"Assessing the Predictive Value of Serum Phosphate for Short-Term Mortality in Acute-on-Chronic Liver Failure Patients"

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ABSTRACT

Background: Acute-on-chronic liver failure (ACLF) is a life-threatening syndrome characterized by acute hepatic decompensation, multiorgan dysfunction, and high short-term mortality. Early identification of patients at increased risk of death is essential for timely intervention and appropriate allocation of critical care resources. Although several prognostic scoring systems are available, they require multiple clinical and laboratory variables. Serum phosphate is an inexpensive, routinely available biochemical parameter that may serve as a simple prognostic biomarker in ACLF.

Aim and Objectives: The study aimed to evaluate the prognostic value of serum phosphate in predicting short-term mortality among patients with ACLF. The objectives were to assess the association between serum phosphate levels and 28-day mortality, evaluate the correlation between serum phosphate and ACLF severity, compare serum phosphate levels between survivors and non-survivors, determine the optimal serum phosphate threshold for mortality prediction, assess its diagnostic performance, and compare its prognostic utility with established scoring systems including MELD, MELD-Na, CLIF-SOFA, CLIF-C ACLF, AARC-ACLF, and Child-Turcotte-Pugh (CTP) scores.

Materials and Methods: This prospective observational study included 68 patients diagnosed with ACLF according to the Asia-Pacific Association for the Study of the Liver (APASL) criteria over a one-year period. Serum phosphate levels were measured on Day 1, Day 3, and Day 7 of hospitalization. Prognostic scores including MELD, MELD-Na, CLIF-SOFA, CLIF-C ACLF, AARC-ACLF, and CTP were calculated using standard methods. Patients were followed for 28 days, and short-term mortality was considered the primary outcome. Statistical analysis included descriptive statistics, comparative tests, correlation analysis, and receiver operating characteristic (ROC) curve analysis.

Results: Among the 68 patients, 58 (85.3%) were males, and the majority (41.2%) were aged 41–50 years. Alcohol-related liver disease was the predominant etiology (73.5%), while alcoholic hepatitis was the most common acute precipitating event (52.9%). Twenty-eight-day mortality was observed in 9 (13.2%) patients. Serum phosphate levels were significantly higher among non-survivors than survivors on Day 1 (6.53 ± 0.58 vs. 3.69 ± 0.86 mg/dL; p=0.005), Day 3 (6.47 ± 0.60 vs. 3.76 ± 0.80 mg/dL; p=0.004), and Day 7 (6.48 ± 0.56 vs. 3.86 ± 0.83 mg/dL; p=0.002). Serum phosphate demonstrated significant positive correlations with AARC, MELD, CTP, CLIF-C ACLF, and CLIF-SOFA scores, with the strongest correlation observed with CLIF-SOFA on Day 7 (r=0.79, p<0.001). Serum phosphate levels increased significantly with increasing ACLF grade (p=0.002). A Day 3 serum phosphate cut-off value of >6.5 mg/dL showed a sensitivity of 88.9%, specificity of 89.8%, and diagnostic accuracy of 89.7% for predicting short-term mortality. ROC analysis demonstrated an AUC of 0.931 for Day 7 serum phosphate, comparable to CLIF-SOFA (AUC=0.948).

Conclusion: Serum phosphate is a simple, inexpensive, and readily available biomarker with excellent prognostic value for predicting short-term mortality in patients with ACLF. Elevated serum phosphate levels were significantly associated with increased disease severity, higher prognostic scores, and poorer 28-day outcomes. Serum phosphate demonstrated diagnostic performance comparable to established prognostic scoring systems and may serve as a valuable adjunct for early risk stratification and clinical decision-making in patients with acute-on-chronic liver failure.

Keywords: Acute-on-chronic liver failure; Serum phosphate; Short-term mortality; Prognostic biomarker; CLIF-SOFA; MELD; AARC-ACLF; CLIF-C ACLF; Liver failure; Prognosis.

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INTRODUCTION

Acute-on-chronic liver failure (ACLF) is a distinct clinical syndrome characterized by an acute deterioration of liver function encephalopathy in patients with previously diagnosed or in patients with underlying chronic liver disease,

resulting in hepatic and extrahepatic organ failure with a high risk of short-term mortality (1). The Asia-Pacific Association for the Study of the Liver (APASL) defines ACLF as an acute hepatic insult manifesting as jaundice (serum bilirubin ≥5 mg/dL) and coagulopathy (INR ≥1.5 or prothrombin activity <40%), complicated within four weeks by ascites and/or hepaticundiagnosed chronic liver disease (2). Despite advances in intensive care, supportive management, and liver transplantation, ACLF continues to be associated with poor outcomes, with reported 28-day mortality ranging from 30% to over 50%, depending on disease severity and the number of organ failures (3).

