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Original Article

Neutrophil–Lymphocyte and Neutrophil–Lymphocyte–Albumin Ratio Prognostic Value in Alcohol-Related Liver Disease

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Abstract

Background: Alcohol-related liver disease (ALD) is a leading cause of preventable morbidity and mortality. The neutrophil-to-lymphocyte ratio (NLR) and neutrophil–lymphocyte-to-albumin (NLA) ratio are inexpensive, readily available biomarkers reflecting inflammatory and synthetic status.

Objective: To evaluate the prognostic utility of neutrophil-to-lymphocyte ratio (NLR) and neutrophil–lymphocyte-to-albumin (NLA) ratio in predicting 30-day and 90-day mortality in ALD.

Methods: This prospective observational study was conducted over 18 months (June 2024–November 2025) at a tertiary care teaching hospital in South India. Seventy consecutive male patients aged >18 years with alcohol-related liver disease were enrolled. NLR was calculated as the ratio of absolute neutrophil count to absolute lymphocyte count, and NLA as NLR divided by serum albumin. Patients were followed up for 90 days after discharge with mortality assessed at admission, 30 days, and at 90 days.

Results: In-hospital mortality was found to be 71.4%, with cumulative mortality of 20.0% at 30 days and 31.2% at 90 days among patients discharged from the hospital. NLR and NLA demonstrated high predictive performance at all time. At admission, NLR ≥8.6 (AUC 0.92) and NLA ≥32.5 (AUC 0.89) were found to be significantly associated with mortality ($p \leq 0.001$). Both markers maintained high sensitivity and specificity at 30 and 90 days.

Conclusion: NLR and NLA are simple, cost-effective prognostic markers that can reliably predict short-term mortality in alcohol-related liver disease. Their integration into routine clinical assessment will enhance early risk stratification and guide timely management decisions in cases of alcoholic liver disease.

Keywords: Alcoholic liver disease, cirrhosis, mortality, neutrophil to lymphocyte ration, serum albumin

Introduction

Alcohol-related liver disease (ALD) remains a major and growing cause of preventable morbidity and mortality worldwide, particularly in regions where harmful alcohol use is rising and access to transplantation is limited.[1] ALD encompasses a clinicopathologic continuum ranging from hepatic steatosis to alcohol-associated hepatitis and ultimately alcohol-associated cirrhosis with portal hypertension and liver failure, with progression influenced by the intensity and duration of alcohol exposure, host susceptibility, nutrition, and intercurrent infections. In the Asia–Pacific region—home to more than half of the global population—liver diseases account for a disproportionate share of global mortality; importantly, the region contributed 54.3% of cirrhosis-related

deaths worldwide in 2015, underscoring the public health relevance of accurate bedside risk stratification in this setting.[2]

Within the ALD spectrum alcohol-associated hepatitis (AH) represents an acute-on-chronic inflammatory syndrome. It is characterized by jaundice, systemic inflammation and high short-term mortality which is often precipitated by recent heavy alcohol intake.[3] Alcohol-associated cirrhosis, the end stage of chronic ALD, is defined by diffuse fibrosis and nodular architectural distortion leading to progressive portal hypertension and a propensity for life-threatening decompensations, including variceal hemorrhage, ascites with spontaneous bacterial peritonitis, hepatic encephalopathy, and hepatocellular carcinoma. Although validated severity models such as the Child–Turcotte–Pugh (CTP) and Model for End-Stage Liver Disease (MELD) scores are widely used to estimate mortality risk and guide referral and prioritization decisions, their predictive performance may vary across phenotypes of acute decompensation.[4]

