https://doi.org/10.31925/farmacia.2026.1.9 **ORIGINAL ARTICLE**

INFLAMMATORY RATIO BIOMARKERS FOR PROGNOSTIC AND THERAPEUTIC GUIDANCE IN CRITICAL COVID-19 CARE

DEJANA D. BAJIĆ [1]*, NEMANJA B. TODOROVIĆ [2], MLADENA N. LALIĆ POPOVIĆ [2], LJILJANA N. ANDRIJEVIĆ [1]

[1]*Department of Biochemistry, Faculty of Medicine, University of Novi Sad, Serbia*
[2]*Department of Pharmacy, Faculty of Medicine, University of Novi Sad, Serbia*

**corresponding author: dejana.bajic@mf.uns.ac.rs*

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Abstract

This study examines the prognostic value of the neutrophil-to-lymphocyte ratio (NLR), fibrinogen-to-albumin ratio (FAR), and C-reactive protein-to-albumin ratio (CAR) as accessible indicators of inflammation and metabolic imbalance in critically ill patients with COVID-19-related sepsis. A total of 133 patients admitted to the intensive care unit were retrospectively analysed. Biomarker values obtained within the first 24 hours of admission were evaluated for their ability to predict 28-day mortality using receiver operating characteristic (ROC) curves and logistic regression analysis. Among the tested ratios, CAR (cut-off 5.5; AUC = 0.665) and NLR (cut-off 25; AUC = 0.663) showed the strongest predictive accuracy for early mortality, whereas FAR demonstrated a weaker association. Elevated CAR and NLR levels were closely linked to poor outcomes, and CAR was identified as the most reliable independent predictor (p = 0.015). These findings suggest that inflammation-based ratios, particularly NLR and CAR, provide simple, cost-effective tools for early risk assessment and can complement personalized therapeutic strategies in critical care.

Rezumat

Acest studiu examinează valoarea prognostică a raportului neutrofile-limfocite (NLR), a raportului fibrinogen-albumină (FAR) și a raportului proteina C reactivă-albumină (CAR) ca indicatori accesibili ai inflamației și dezechilibrului metabolic la pacienții critici cu sepsis asociat COVID-19. Un total de 133 de pacienți internați în unitatea de terapie intensivă au fost analizați retrospectiv. Valorile biomarkerilor determinate în primele 24 de ore de la internare au fost evaluate în ceea ce privește capacitatea lor de a prezice mortalitatea la 28 de zile, utilizând curbe de tip „receiver operating characteristic" (ROC) și analiză de regresie logistică. Dintre rapoartele investigate, CAR (prag 5,5; AUC = 0,665) și NLR (prag 25; AUC = 0,663) au demonstrat cea mai bună acuratețe predictivă pentru mortalitatea precoce, în timp ce FAR a prezentat o asociere mai slabă. Nivelurile crescute ale CAR și NLR au fost strâns corelate cu evoluții nefavorabile, iar CAR a fost identificat drept cel mai fiabil predictor independent (p = 0,015). Aceste rezultate sugerează că rapoartele bazate pe inflamație, în special NLR și CAR, reprezintă instrumente simple și cost-eficiente pentru evaluarea precoce a riscului și pot completa strategiile terapeutice personalizate în îngrijirea critică.

Keywords: biomarkers, COVID-19, inflammation, prognosis

Introduction

Biomarkers have long been essential tools in clinical medicine and pharmaceutical research, helping physicians diagnose diseases, monitor progression, and predict patient outcomes. Traditionally, single-parameter biomarkers offered useful but limited insight into isolated physiological or pathological processes. In recent years, greater attention has been given to *ratio biomarkers*, which combine two or more laboratory parameters to better capture the complex interplay between inflammation, immunity, and metabolism. These derived indices - such as the neutrophil-to-lymphocyte ratio (NLR), fibrinogen-to-albumin ratio (FAR), and C-reactive protein-to-albumin ratio (CAR) - reflect both inflammatory and metabolic changes, providing a more integrated picture of systemic dysfunction (1-5).