The clinical course of ACLF is highly dynamic and unpredictable. Patients may rapidly progress from compensated chronic liver disease to multiorgan dysfunction due to an exaggerated systemic inflammatory response, immune dysregulation, circulatory disturbances, and metabolic derangements (4). Early recognition of patients at high risk of mortality is therefore essential for timely initiation of intensive management, prioritization for liver transplantation, and optimal utilization of healthcare resources (5). Several prognostic scoring systems, including the Model for End-stage Liver Disease (MELD), MELD-Sodium (MELD-Na), Chronic Liver Failure-Sequential Organ Failure Assessment (CLIF-SOFA), Chronic Liver Failure Consortium ACLF (CLIF-C ACLF), Child-Turcotte-Pugh (CTP), and APASL ACLF Research Consortium (AARC-ACLF) scores, are widely used for prognostic assessment. However, these scoring systems require multiple clinical and laboratory variables, limiting their rapid applicability in certain clinical settings (6).

Serum phosphate is an essential intracellular electrolyte involved in numerous physiological processes, including energy metabolism, adenosine triphosphate synthesis, cellular signaling, membrane integrity, and acid-base homeostasis (7). Alterations in phosphate metabolism are common among critically ill patients and may reflect the severity of systemic illness. In liver disease, disturbances in phosphate homeostasis may occur due to impaired hepatic metabolism, renal dysfunction, intracellular phosphate shifts, nutritional deficiencies, and the systemic inflammatory response associated with ACLF (8). Emerging evidence suggests that abnormal serum phosphate levels may correlate with disease severity and adverse clinical outcomes in critically ill patients, making phosphate a potential prognostic biomarker (9).

Unlike complex prognostic scores, serum phosphate estimation is inexpensive, widely available, rapidly obtainable, and routinely performed in most clinical laboratories. If serum phosphate demonstrates adequate predictive performance for short-term mortality, it could provide clinicians with a simple adjunctive tool for early risk stratification, particularly in resource-limited healthcare settings (9). Furthermore, combining serum phosphate with established prognostic scoring systems may improve overall prognostic accuracy and facilitate better clinical decision-making (10).

Although previous studies have explored various biochemical markers in ACLF, the prognostic significance of serum phosphate remains insufficiently investigated. Limited data are available regarding its relationship with disease severity, established prognostic scores, and short-term mortality in patients with ACLF

(11). Therefore, the present study was undertaken to assess the predictive value of serum phosphate for 28-day mortality in patients with acute-on-chronic liver failure, evaluate its association with disease severity, determine its optimal prognostic threshold, assess its diagnostic performance, and compare its predictive ability with established prognostic scoring systems including MELD, MELD-Na, CLIF-SOFA, CLIF-C
ACLF, and AARC-ACLF scores. The findings of this study may help establish serum phosphate as a simple, readily available, and cost-effective biomarker for

prognostic assessment in patients with acute-on-chronic liver failure.

AIM AND OBJECTIVES

Aim

To study the prognostic value of serum phosphate levels in predicting short-term mortality in patients with acute-on-chronic liver failure.

Objectives Primary

Objective

- To assess the association between serum phosphate levels and short-term mortality in patients with acute-on-chronic liver failure.

Secondary Objectives

- To evaluate the correlation between serum phosphate levels and severity of ACLF.
- To compare serum phosphate levels between survivors and non-survivors.
- To determine the threshold value of serum phosphate for prediction of short-term mortality.
- To assess the sensitivity, specificity and predictive value of serum phosphate in ACLF prognostication.
- To compare serum phosphate with established prognostic scoring systems such as MELD, MELD-Na, CLIF-SOFA, CLIF-C ACLF and
AARC-ACLF scores.

The present study is intended to determine whether serum phosphate can serve as a simple, inexpensive and easily available prognostic biomarker in ACLF patients. Early identification of high-risk patients may help improve clinical monitoring, treatment prioritization and overall prognostic assessment in acute-on-chronic liver failure.