Serum albumin is a readily measurable marker of hepatic synthetic capacity and systemic illness severity. It has long been considered a cardinal marker of decompensated cirrhosis. Hypoalbuminemia reflects not only reduced hepatocellular synthesis but also inflammation-driven capillary leak. The factors responsible for hypoalbuminemia include hemodilution and increased catabolism. Consequently, low albumin levels correlate with circulatory dysfunction, infection risk and adverse outcomes in cases of chronic liver disease. Large cohort data support albumin as an independent predictor of mortality in both compensated and decompensated cirrhosis. Similarly, the neutrophil-to-lymphocyte ratio (NLR) has emerged as an important index of systemic inflammation as well as immune dysregulation. Higher neutrophil counts are suggestive of heightened inflammatory activation, whereas relative lymphopenia may suggest impaired immune competence and malnutrition. These features are common in advanced ALD. Recent work in alcoholic cirrhosis suggests that NLR and composite indices incorporating albumin (often termed neutrophil-to-lymphocyte-to-albumin measures) can stratify short-term mortality risk using routine laboratory parameters, making them appealing candidates for bedside prognostication.[5]

The present study evaluates the prognostic value of NLR and the neutrophil–lymphocyte-to-albumin ratio as readily available inflammatory-synthetic composite markers to predict 30-day and 90-day mortality in alcohol-related liver disease, with the aim of identifying feasible risk stratification tools that can complement established scores and support timely escalation of care.

Methods

This prospective observational study was conducted in the Department of General Medicine of Basaveshwar Teaching and General Hospital (attached to Mahadevappa Rampure Medical College, Kalaburagi after obtaining permission from institutional ethics committee (IEC-Reg No ECR/889/InstEC). The duration of the study was 18 months extending from June 2024–November 2025. 70 patients diagnosed with alcohol-related liver disease (ARLD) were included in this study. Patients aged more than 18 years with a confirmed diagnosis of alcohol-related liver disease were included in the study. Individuals with conditions that could alter inflammatory markers were excluded. These included patients with secondary immunodeficiency states such as HIV infection, hepatocellular carcinoma or other malignancies, those receiving corticosteroids or cytotoxic drugs, and patients with any ongoing infection at the time of evaluation.The sample size of 70 was determined based on feasibility within the study duration and expected inpatient load while considering a confidence level of 95% and an anticipated mortality proportion derived from prior regional hospital data on ARLD. All enrolled patients were male. This reflects the epidemiological pattern of alcohol-related liver disease in this tertiary care setting where the overwhelming majority of ALD cases are men due to sociocultural drinking patterns. All consecutive eligible patients presenting to the inpatient and outpatient departments during the study period were enrolled using a non-probability consecutive sampling method. Written informed consent was obtained from all patients prior to enrolment, and the study was conducted in accordance with institutional ethical standards.

Patients attending the Medicine inpatient and outpatient departments who fulfilled the eligibility criteria were enrolled in this study. Detailed clinical details were collected using a structured and predesigned proforma. Baseline demographic details including age and gender distribution was

recorded. A detailed history was taken particularly regarding duration and quantity of alcohol consumption. At admission, all patients underwent thorough clinical examination and laboratory investigations. These included Complete Blood Count (CBC), Liver Function Tests (LFT), Serum Proteins, Serum Electrolytes, Renal Function Tests (RFT), Prothrombin Time and International Normalized Ratio (PT-INR). An Ultrasound abdomen was done in all cases. In patients with ascites, ascitic fluid analysis was performed as indicated. Blood samples were collected under aseptic precautions at the time of admission. NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. The neutrophil–lymphocyte-to-albumin (NLA) ratio was calculated using the formula: NLA = (Absolute Neutrophil Count / Absolute Lymphocyte Count) / Serum Albumin (g/dL). Both NLR and NLA ratios were recorded at admission for all patients.

All enrolled patients were followed up for a period of 90 days. Follow-up assessments were conducted at 30 days and 90 days either through outpatient visits, during subsequent inpatient admissions, or via telephonic communication when necessary. During follow-up, clinical status and survival outcomes were documented. Repeat laboratory investigations including CBC and serum albumin were performed during follow-up visits, and NLR and NLA ratios were recalculated at 30 days and 90 days. The primary outcome measure was mortality at 30 days and 90 days. Patients who were lost to follow-up were contacted telephonically to ascertain survival status.