In critically ill patients, particularly those with sepsis and severe COVID-19, the clinical relevance of ratio biomarkers becomes more evident. Both conditions share similar biological mechanisms, including immune dysregulation, cytokine overactivation, and metabolic imbalance, which often result in organ failure and high mortality. In such patients, simple and rapidly obtainable markers like NLR, FAR, and CAR can serve as practical tools for assessing disease severity, identifying high-risk individuals, and guiding early intervention (6-9). Because they are calculated from routine laboratory data, these ratios offer a cost-effective and accessible method for risk stratification, especially in settings with limited resources.

The early phase of intensive care admission is critical for evaluating the patient's physiological state and initiating appropriate therapy. Understanding which biomarkers can predict short-term mortality during this period may help clinicians make timely, evidence-based decisions.

The present study examines the prognostic value of three ratio biomarkers - NLR, FAR, and CAR - in patients with confirmed COVID-19 and sepsis admitted to the intensive care unit (ICU). The analysis focuses on values measured within the first 24 hours of admission and their relationship to 28-day mortality. By assessing the predictive accuracy of these markers, this study aims to clarify their role in early risk assessment, support individualized therapeutic planning, and contribute to improving outcomes in this highly vulnerable patient population (10-12).

Materials and Methods

Study design and ethical approval

This retrospective observational study was conducted at the Institute for Pulmonary Diseases of Vojvodina, Sremska Kamenica, within the Clinic for Intensive Medicine and Vascular Pulmonary Diseases, Department for Intensive Care and Intoxications Level 3. The study period extended from November 2020 to February 2022 and included 133 adult patients admitted to the Intensive Care Unit (ICU). Ethical approval was obtained from the Ethics Committee of the Institute for Pulmonary Diseases of Vojvodina (Protocol No. 9-II/3, February 24, 2022) and from the Ethics Committee of the Faculty of Medicine, University of Novi Sad (Protocol No. 01-39/190/1, May 13, 2022). The study was conducted in accordance with the Declaration of Helsinki and institutional ethical standards.

Patient selection and data collection

Eligible participants were adults (≥ 18 years) with a confirmed COVID-19 infection, as verified by RT-PCR or rapid antigen testing from nasopharyngeal swabs. All patients were critically ill at ICU admission, presenting with life-threatening conditions and a high risk of imminent death. Sepsis was diagnosed according to the Sepsis-3 criteria, requiring confirmed or suspected infection and an acute increase in the Sequential Organ Failure Assessment (SOFA) score of ≥ 2 points.

Exclusion criteria were applied to ensure data consistency and eliminate potential confounders. The study excluded immunocompromised patients (HIV-positive individuals with AIDS, post-transplant recipients), pregnant or breastfeeding women, and patients with active malignancies, highly active autoimmune diseases, or ICU stays shorter than four hours. These conditions may significantly alter immune and metabolic responses, confounding biomarker interpretation and outcome analysis.

The study analyzed three biomarkers: the neutrophil-to-lymphocyte ratio (NLR), fibrinogen-to-albumin ratio (FAR), and C-reactive protein-to-albumin ratio (CAR). NLR was obtained by dividing the absolute neutrophil count by the absolute lymphocyte count from a complete blood count (CBC) performed using whole blood with K_2EDTA anticoagulant on the *Beckman Coulter DxH 900* analyzer (Nyon, Switzerland). FAR was calculated by dividing the fibrinogen concentration in plasma, determined by the Clauss method on *ACL TOP CTS 300* (Instrumentation Laboratory, Bedford, MA, USA), by the serum albumin concentration measured using the Bromocresol Green colorimetric method on *Cobas c311* (Roche Diagnostics, Basel, Switzerland). CAR was computed by dividing the C-reactive protein concentration obtained from venous blood without anticoagulants, measured by the immunoturbidimetric method on *Cobas c311* (Roche Diagnostics, Basel, Switzerland), by the albumin concentration. All laboratory parameters were collected within the first 24 hours of ICU admission.