MATERIALS AND METHODS

This prospective observational study was conducted over a period of one year in the Department of General Medicine at Jawaharlal Nehru Medical College. "A total of 68 patients aged 18–80 years diagnosed with acute-on-chronic liver failure (ACLF) according to the Asia-Pacific Association for the Study of the Liver (APASL) criteria were enrolled after obtaining approval from the Institutional Ethics Committee and written informed consent. The sample size was calculated using the sensitivity reported by Wagh et al. with a fixed precision of 10%. Patients with hypo- or hyperparathyroidism, hypervitaminosis D, chronic kidney disease, malignancy, HIV infection, pregnancy or lactation, and those unwilling to participate were excluded. Sociodemographic details, clinical history, physical examination findings, etiology of chronic liver disease, and laboratory investigations were recorded using a

predesigned semi-structured proforma. Chronic liver disease was confirmed using appropriate clinical, radiological, and endoscopic investigations, including hepato-porto-splenic Doppler ultrasonography, FibroScan, computed tomography of the abdomen, and oesophagogastroduodenoscopy for detection of varices.

Serum phosphate levels were estimated by the colorimetric method, while serum arterial lactate was measured using the spectrophotometric method. ACLF severity was graded according to the APASL 2019 definition using the AARC-ACLF score, with scores of 5–7 classified as Grade I, 8–10 as Grade II, and 11–15 as Grade III. Prognostic scores including Child-Turcotte-Pugh (CTP), Model for End-stage Liver Disease (MELD), MELD-Sodium (MELD-Na), Chronic Liver Failure-Sequential Organ Failure Assessment (CLIF-SOFA), Chronic Liver Failure Consortium ACLF (CLIF-C ACLF), and APASL ACLF Research Consortium (AARC-ACLF) scores were calculated using standard validated equations. All patients were followed throughout hospitalization and for 28 days after admission through hospital visits and/or telephonic follow-up. Short-term mortality within 28 days was considered the primary study outcome.

Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) version 22.0. Continuous variables were expressed as mean ± standard deviation or median with interquartile range depending on data distribution, while categorical variables were presented as frequency and percentage. Comparisons between survivors and non-survivors were performed using the Independent Student's *t*-test or Mann–Whitney *U* test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables, as appropriate. Correlation between serum phosphate levels and prognostic scoring systems was assessed using Pearson's or Spearman's correlation coefficient". Receiver operating characteristic (ROC) curve analysis was performed to determine the optimal serum phosphate threshold for predicting 28-day mortality and to evaluate its sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy. A p-value of <0.05 was considered statistically significant for all analyses.

RESULTS

Table 1. Distribution of Study Participants According to Gender (N=68)

Gender	n	%
Male	58	85.3
Female	10	14.7
Total	68	100.0

In the present study, out of a total of 68 study participants, 58 (85.3%) were males and 10 (14.7%) were females. "Thus, males constituted the majority of the study population. The total number of participants included in the study was 68 (100.0%).

Table 2. Distribution of Study Participants According to Age Group (N=68)

Age Group (Years)	n	%
18–30	6	8.8
31–40	18	26.5
41–50	28	41.2
51–60	11	16.2
>60	5	7.3
Total	68	100.0

In the present study, out of a total of 68 study participants, 6 (8.8%) were in the 18–30 years age group,
18 (26.5%) were in the 31–40 years age group, 28 (41.2%) were in the 41–50 years age group, 11 (16.2%) were in the 51–60 years age group, and 5 (7.3%) were aged more than 60 years. The highest proportion of study participants belonged to the 41–50 years age group, comprising 28 (41.2%) participants. The total number of participants included in the study was 68 (100.0%).

Table 3. Distribution According to Etiology of Chronic Liver Disease (N=68)

Etiology	n	%
Alcohol-related liver disease	50	73.5
NAFLD	2	2.9
Autoimmune hepatitis	5	7.4
Chronic hepatitis B	4	5.9
Budd-Chiari syndrome	1	1.5
Alcohol + Hepatitis B	1	1.5
Wilson disease	1	1.5
Unknown etiology	4	5.9
Total	68	100.0

In the present study, out of a total of 68 study participants, alcohol-related liver disease was observed in 50 (73.5%) participants, NAFLD in 2 (2.9%) participants, autoimmune hepatitis in 5 (7.4%) participants, chronic hepatitis B in 4 (5.9%) participants, Budd-Chiari syndrome in 1 (1.5%) participant, alcohol + hepatitis B in 1 (1.5%) participant, Wilson disease in 1 (1.5%) participant, and unknown etiology in 4 (5.9%) participants. Alcohol-related liver disease was the most common etiology of chronic liver disease among the study participants. The total number of participants included in the study was 68 (100.0%).

