] The burden of liver disease in India is significant because it alone contributed to 18.3% of the two million global liver disease–related deaths in 2015.[2] The common etiologies of CLD are Alcoholic liver disease, Non-alcoholic fatty liver disease (NAFLD/NASH), chronic viral hepatitis (hepatitis B, C, and D infections), genetic causes (alpha-1 antitrypsin deficiency, hereditary hemochromatosis, wilson disease), autoimmune causes, drugs, idiopathic/cryptogenic.[1] Chronic liver disease is frequently associated with haematological abnormalities such as anemia, decreased platelet count, increased total leukocyte count and biochemical abnormalities which reflect in different values of LFT and RFT.

MELD Na Score has been used as a predictor of survival in patients awaiting liver transplantation and to predict the risk of mortality in patients with cirrhosis. There is fair amount of mortality associated with CLD so it is important to identify the predictive markers of mortality. The aim of this study is to assess the changes in hematological and biochemical parameters among CLD patients, their correlation with Model for End- stage Liver Disease – Sodium (MELD Na) Score and predict 28day mortality to enable early identification and timely intervention of high-risk patients. Thus, helping to reduce the disease burden. The objectives of the study were -

- To estimate the Model for End-stage Liver Disease– Sodium (MELD Na) score for severity of chronic liver disease.
- To measure the changes in hematological parameters (Total Leukocyte Count (TLC), Platelets, Hemoglobin, Platelet to White Blood Cell ratio (PWR), Neutrophil to Lymphocyte ratio(NLR) among CLD patients.
- To study LFT among CLD patients.
- To measure the association between MELD score and the above hematological and biochemical parameters.
- Using hematological and biochemical changes to predict 28 day mortality.

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Materials and Methods

This was a longitudinal prospective study on 205 patients with CLD, conducted from August 2023 to January 2025, in a tertiary care centre of central India. The study was approved by Institutional Ethics Committee. Written informed consent was obtained.

Inclusion Criteria-

- Patients >14 years of age.
- Duration of disease >6 months
- All patients with diagnosis of Chronic Liver Disease.

Exclusion Criteria:

- Hepatitis A, Hepatitis E patients.
- Patients on treatment for Anemia.
- Patients on drugs (Chemotherapeutic agents, Antiepileptics, Methotrexate, Doxorubicin) causing bone marrow suppression.

Patients were selected according to the inclusion and exclusion criteria. Careful history and detailed clinical examination was carried out for each patient. Under all aseptic conditions blood samples were collected and analysed for complete blood count by Zybio Z3 analyser, biochemical analysis (using Beckman Coulter D x C 700 AU), Prothrombin Time (PT/INR) using Yumizen G200. We followed up the patients upto 28 days to assess the outcome of disease.

MELD Score and MELD Sodium Score was calculated for each study subject using –

MELD Score= 3.78 x log (serum total bilirubin) + 11.2 x log (INR) + 9.57 x log (serum creatinine) + 6.43.

MELD Sodium (MELD Na) = MELD + 1.32 x (137-Na) - [0.033 x MELD x (137-Na)]

They were grouped depending on the MELD Sodium Score as follows:

MELD Na Score	MELD Na Group
40 or more	5
30–39	4
20–29	3
10–19	2
< 9	1

Hematological [Total Leukocyte Count (TLC), Platelets, Hemoglobin, Platelet to White Blood Cell ratio (PWR), Neutrophil to Lymphocyte ratio(NLR)] and Biochemical (Serum Bilirubin, AST, ALT) parameters were expressed in different MELD Na Groups and survivors/ non- survivors. Statistical Analysis was done.

Ethical committee approval was received. (Approval no: IEC/2023/7335 - 61, Date: 18- 08-2023). Written informed consent was obtained from the patients who agreed to take part in the study.