Statistical analysis was performed using SPSS 23.0 software Continuous variables were expressed as mean ± standard deviation (SD). Categorical variables were expressed as frequencies and percentages. The association between NLR, NLA ratio, and mortality was analyzed using appropriate statistical tests such as the independent t-test or Mann–Whitney U test for continuous variables and Chi-square test or Fisher's exact test for categorical variables. Receiver Operating Characteristic (ROC) curve analysis was performed to determine the predictive accuracy and optimal cutoff values of NLR and NLA ratio for mortality prediction. A p-value of <0.05 was considered statistically significant.

Results

All cases of alcoholic liver disease included in this study were males. The majority of patients belonged to the 31–40 years age group (30.0%), followed closely by 41–50 years (28.6%). Patients aged 51–60 years constituted 17.1%, while 21–30 years accounted for 15.7%. The least represented group was those aged >60 years (8.6%) (Table 1).

Out of 70 patients enrolled, mortality at admission was 71.4%, with 28.6% discharged for follow-up. Among discharged patients, mortality at 30 days was 20.0%. By 90 days, mortality increased to 31.2%, indicating progressive cumulative mortality over time (Table 2).

Non-surviving patients demonstrated significantly lower hemoglobin, lymphocyte count, total protein, and albumin levels, along with significantly higher total leukocyte count, neutrophil percentage, urea, creatinine, INR, PT, and total bilirubin compared to survivors. Age, serum sodium, potassium, platelet count, liver enzymes (SGOT, SGPT, ALP), direct and indirect bilirubin, and globulin levels did not differ significantly between groups (Table 3).

Both NLR and NLA demonstrated strong

Table 1 Age-Wise Distribution Of Patients Included in the Study (n=70)

Age	Number of Cases	%
21–30	11	15.7
31–40	21	30.0
41–50	20	28.6
51–60	12	17.1
>60	6	8.6

Table 2 Distribution Of Mortality And Follow-Up Status At Admission, 30 Days, And 90 Days Among Enrolled Patients (n=70)

Time interval	Follow-up	Follow-up (%)	Died	Died (%)	Total
At Admission	20	28.6	50	71.4	70
30 days	16	80.0	4	20.0	20
90 days	11	68.8	5	31.2	16

Table 3 Comparison of Baseline Hematological and Biochemical Parameters Between Surviving and Non-Surviving Patients

Parameter	Surviving (n=20)	Non-surviving (n=50)	Test Value and p-value
	Mean ± SD	Mean ± SD	
Age	42.80 ± 14.74	43.72 ± 10.01	p=0.764, NS
Hemoglobin	11.43 ± 3.52	8.38 ± 2.38	p<0.001, HS
Total Count	7685 ± 2998.99	14901 ± 8844.46	p=0.001, HS
Neutrophil	68.55 ± 11.39	87.30 ± 4.47	p<0.001, HS
Lymphocyte	26.55 ± 10.85	8.48 ± 3.58	p<0.001, HS
Urea	16.36 ± 8.30	50.76 ± 41.27	p<0.001, HS
Creatinine	0.765 ± 0.29	1.55 ± 1.24	p=0.007, HS
Sodium	135.70 ± 5.89	134.06 ± 6.87	p=0.352, NS
Potassium	4.03 ± 0.81	4.37 ± 1.12	p=0.227, NS
INR	1.26 ± 0.33	2.03 ± 0.86	p<0.001, HS
PT	16.36 ± 4.44	23.98 ± 9.89	p=0.003, HS
Total Bilirubin	4.36 ± 4.14	9.38 ± 11.20	p=0.031, S
Direct Bilirubin	2.68 ± 3.74	5.75 ± 9.29	p=0.158, NS
Indirect Bilirubin	1.32 ± 0.84	2.99 ± 4.88	p=0.136, NS
Platelet	1.81 ± 0.75	1.79 ± 1.05	p=0.949, NS
SGOT	143.15 ± 66.22	132.60 ± 142.62	p=0.753, NS
SGPT	54.10 ± 33.05	48.22 ± 40.83	p=0.569, NS
ALP	166.40 ± 94.09	153.08 ± 72.14	p=0.526, NS
Total Protein	7.16 ± 0.91	6.21 ± 1.17	p=0.002, HS
Albumin	3.07 ± 0.77	2.43 ± 0.57	p<0.001, HS
Globulin	4.09 ± 0.93	3.73 ± 1.03	p=0.201, NS