Table 4. Distribution According to ACLF Grade (N=68)

ACLF Grade	n	%
Grade I	33	48.5
Grade II	26	38.2
Grade III	9	13.2
Total	68	100.0

In the present study, out of a total of 68 study participants, 33 (48.5%) had ACLF Grade I, 26 (38.2%) had ACLF Grade II, and 9 (13.2%) had ACLF Grade III. ACLF Grade I was the most common grade among the study participants. The total number of participants included in the study was 68 (100.0%).

Table 5. Distribution According to 28-Day Outcome (N=68)

Outcome	n	%
Survivor	59	86.8
Non-survivor	9	13.2
Total	68	100.0

In the present study, out of a total of 68 study participants, 59 (86.8%) were survivors and 9 (13.2%) were non-survivors at 28 days. The majority of the study participants were survivors. The total number of participants included in the study was 68 (100.0%).

Table 6. Descriptive Analysis of Laboratory Parameters (N=68)

Parameter	Mean ± SD
Hemoglobin (g/dL)	9.3 ± 2.1
Platelet count (/mm³)	135200 ± 68900
Total bilirubin (mg/dL)	13.4 ± 7.6
Serum albumin (g/dL)	2.6 ± 0.5
INR	2.06 ± 0.45
Serum phosphate (mg/dL)	4.1 ± 1.3
Serum creatinine (mg/dL)	1.1 ± 0.8
Serum lactate (mmol/L)	1.7 ± 0.9

In the present study, the mean hemoglobin level was 9.3 ± 2.1 g/dL, the mean platelet count was 135200 ± 68900/mm³, the mean total bilirubin level was 13.4 ± 7.6 mg/dL, the mean serum albumin level was 2.6 ± 0.5 g/dL, the mean INR was 2.06 ± 0.45, the mean serum phosphate level was 4.1 ± 1.3 mg/dL, the mean serum creatinine level was 1.1 ± 0.8 mg/dL, and the mean serum lactate level was 1.7 ± 0.9 mmol/L.

Table 7. Comparison of Serum Phosphate Levels Between Survivors and Non-Survivors

Parameter	Survivors Mean ± SD	Non-survivors Mean ± SD	t-value	p-value
Day 1	3.69 ± 0.86	6.53 ± 0.58	9.87	0.005
Day 3	3.76 ± 0.80	6.47 ± 0.60	10.21	0.004
Day 7	3.86 ± 0.83	6.48 ± 0.56	9.95	0.002

In the present study, on Day 1, the mean serum phosphate level was 3.69 ± 0.86 mg/dL among survivors and 6.53 ± 0.58 mg/dL among non-survivors, with a t-value of 9.87 and p-value of 0.005. On Day 3, the mean serum phosphate level was 3.76 ± 0.80 mg/dL among survivors and 6.47 ± 0.60 mg/dL among non-survivors, with a t-value of 10.21 and p-value of 0.004. On Day 7, the mean serum phosphate level was 3.86 ± 0.83 mg/dL among survivors and 6.48 ± 0.56 mg/dL among non-survivors, with a t-value of 9.95 and p-value of 0.002.

Table 8. Association Between Serum Phosphate Category and 28-Day Mortality

Serum Phosphate Category	Survivors n (%)	Non-survivors n (%)	Total n (%)	p-value
<2.5 mg/dL	2 (100.0)	0 (0.0)	2 (2.9)	<0.001
2.5–3.5 mg/dL	26 (100.0)	0 (0.0)	26 (38.2)	
3.6–4.5 mg/dL	24 (100.0)	0 (0.0)	24 (35.3)	
>4.5 mg/dL	7 (43.7)	9 (56.3)	16 (23.5)	

In the present study, among study participants with serum phosphate level <2.5 mg/dL, 2 (100.0%) were

survivors and 0 (0.0%) were non-survivors, with a total of 2 (2.9%) participants. Among participants with serum phosphate level 2.5–3.5 mg/dL, 26 (100.0%) were survivors and 0 (0.0%) were non-survivors, with a total of 26 (38.2%) participants. Among participants with serum phosphate level 3.6–4.5 mg/dL, 24 (100.0%) were survivors and 0 (0.0%) were non-survivors, with a total of 24 (35.3%) participants. Among participants with serum phosphate level >4.5 mg/dL, 7 (43.7%) were survivors and 9 (56.3%) were non-survivors, with a total of 16 (23.5%) participants. The association between serum phosphate category and 28-day mortality was statistically significant with a p-value of <0.001.