Statistical analysis

Data was analyzed using *IBM SPSS Statistics* software, version 26.0 (Chicago, IL, USA). Statistical significance was set at $\alpha = 0.05$, with $p < 0.05$ considered significant. The Shapiro–Wilk test assessed normality of distribution. Differences between survivors and non-survivors were evaluated using the Mann–Whitney U test for continuous variables and the Chi-square test for categorical data. Median values were used as cut-off points for NLR, FAR, and CAR. Logistic regression analysis identified potential predictors of 28-day mortality. Receiver operating characteristic (ROC) curve analysis was used to assess the prognostic performance of biomarkers, with the area under the curve (AUC) quantifying discriminatory accuracy between survivors and non-survivors.

Results and Discussion

Patient characteristics and mortality

The study included 133 patients, of whom 90 were male and 43 females. Within 28 days, 45 patients survived, whereas 88 did not. Mortality was higher among males (72.2%, 65/90) compared to females (53.5%, 23/43), indicating an elevated risk of short-term death in men. Age distribution (Figure 1) showed that deceased males were generally older, particularly between 60 and 80 years, while survivors of both sexes were younger and more evenly distributed, highlighting the influence of advanced age on 28-day mortality.

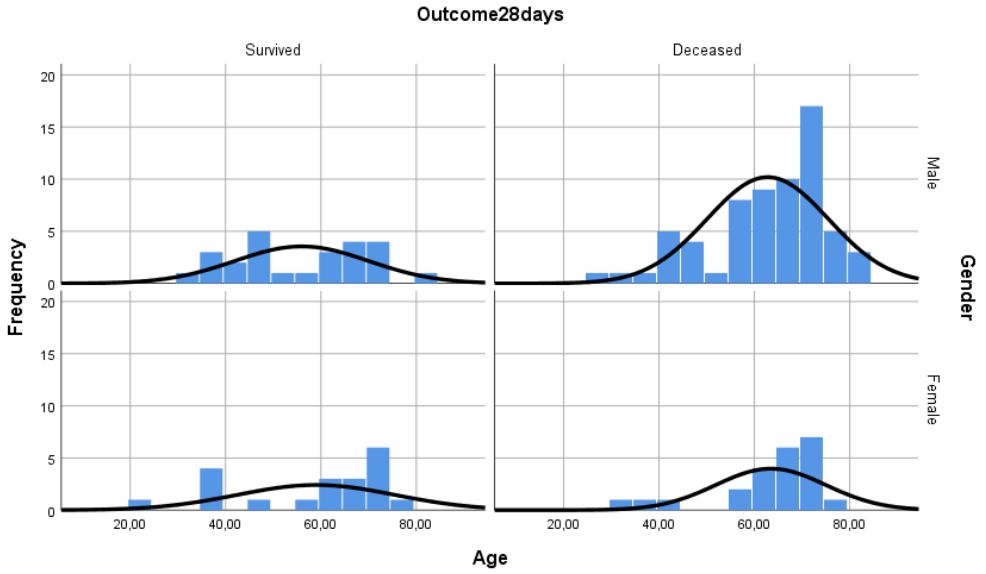

Figure 1.
Age distribution of survivors and deceased patients stratified by gender

Inflammatory ratio biomarkers and distribution
Significant differences between survivors and non-survivors were observed for NLR (p = 0.002), CAR (p = 0.002), and FAR (p = 0.033), although FAR demonstrated a weaker association. Elevated NLR was strongly associated with increased mortality. As illustrated in Figure 2, deceased patients of both sexes had NLR values primarily ranging from 20 to 40, with some exceeding 100. In contrast, survivors mostly exhibited values below 25. Male non-survivors showed greater variability in NLR, reflecting a more heterogeneous inflammatory response.