Statistical Analysis: It was done using SPSS software version 27.0. Continuous variables were expressed in form of Median and IQR2-3(Inter Quartile range) and categorical data was expressed as percentage. Difference in variables with MELD Group was analyzed using Kruskal- Wallis test, with outcome using Mann – Whitney test. Multiple logistic regression was applied to identify independent predictors of 28-day mortality. Receiver Operating Characteristics (ROC) curve was used to analyze the performance of measured variables and ratios studied. A p value < 0.05 was considered statistically significant.

Results

Patient Characteristics

A total of 205 patients with CLD were included in this study, out of which 197 were males and 8 were females. Mean ± SD age at presentation was 42.92 ± 11.34 years. The most common etiology was alcohol (74.23%) followed by Hepatitis B virus (10.7%), cryptogenic (7.8%), NASH (3.4%), Hepatitis C virus (2.9%), wilson's Disease (0.97%). Among 205 patients, 139 survived and 66 died after 28 days of admission. Maximum patients had a MELD Na Score between 10 – 19; Group 2.

Baseline characteristics of study subjects are shown in [Table 1].

Mortality and MELD Na Score [Table 2]

Maximum number of patients have the MELD Sodium score between 10 to 19 (Group- 2), amongst them 69.4% are survivors and 30.6% are non- survivors. Patients having MELD Sodium score of < or equal to 9 (Group 1) have the highest survival percent of 89.5%. It is also evident that as the MELD Sodium score increases the survival percentage decreases and the mortality percentage increases ($p< 0.001$)

Hematological and biochemical parameters across different MELD Na Groups [Table 3].

Hematological and biochemical parameters including Total Leucocyte Count, NLR, Serum Bilirubin, AST and ALT increased significantly with increase in MELD Na Score. Platelet Count, PWR significantly decreased with increase in MELD Na score. Hemoglobin values did not show significant correlation with MELD Na score.

Comparison of hematological and biochemical parameters with 28day Outcome [Table 4].

Amongst the hematological parameters TLC in non- survivors [Median/IQR (2-3) - 11.74/(7.22- 15.89)] was significantly higher compared to survivors [Median/IQR (2-3) - 8.14 / (5.77- 13.08)] with p- value of 0.003. PWR was significantly lower in non- survivors [Median/IQR (2-3) - 11.05/(8.76- 15.45)]compared to survivors [16.43/(9.75 – 26.38)] with p value of 0.002.

All the Biochemical parameters serum bilirubin [Survivors – 2.04/(0.9- 4.60); Non- Survivors- 5.79/ (3.39- 15.41)], AST [Survivors – 56/(30.05- 100.6); Non- Survivors- 102/ (53.25- 196.25)] and ALT [Survivors – 29/ (18.5- 43.2); Non- Survivors – 42.35/ (27 – 75.5)] were significantly higher in non-survivors compared to survivors.(p- value - <0.001)

Multivariate analysis of hematological and biochemical parameters and their ratios [Table 5]

Serum bilirubin value at the time of admission was one of the strongest predictors of mortality, with a hazard ratio of 1.04 (95% CI: 1.00–1.07, p <0.05). This reflects a 4% increase in risk of death per 1 mg/dL increase in bilirubin.

ROC curve analysis in different variables. [Figure 1]

In Table no.6 among the parameters analyzed, serum bilirubin and AST demonstrated good predictive accuracy with an AUC of 0.756 and 0.701 respectively, the optimal cutoff for serum bilirubin was identified at 3.2 mg/dL, (sensitivity of 77.3% and specificity of 67.6%) and for AST at 59.65 U/L, (sensitivity of

71.2% and specificity of 52.5%).