Table 9. Diagnostic Performance of Serum Phosphate for Prediction of Short-Term Mortality

Day	Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Day 1	>6.5 mg/dL	77.8	76.3	35.0	95.6	76.5
Day 3	>6.5 mg/dL	88.9	89.8	57.1	98.1	89.7
Day 7	>6.5 mg/dL	88.9	86.4	50.0	98.0	86.8

In the present study, on Day 1, a serum phosphate cut-off value of >6.5 mg/dL showed a sensitivity of 77.8%, specificity of 76.3%, positive predictive value (PPV) of 35.0%, negative predictive value (NPV) of 95.6%, and diagnostic accuracy of 76.5% for predicting short-term mortality. On Day 3, a serum phosphate cut-off value of >6.5 mg/dL showed a sensitivity of 88.9%, specificity of 89.8%, PPV of 57.1%, NPV of 98.1%, and diagnostic accuracy of 89.7%. On Day 7, a serum phosphate cut-off value of >6.5 mg/dL showed a sensitivity of 88.9%, specificity of 86.4%, PPV of 50.0%, NPV of 98.0%, and diagnostic accuracy of 86.8% for predicting short-term mortality.

Table 10. Comparison of Prognostic Scores Between Survivors and Non-Survivors

Score	Survivors Mean ± SD	Non-survivors Mean ± SD	t-value	p-value
CTP	7.8 ± 1.1	12.0 ± 0.8	11.62	<0.005
MELD	23.1 ± 3.0	33.2 ± 4.1	9.44	<0.005
MELD-Na	24.6 ± 3.2	35.1 ± 4.1	9.73	<0.005
AARC	7.0 ± 0.7	12.0 ± 0.8	18.12	<0.005
CLIF-C ACLF	28.2 ± 2.6	72.5 ± 3.6	41.24	<0.005
CLIF-SOFA	11.3 ± 1.0	1 ± 1.8	16.92	<0.005

In the present study, the mean CTP score was 7.8 ± 1.1 among survivors and 12.0 ± 0.8 among non-survivors, with a t-value of 11.62 and p-value of <0.005. The mean MELD score was 23.1 ± 3.0 among survivors and 33.2 ± 4.1 among non-survivors, with a t-value of 9.44 and p-value of <0.005. The mean MELD-Na score was 24.6 ± 3.2 among survivors and 35.1 ± 4.1 among non-survivors, with a t-value of 9.73 and p-value of <0.005. The mean AARC score was 7.0 ± 0.7 among survivors and 12.0 ± 0.8 among non-survivors, with a t-value of 18.12 and p-value of <0.005. The mean CLIF-C ACLF score was 28.2 ± 2.6 among survivors and 72.5 ± 3.6 among non-survivors, with a t-value of 41.24 and p-value of <0.005. The mean CLIF-SOFA score was 11.3 ± 1.0 among survivors and 17.8 ± 1.8 among non-survivors, with a t-value of 16.92 and p-value of <0.005.

Table 11. Correlation of Serum Phosphate with Prognostic Scores

Prognostic Score	Day 1 r (p-value)	Day 3 r (p-value)	Day 7 r (p-value)
AARC	0.48 (0.003)	0.69 (<0.001)	0.72 (<0.001)
CLIF-SOFA	0.52 (0.001)	0.74 (<0.001)	0.79 (<0.001)
CLIF-C ACLF	0.50 (0.020)	0.67 (<0.001)	0.72 (<0.001)
MELD	0.45 (0.008)	0.62 (<0.001)	0.67 (<0.001)
CTP	0.39 (0.0018)	0.55 (0.004)	0.58 (0.001)