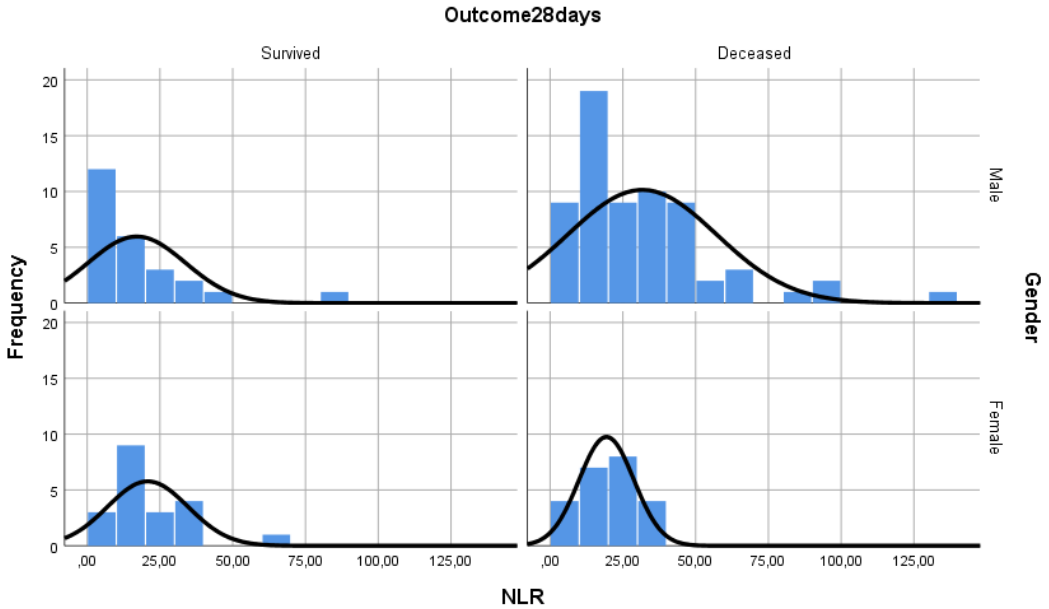

Figure 2.
Distribution of NLR among survivors and deceased by gender

CAR values were higher among deceased patients, particularly males, suggesting a correlation with increased mortality risk. Figure 3 demonstrates that survivors generally had lower CAR levels, mostly between 0 and 10, whereas deceased patients showed a broader distribution with a rightward shift. This trend was more pronounced in males; females exhibited a similar pattern, but less markedly. The shift in CAR distribution among non-survivors supports its potential role as a prognostic marker.