Table 1: Baseline characteristics of study subjects (N = 205)

Characteristics	Percentage (%)
Gender	
Male	96.09% (197)
Female	3.91% (8)
Age (in years)	
< 30	13.60% (28)
31- 50	63.53% (130)
51-70	21.90% (45)
>70	0.97% (2)
Etiology	
Alcohol	74.23% (152)
Hepatitis B Virus	10.7% (22)
Cryptogenic	7.8% (16)
NASH [a]	3.4% (7)
Hepatitis C Virus	2.9% (6)
Wilson's Disease	0.97% (2)
MELD Na Group [b]	
1 (< or equal to 9)	27.8% (57)
2 (10 – 19)	47.8% (98)
3 (20 – 29)	21.0% (43)
4 (30 – 39)	03.4% (7)
5 (40 or more)	0
28day Outcome	
Survivor	67.8% (139)
Non - survivor	32.20% (66)

a- NASH – Non – Alcoholic Steatohepatitis ; b - MELD Na – Model for End-stage Liver Disease with Sodium

Table 2: Shows distribution of outcome of the patients after 30 day follow up with MELD Na Score

MELD Na [a] Score	MELD Na group	Survivor	Non- survivor	Total
< or equal to 9	1	51 (89.5%)	6 (10.5%)	57
10 to19	2	68 (69.4%)	30 (30.6%)	98
20 to 29	3	17 (39.5%)	26 (60.4%)	43
30 to 39	4	3 (42.8%)	4 (57.14%)	7
40 or more	5	0	0	0

a - MELD Na – Model for End-stage Liver Disease with Sodium
Chi-Square = 30.11, p value = <0.001

Table 3: Distribution of Hematological and Biochemical parameters across different MELD Groups

Variable	MELD Na GROUP (Median/IQR2-3)					p- value
	1	2	3	4	5	
Hemoglobin(g/dl)	8.9/ (6.2- 11.6)	8.8/ (7.5-10.2)	9.4/ (7.2-10.5)	7.5/ (7.4-7.9)	0	0.280
TLC [a] (10^3/µl)	6.330 (4.09-8.38)	9.615 (6.54- 13.77)	13.840 (9.00- 17.07)	23.570 (9.97- 26.58)	0	<0.001
Platelet ($x10^3$/ µl)	127 (53.00- 239.00)	134 (83.25- 203)	110 (70-150)	90 (50.00- 98.50)	0	0.036
NLR [b]	3.03 (2.10- 5.53)	3.74 (2.51- 6.8)	5.24 (3.40- 7.30)	5.69 (4.33- 8.03)	0	0.009
PWR [c]	21.07 (13.19- 35.8)	15.01 (9.87- 23.30)	10.07 (5.76- 13.35)	4.11 (2.87- 5.68)	0	<0.001
Serum Bilirubin (mg/dl)	0.96 (0.50- 1.93)	3.02 (1.72- 6.32)	11.05 (5.18- 15.29)	16.94 (5.35- 22.87)	0	<0.001
AST [d] (U/L)	33.9 (24.8- 80.1)	62 (38.5- 107.5)	111.5 (77.9- 191)	114.5 (68.5- 138.85)	0	<0.001
ALT [e] (U/L)	24 (16- 40)	34 (22- 50.65)	41 (28.4- 62.6)	32 (27- 42.5)	0	0.002

(a- TLC – Total Leucocyte Count, b- Neutrophil to Lymphocyte Ratio, c- Platelet to WBC ratio, d- AST – Serum Glutamic Oxaloacetic Transaminase, e- ALT – Serum Glutamic Pyruvic Transaminase)

Table 4: Comparison of hematological and biochemical parameters with 28day outcome.

Variable	Survivor (Median/IQR2-3)	Non- Survivor (Median/IQR2-3)	p- value
Hemoglobin (g/dl)	8.9 (6.85- 10.8)	8.65 (7.42- 10.07)	0.891
TLC [a] ($x10^3$/µl)	8.14 (5.77- 13.08)	11.74 (7.22- 15.89)	0.003
Platelet Count ($x10^3$/µl)	129 (61- 209)	119 (84.7- 174.5)	0.647
NLR [b]	3.31 (2.23- 6.55)	4.70 (3.46- 6.68)	0.075
PWR [c]	16.43 (9.75- 26.38)	11.05 (8.76- 15.45)	0.002
Serum Bilirubin (mg/dl)	2.04 (0.9- 4.60)	5.79 (3.39- 15.41)	<0.001
AST [d] (U/L)	56 (30.05- 100.6)	102 (53.25- 196.25)	<0.001
ALT [e] (U/L)	29 (18.5- 43.2)	42.35 (27- 75.5)	<0.001

(a- TLC – Total Leucocyte Count, b- Neutrophil to Lymphocyte Ratio, c- Platelet to WBC ratio d- AST – Serum Glutamic Oxaloacetic Transaminase, e- ALT – Serum Glutamic Pyruvic Transaminase)

Table 5: Multivariate analysis of hematological and biochemical parameters and their ratios.