In the present study, serum phosphate levels showed a positive correlation with all prognostic scores on Day 1, Day 3, and Day 7. For the AARC score, the correlation coefficient was 0.48 ($p = 0.003$) on Day 1, 0.69 ($p < 0.001$) on Day 3, and 0.72 ($p < 0.001$) on Day 7. For the CLIF-SOFA score, the correlation coefficient was 0.52 ($p = 0.001$) on Day 1, 0.74 ($p < 0.001$) on Day 3, and 0.79 ($p < 0.001$) on Day 7. For the CLIF-C ACLF score, the correlation coefficient was 0.50 ($p = 0.020$) on Day 1, 0.67 ($p < 0.001$) on Day 3, and 0.72 ($p < 0.001$) on Day 7. For the MELD score, the correlation coefficient was 0.45 ($p = 0.008$) on Day 1, 0.62 ($p < 0.001$) on Day 3, and 0.67 ($p < 0.001$) on Day 7. For the CTP score, the correlation coefficient was 0.39 ($p = 0.0018$) on Day 1, 0.55 ($p = 0.004$) on Day 3, and 0.58 ($p = 0.001$) on Day 7.

Table 12. Comparison of Serum Phosphate Levels According to ACLF Grade

ACLF Grade	Day 1	Day 3	Day 7	p-value
Grade I	3.3 ± 0.8	3.2 ± 0.7	3.1 ± 0.7	
Grade II	4.5 ± 1.1	4.8 ± 1.2	5.0 ± 1.3	
Grade III	6.2 ± 1.6	6.8 ± 1.7	7.2 ± 1.8	**0.002**

In the present study, serum phosphate levels showed a positive correlation with all prognostic scores on Day 1, Day 3, and Day 7. For the AARC score, the correlation coefficient was 0.48 ($p = 0.003$) on Day 1, 0.69 ($p < 0.001$) on Day 3, and 0.72 ($p < 0.001$) on Day 7. For the CLIF-SOFA score, the correlation coefficient was 0.52 ($p = 0.001$) on Day 1, 0.74 ($p < 0.001$) on Day 3, and 0.79 ($p < 0.001$) on Day 7. For the CLIF-C ACLF score, the correlation coefficient was 0.50 ($p = 0.020$) on Day 1, 0.67 ($p < 0.001$) on Day 3, and 0.72 ($p < 0.001$) on Day 7. For the MELD score, the correlation coefficient was 0.45 ($p = 0.008$) on Day 1, 0.62 ($p < 0.001$) on Day 3, and 0.67 ($p < 0.001$) on Day 7. For the CTP score, the correlation coefficient was 0.39 ($p = 0.0018$) on Day 1, 0.55 ($p = 0.004$) on Day 3, and 0.58 ($p = 0.001$) on Day 7.

Table 13. ROC Curve Analysis of Serum Phosphate and Prognostic Scores

Parameter	AUC	95% CI	p-value
Serum phosphate Day 7	0.931	0.867–0.995	<0.001
CLIF-SOFA	0.948	0.889–1.000	<0.001
CLIF-C ACLF	0.884	0.789–0.979	<0.001
AARC	0.862	0.756–0.968	<0.001
MELD	0.812	0.690–0.934	<0.001
CTP	0.801	0.674–0.928	<0.001

In the present study, serum phosphate on Day 7 showed an AUC of 0.931 with a 95% confidence interval (CI) of 0.867–0.995 and a p-value of <0.001. CLIF-SOFA showed an AUC of 0.948 with a 95% CI of 0.889–1.000 and a p-value of <0.001. CLIF-C ACLF showed an AUC of 0.884 with a 95% CI of 0.789–0.979 and a p-value of <0.001. AARC showed an AUC of 0.862 with a 95% CI of 0.756–0.968 and a p-value of <0.001. MELD showed an AUC of 0.812 with a 95% CI of 0.690–0.934 and a p-value of <0.001". CTP showed an AUC of 0.801 with a 95% CI of 0.674–0.928 and a p-value of <0.001.

DISCUSSION

The present study evaluated the prognostic value of serum phosphate in predicting 28-day mortality among patients with acute-on-chronic liver failure (ACLF). Early identification of patients at increased risk of mortality remains essential because ACLF is characterized by rapid progression, multiorgan dysfunction, and high short-term mortality. In the present study, males constituted the majority of the study population (85.3%), with most patients belonging to the 41–50-year age group (41.2%). Alcohol-related liver disease was the predominant underlying etiology (73.5%), and alcoholic hepatitis was the most frequent acute precipitating event (52.9%). Similar demographic and etiological profiles have been reported by Wagh et al. (2024), Ramzan et al. (2020), Lin et al. (2020), Nagel et al. (2023), and Jiang et al. (2025), all of whom observed a predominance of middle-aged male patients with alcohol-related chronic liver disease among ACLF cohorts (12–16).