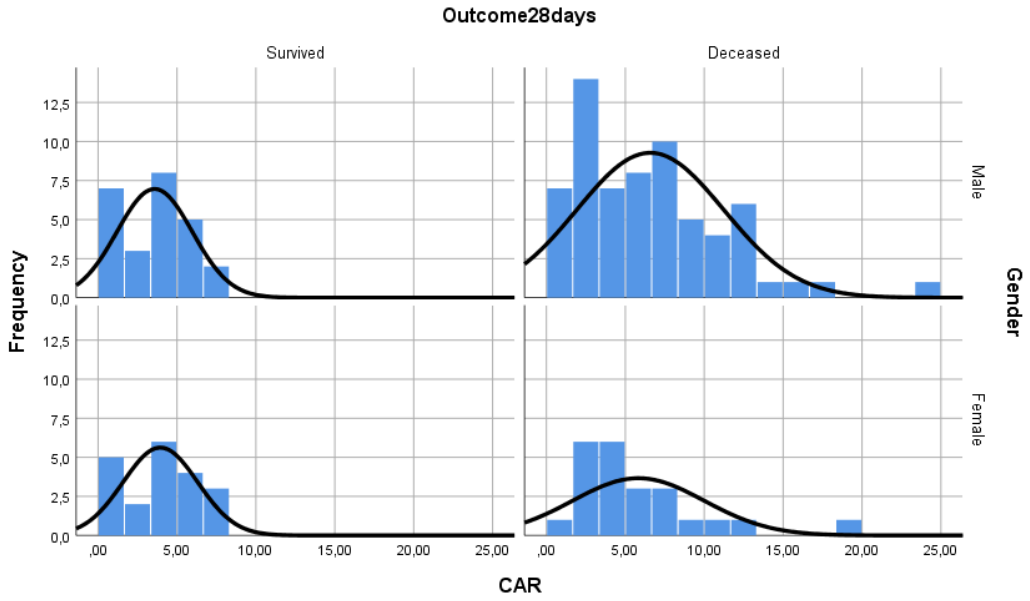

Figure 3.
Distribution of CAR among survivors and deceased by gender

Predictive Performance and Risk Stratification
ROC curve analysis indicated that CAR (AUC = 0.665, p = 0.002) and NLR (AUC = 0.663, p = 0.002) demonstrated moderate discriminative ability for 28-day mortality. FAR showed lower predictive accuracy (AUC = 0.613, p = 0.033), while ICU stay duration did not predict mortality (AUC = 0.532, p = 0.541) (Figure 4, Table I).

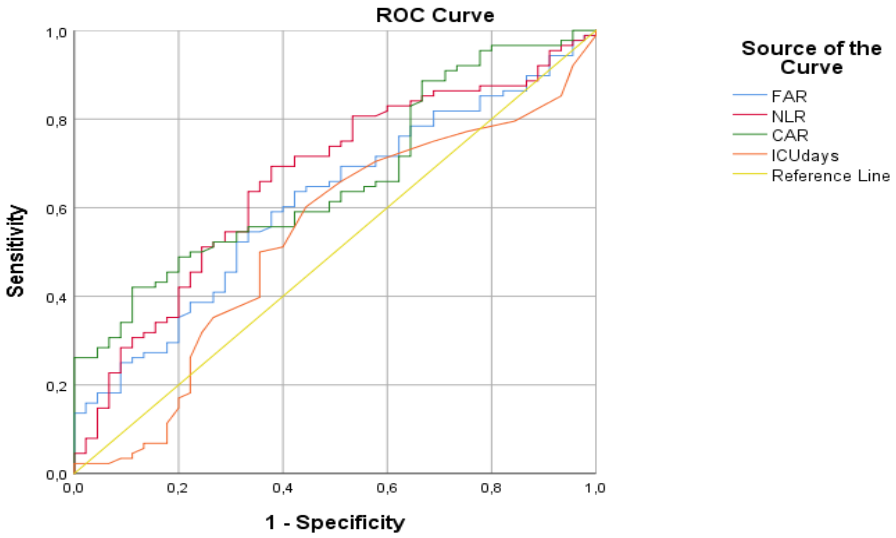

Figure 4.
Viscosity curves and the statistical mean of differences expressed by the regression lines

Table I
Area under the curve for FAR, NLR, CAR, and ICU days

				Asymptotic 95% Confidence Interval	
Test Variable	**Area**	**Standard Error**	**Asymptotic Sig.**	**Lower Bound**	**Upper Bound**
FAR	0.613	0.050	0.033	0.516	0.711
NLR	0.663	0.049	0.002	0.567	0.760
CAR	0.665	0.047	0.002	0.572	0.758
ICU days	0.532	0.054	0.541	0.426	0.639

Logistic regression suggested CAR as the most robust marker (p = 0.015, OR = 1.225), while NLR showed a borderline effect (p = 0.055, OR = 1.025). FAR, age, and gender did not reach statistical significance.