Serial Number	Variable	Hazard Ratio	p-value	Lower 95%	Upper 95%
1	Hb	0.98	0.801	0.89	1.09
2	TLC [a]	1.00	0.369	1.00	1.01
3	Platelet	0.99	0.223	0.99	1.00
4	NLR [b]	1.00	0.666	0.97	0.93
5	PWR [c]	0.97	0.160	0.935	1.01
6	S. Bilirubin	1.04	0.016	1.00	1.07
7	AST [d]	1.00	0.131	0.99	1.00
8	ALT [e]	0.99	0.679	0.99	1.00

(a- TLC – Total Leucocyte Count, b- Neutrophil to Lymphocyte Ratio, c- Platelet to WBC ratio d- AST – Serum Glutamic Oxaloacetic Transaminase, e- ALT – Serum Glutamic Pyruvic Transaminase)

Table 6: ROC curve analysis for hematological and biochemical parameters

Parameters	AUC	Optimal Cutoff	Sensitivity	Specificity
Hemoglobin	0.494	7.35 g/dl	77.3%	30.2%
TLC [a]	0.628	8455/µl	68.2%	54.7%
Platelet	0.480	89,500/µl	71.2%	31.7%
NLR [b]	0.577	3.5	74.2%	52.5%
PWR [c]	0.366	9.03	71.2%	21.6%
S. Bilirubin	0.756	3.2 mg/dl	77.3%	67.6%
AST [d]	0.701	59.65 U/L	71.2%	52.5%
ALT [e]	0.666	29.5 U/L	71.2%	50.4%

(a- TLC – Total Leucocyte Count, b- Neutrophil to Lymphocyte Ratio, c- Platelet to WBC ratio d- AST – Serum Glutamic Oxaloacetic Transaminase, e- ALT – Serum Glutamic Pyruvic Transaminase)

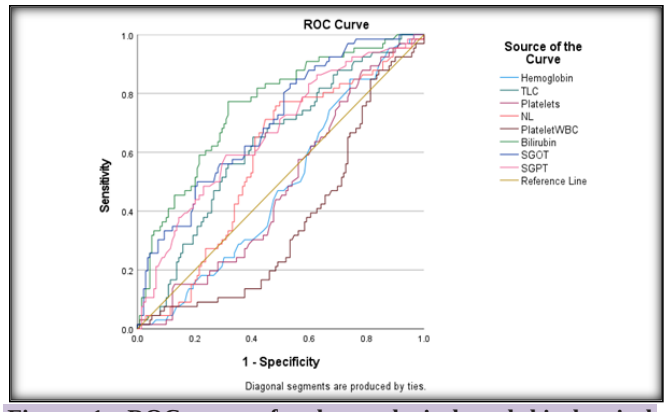

Figure 1: ROC curve for hematological and biochemical parameters.

Discussion

In this prospective longitudinal study, out of 205 patients included, 96.09% (197) were males and 3.91% (8) were females. The similar findings were seen in a study by Arul et al. (2019) on 100 CLD patients, out of which 15% were females and 85% were males.[3] These results were probably due to higher alcohol related CLD in males, specially in Indian subcontinent. The mean age ± SD for all patients in this study was 42.92 ± 11.34 years. In a study by Mehta et al. (2023) on 150 CLD patients mean age ± SD for all patients was 49.82 ± 11.63 years.[4] This reflects that CLD often affects individuals in their most economically productive years, posing a major burden on families and the healthcare system.