Table 4 Composite Diagnostic Value of Prognostic Scores in Predicting Mortality at Admission, 30 Days, and 90 Days

Time Period	Prognostic Score	Cut off	Specificity (%)	Sensitivity (%)	PPV	NPV	AUC (95% CI)	p-value
At Admission	NLR	8.6	92.5	76.8	62.0%	90.0%	0.92 (0.76–0.95)	p=0.001
	NLA	32.5	89.4	74.6	69.0%	94.0%	0.89 (0.69–0.92)	p<0.001
30 Days	NLR	3.45	90.4	81.0	69.3%	87.9%	0.89 (0.75–0.93)	p<0.001
	NLA	12.10	85.23	79.4	63.5%	85.7%	0.86 (0.69–0.90)	p=0.008
90 Days	NLR	3.80	94.41	78.1	0.69	0.93	0.92 (0.78–0.96)	p=0.001
	NLA	16.5	90.34	76.53	0.73	0.92	0.90 (0.72–0.95)	p=0.001

diagnostic performance in predicting mortality at admission, 30 days, and 90 days, with consistently high specificity, sensitivity, and AUC values across all time points. NLR showed marginally higher AUC values compared to NLA at each interval. All results were statistically significant (Table 4).

Discussion

In this cohort of 70 men with alcohol-related liver disease (ALD) demonstrated a strikingly high early mortality, with most deaths occurring during the index admission and additional attrition through 30- and 90-day follow-up. This pattern aligns with the concept that ALD-related decompensation is frequently driven by an "inflammation–immune dysfunction" phenotype superimposed on impaired hepatic reserve. Hasa *et al.* emphasized the role of bacterial translocation, immune activation and cytokine-driven systemic inflammation in progression of liver disease from steatosis to alcoholic hepatitis and cirrhosis.[6] The significantly high in-hospital mortality of 71.4% in this study reflects the advanced disease severity at presentation with most patients demonstrating features of acute-on-chronic liver failure. This tertiary referral center predominantly receives late-stage cases transferred after initial management failure elsewhere contributing to high mortality seen in this study.

Similarly, Biyik showed that the NLR can independently predict mortality in cases of cirrhosis even after accounting for Child–Turcotte–Pugh (CTP) and MELD scores. These findings reinforce the immune dysregulation that conveys risk beyond conventional liver severity metrics. Against this background, findings of this study that NLR- and albumin-integrated metrics can reliably predict outcomes in ALD is clinically coherent. It can be confidently said that decompensation in ALD is not merely "hepatic failure," but a systemic inflammatory state with measurable hematologic parameters.

At admission, an NLR cut-off of 8.6 was found to have high specificity and a corresponding neutrophil–lymphocyte-to-albumin ratio (NLAR) cut-off of 32.5, with values above these thresholds strongly associated with death. These cut-points are directionally consistent with the existing cirrhosis literature, although thresholds differ across populations and clinical contexts. In cases of hepatic cirrhosis Dewi *et al.* reported marked separation of mean NLR between survivors and non-survivors and demonstrated that NLR remained prognostic independent of MELD/CTP, supporting the observation that admission NLR captures risk not fully reflected by traditional scoring.[7]

Importantly, hospitalized cohorts often exhibit higher inflammatory burden and intercurrent triggers (infection, bleeding, encephalopathy), which can shift optimal cut-offs upward. In this regard, Chiriac S and colleagues found that among hospitalized cirrhotic patients, NLR contributed to predicting short-term survival , underscoring that in patients with advanced disease may require higher decision thresholds than outpatient "stable" cohorts.[8] The strong discrimination at admission likely reflects both the severity mix (predominance of cirrhosis) and the systemic inflammatory milieu typical of ALD-related decompensation.