The principal finding of the present study was the significant association between elevated serum phosphate levels and short-term mortality. Serum phosphate levels were consistently higher among non-survivors than survivors on Day 1 (6.53 ± 0.58 vs. 3.69 ± 0.86 mg/dL), Day 3 (6.47 ± 0.60 vs. 3.76 ± 0.80 mg/dL), and Day 7 (6.48 ± 0.56 vs. 3.86 ± 0.83 mg/dL), with statistically significant differences at each assessment. Furthermore, mortality occurred exclusively among patients with serum phosphate levels greater than 4.5 mg/dL, demonstrating a strong association between hyperphosphatemia and adverse outcome. These observations are in close agreement with Wagh et al. (2024), who first demonstrated the prognostic significance of serum phosphate in ACLF and reported significantly higher phosphate concentrations among non-survivors (12). Similar conclusions regarding the prognostic importance of biochemical derangements and organ dysfunction were reported by Jiang et al. (2025) and Shen et al. (2024) (16,17).

Serial assessment revealed that serum phosphate correlated positively with disease severity throughout

hospitalization. Serum phosphate showed significant positive correlations with AARC, MELD, Child–Turcotte–Pugh (CTP), CLIF-C ACLF, and particularly CLIF-SOFA scores, with the strongest correlation observed with CLIF-SOFA on Day 7 ($r = 0.79$, $p < 0.001$). Serum phosphate levels also increased progressively from ACLF Grade I to Grade III, indicating that worsening ACLF severity was associated with increasing phosphate concentrations. These findings support the concept that phosphate elevation reflects progressive metabolic disturbance and multiorgan dysfunction. Comparable observations have been reported by Dhiman et al. (2014), Lin et al. (2020), Ramzan et al. (2020), Nagel et al. (2023), and Rashed and Soldera (2022), who demonstrated that higher organ failure scores are strongly associated with increasing mortality risk in ACLF (13–15,18,19).

The present study also demonstrated excellent diagnostic performance of serum phosphate. A serum phosphate cut-off value of >6.5 mg/dL on Day 3 yielded a sensitivity of 88.9%, specificity of 89.8%, diagnostic accuracy of 89.7%, and a negative predictive value of 98.1% for predicting 28-day mortality. Receiver operating characteristic analysis showed an AUC of 0.931 for Day 7 serum phosphate, which was comparable to CLIF-SOFA (AUC 0.948) and superior to CLIF-C ACLF, AARC, MELD, and CTP scores. Similar findings were reported by Wagh et al. (2024), who demonstrated that Day 3 serum phosphate achieved prognostic performance approaching that of CLIF-SOFA (12). Likewise, Ramzan et al. (2020), Lin et al. (2020), Nagel et al. (2023), Lee et al. (2015), and Acharya et al. (2020) confirmed the excellent predictive ability of established prognostic scores, supporting comparison with the present findings (13–15,20).

Overall, the present study demonstrates that serum phosphate is closely associated with ACLF severity, established prognostic scores, and short-term mortality. As serum phosphate estimation is inexpensive, widely available, and routinely performed, it represents a practical biomarker for early risk stratification in ACLF. Although CLIF-SOFA demonstrated the highest prognostic accuracy, serum phosphate provided comparable predictive performance while requiring only a single laboratory measurement. These findings suggest that serum phosphate may serve as a valuable adjunct to established prognostic scoring systems for identifying high-risk ACLF patients and facilitating timely clinical decision-making.

CONCLUSION

The present study demonstrated that serum phosphate is a valuable prognostic biomarker for predicting short-term mortality in patients with acute-on-chronic liver failure. Higher serum phosphate levels were significantly associated with increased 28-day mortality, greater ACLF severity, and higher values of established prognostic scores including MELD, MELD-Na, CLIF-SOFA, CLIF-C ACLF, AARC-ACLF, and CTP. Serum phosphate showed excellent diagnostic performance, particularly on Day 3 and Day 7, with high sensitivity, specificity, and overall predictive accuracy. Progressive elevation of serum phosphate with increasing ACLF grade further supports its association with worsening disease severity. Although CLIF-SOFA demonstrated the highest prognostic accuracy, serum phosphate provided comparable predictive performance while being inexpensive, readily available, and easy to measure. Therefore, serum phosphate may serve as a practical adjunct to established prognostic scoring systems for early risk stratification, timely clinical decision-making, and identification of high-risk ACLF patients requiring intensive monitoring and management.

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