In our study, the most common cause of chronic liver disease (CLD) was alcohol consumption, accounting for 152 cases (74.23%). This was followed by Hepatitis B virus (22 cases, 10.7%). In Mehta et al.'s 2023 study similar findings were observed with alcohol accounting for etiology in 50.34% of cases.[4]

In our study, 32.2% (66) of the participants were non-survivors, while 67.8% (139) were survivors. In a study by Devarbhavi et al. (2023) reported that liver disease causes around two million deaths each year, making up 4% of total global mortality, or roughly one in every 25 deaths.[5] This indicates that there is fair amount of mortality associated with CLD and the importance of identifying predictive markers of mortality.

In this study, most patients had a MELD Na Score between 10 to 19 (Group – 2). The mortality rates were 10.5%, 30.6%, 60.4%, 57.14% for MELD Sodium Group 1,2,3, 4 respectively. There is a clear inverse relationship between MELD Na score and survival. Results of a study by Elhence et al,[6] (2022) aligned with the observations of this study. They demonstrated that mortality increases with worsening MELD class, significantly decreased 28-day survival was observed among patients with MELD ≥20 (log-rank P <0.001). This reinforces the established role of MELD score in prognostication of CLD patients.

In this study [Table 3], significant trends were observed in key hematological and biochemical parameters with increasing MELD Na scores, reflecting the systemic impact of worsening hepatic function. The TLC increased significantly with MELD Na progression, rising from a median /IQR(2-3) of 6,330 /(4090-8380) / µL in Group 1 to 23,570 /(9970- 26580) / µL in Group 4 ($p < 0.001$). These findings are comparable with a study conducted by Xu H et al. (2025)7, on 247 patients with acute - on – chronic liver failure. This marked leukocytosis may reflect systemic inflammation, endotoxemia, or infection, all of which are known to complicate advanced liver disease.

In this study, there was a statistically significant decline in platelet counts with increasing MELD Na ($p = 0.036$), falling from median /IQR(2-3) of 127 / (53.00- 239.00) $x10^3$ /µL in MELD Na Group 1 to 90/ (50.00 - 98.5) $x10^3$ /µL in MELD Na

Group 4. A similar study by Jain et al. (2016)[8] found a sharp drop in platelets from 3,80,000/μL in MELD Na group 1 to 1,00,000/μL in MELD Na group 5 ($p < 0.01$). All these studies suggest that platelet count decreases with increase in severity of liver disease. This is consistent with portal hypertension-induced hypersplenism, decreased thrombopoietin synthesis, and bone marrow suppression.

In this study, the NLR increased progressively from MELD Na Group 1 [median /IQR(2-3): 3.03/ (2.10- 5.53)] to MELD Na Group 4 [median /IQR(2-3) 5.69/ (4.33- 8.03)], with statistical significance ($p = 0.009$). There was the sharp decline in PWR with advancing MELD Na ($p < 0.001$), dropping from median /IQR(2-3) :21.07/ (13.19- 35.8) in MELD Na 1 to 4.11/ (2.87 – 5.68) in MELD Na 4. This progressive rise suggests that systemic inflammation intensifies with worsening hepatic dysfunction. Similar findings were reported by Xu H et al,[7] (2025) in their study.

In this study all the three biochemical parameters (Serum Bilirubin, AST, ALT) showed a positive correlation with MELD Na Score. The median /IQR2-3 value of serum bilirubin in MELD Na 1 was median /IQR(2-3) : 0.96 / (0.50 – 1.93) and in MELD Na 4 was median /IQR(2-3) : 16.94 / (5.35 – 22.87) with a p value of <0.001. These findings are comparable with study conducted by Tomar MS et al. (2023).[9] For AST, value in MELD Na 1 was median /IQR(2-3) : 33.9/ (24.8- 80.1) and 114.5/ (68.5- 138.85) in MELD Na 4 ($p<0.001$). For ALT, value in MELD Na 1 was median /IQR(2-3): 24/ (16- 40) and 32/ (27- 42.5) in MELD Na 4 ($p= 0.002$). In the study by Tomar MS et al,[9] (2023) there was a non- significant rise in the levels of these enzymes with increase in CTP Score.