A key contribution of this study is the demonstration that incorporating albumin into NLR (NLAR) further strengthened mortality prediction. Albumin is not only a marker of hepatic synthetic function and nutritional status; it is also a negative acute-phase reactant that falls with systemic inflammation, thereby integrating "liver reserve" and "inflammatory load" in a single composite. This conceptual advantage mirrors findings in alcoholic cirrhosis reported by Zhang M and colleagues, who proposed an NLR/albumin-derived biomarker (their NLA) and showed it outperformed NLR alone for predicting 30-day mortality, with a clinically usable cut-off in their male alcoholic cirrhosis cohort.[9] 30-day analyses similarly identified lower follow-up cut-offs for both NLR (3.45) and NLAR (12.10) than at admission, which may reflect survivor bias (patients who lived beyond the index admission likely had partial resolution of acute inflammatory triggers) and the dynamic nature of inflammation in cirrhosis. These findings were further supported by study by Maccali *et al* who reported that NLR assessed at 48 hours were independently associated with short-term mortality in acutely decompensated cirrhosis.[10] These findings indicate that serial measurement of NLR can add prognostic value beyond a single baseline value.

By 90 days, identified cut-offs (NLR 3.80; NLAR 16.5) continued to discriminate mortality, supporting the durability of inflammatory and nutrition-synthetic signals as risk markers beyond the immediate hospitalization window. In a propensity score–matched analysis, Deng *et al.* reported that NLR >8.9 was a feasible and clinically meaningful cut-off associated with 90-day mortality in

cirrhosis, independent of age, sex, CTP, and MELD, and suggested incremental value when combined with conventional systems.[11] Although 90-day threshold in this study is lower, the difference is plausibly explained by cohort composition, timing of measurement (post-acute stabilization among survivors vs baseline in a broader cirrhotic population), and variability in precipitating events and supportive care. Extending the discussion to broader short-term outcomes, Liu *et al*. (in large multicenter cohorts) described a non-linear association between baseline NLR and 90-day transplant-free mortality, highlighting that risk relationships may not be strictly linear across the entire NLR range and that clinically relevant inflection points can exist.[12] This nonlinearity provides one explanation for why different studies yield different "optimal" cut-offs and supports approach of empirically deriving thresholds within the ALD cohort rather than importing a single universal value.

Clinically, the findings support NLR and NLAR as practical, low-cost adjuncts to established prognostic tools in ALD. This is important particularly in settings where rapid risk stratification is needed. The significant association of higher NLR/NLAR with mortality in this study is similar evidence from both stable and hospitalized cirrhosis populations as also reported by, Rice *et al.* following non-elective hospitalization.[13] in inpatient cirrhosis. From an implementation perspective, NLAR may be especially useful in ALD because it partially embeds two major prognostic domains—systemic inflammation and hepatic synthetic failure—without requiring complex calculations. Nevertheless, this study's limitations should temper interpretation: the single-center design, modest sample size, and all-male cohort may limit generalizability; the absence of direct statistical comparison with established prognostic scores such as MELD and Child–Pugh limits assessment of incremental predictive value; moreover, intercurrent infection, gastrointestinal bleeding, renal dysfunction and treatment heterogeneity can confound inflammatory markers.

In conclusion both neutrophil–lymphocyte ratio (NLR) and neutrophil–lymphocyte–albumin ratio (NLAR/NLA) significantly predicted mortality. Higher values above validated cut-offs at the time of admission and at 30 and 90 days were significantly associated with mortality showing good sensitivity and specificity. These readily available markers reflect systemic inflammation, immune dysregulation and liver dysfunction. These ratios be incorporated into routine care to improve prognostic stratification and management in cases of alcohol related liver disease.

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