In our study, TLC was significantly higher among non-survivors median /IQR(2-3) : 11.74/ (7.22–15.89) $\times 10^3/\mu L$ compared to survivors median /IQR(2-3) :8.14/ (5.77–13.08) $\times 10^3/\mu L$], with a p-value of 0.003. The PWR in our study was significantly lower in non-survivors [median /IQR(2-3) 11.05/ (8.76- 15.45)] compared to survivors [median /IQR2-3: 16.43/ (9.75- 26.38)], with a p-value of 0.002. These findings are comparable with a study conducted by Liu XL et al (2020).[10]

A comparative analysis of liver function parameters between survivors and non-survivors revealed statistically significant differences in all three measured biomarkers: serum bilirubin, SGOT (AST), and SGPT (ALT). In this study, the serum bilirubin level in non-survivors was median /IQR(2-3) : 5.79/ (3.39–15.41)mg/dl, significantly higher than survivors median /IQR(2-3) :2.04/ (0.90–4.60) mg/dl; $p < 0.001$). This marked elevation in bilirubin suggests that non-survivors experienced more profound hepatic dysfunction. Similar findings were reported by Xu H et al,[7] (2025) in their study.

AST levels in this study were significantly higher ($p<0.001$) in non-survivors [median /IQR(2-3) : 102.00 /(53.25–196.25) U/L] compared to survivors [median /IQR(2-3) : 56.00 /(30.05–100.60) U/L]. ALT also demonstrated significantly higher values in non-survivors [median /IQR(2-3) : 42.35 /(27- 75.5)U/L] versus survivors [median /IQR(2-3) : 29.00 /(18.5- 43.2)] ($p<0.001$). These findings are comparable with a study conducted by Liu XL et al (2020).[10]

The consistent elevation of all three parameters in non-survivors, coupled with highly significant p-values (<0.001), suggests that hepatic dysfunction is strongly associated with mortality.

In this study, the multivariate cox proportional hazards regression model identified only serum bilirubin as independent predictor of mortality in patients with chronic liver disease with a hazard ratio of 1.04 (95% CI: 1.00–1.07, $p <0.05$). These results are comparable with a study by Xu X et al,[11] (2021) where serum bilirubin was the independent predictor of mortality in ACLF patients with a hazard ratio of 1.002 and p value of 0.013.

In this study on ROC curve analysis serum bilirubin yielded the highest AUC of 0.756, AST yielded the AUC of 0.701, both of them indicating good discriminatory ability for non- survival with cut- off value of 3.2 mg/dl (Sensitivity = 77.3%, Specificity = 67.6%) and 59.65 U/L (Sensitivity = 71.2% , Specificity = 52.5%) respectively. These results are similar to a study by Velázquez LJA et al,[12] (2014) on 65 patients of acute-on-chronic liver failure, where serum bilirubin had the AUC of 0.746. This highlights their potential utility in clinical settings to discriminate non- survivors from survivors and guide timely interventions.

Conclusion

In this study, there was increase in mortality with increase in MELD Na Score. As MELD Na score increased from MELD Na group 1 to 4, TLC and NLR increased, while platelet count and PWR decreased significantly. Serum bilirubin, ALT, and AST also increased significantly with increase in MELD scores. Non-survivors had significantly higher TLC, serum bilirubin, AST, ALT, and lower PWR than survivors. Multivariate analysis identified serum bilirubin as the only independent predictor of mortality.

ROC analysis showed serum bilirubin (AUC = 0.756) and AST (AUC = 0.701) had the good predictive accuracy with an optimal cutoff of 3.2 mg/dL (sensitivity 77.3%, specificity 67.6%) for serum bilirubin and a cut off of 59.65 U/L (sensitivity of 71.2%, specificity of 52.5%) for AST.

These parameters can help in early identification of high-risk patients and guide timely interventions to reduce morbidity and mortality.

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Conflicts of interest

There are no conflicts of interest.

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