Patients were stratified into low- and high-risk groups (Figure 5) using median cut-off values for NLR (25), CAR (5.5), and FAR (21). Figure 6 shows that patients with NLR above 25 had markedly higher mortality (38 deceased *vs*. 10 survived) compared to those with NLR ≤ 25 (50 deceased *vs*. 35 survived; p = 0.017). Similarly, Figure 7 illustrates that patients with CAR > 5.5 had an 81.8% mortality rate, while those with CAR ≤ 5.5 had a 55.1% mortality rate (p = 0.001), confirming CAR as a strong prognostic indicator. FAR did not show a significant association with mortality (χ^2 = 2.448, p = 0.118; Fisher's exact p = 0.156; likelihood ratio χ^2 = 2.545, p = 0.111), suggesting that observed differences were likely due to chance.

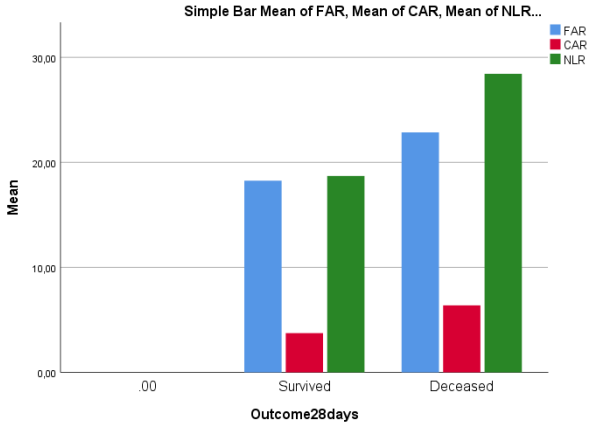

Figure 5.
Mean values of FAR, CAR, and NLR in survivors *vs*. deceased patients

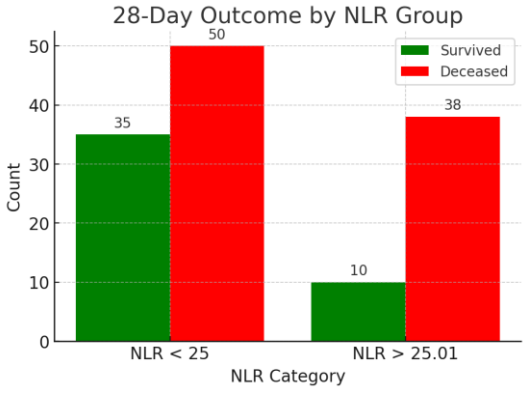

Figure 6.
28-day survival outcomes in patients with NLR < 25 and NLR > 25

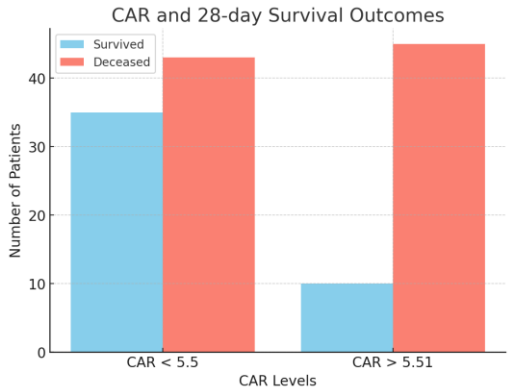

Figure 7.
28-day survival outcomes in patients with CAR < 5.5 and CAR > 5.51

Traditional single biomarkers, such as CRP or albumin, provide useful information but often fail to capture the multifaceted nature of critical illness. Ratio biomarkers (NLR, CAR, FAR) combine related parameters to reflect inflammation, immune response, and nutritional/metabolic status, offering a more integrated perspective. This approach reduces individual variability and may improve early risk stratification compared to single markers (13-15).

By combining two related variables, these ratios reduce individual variability and increase specificity. For instance, CAR reflects both systemic inflammation (CRP) and nutritional status (albumin), making it a more reliable predictor of mortality than either component alone (4, 15-17). NLR highlights neutrophil-driven inflammation alongside lymphocyte suppression, while FAR links coagulation and nutrition—both crucial factors in critical illness (14-16).

In this study, higher NLR and CAR were consistently associated with 28-day mortality, with CAR showing the strongest association (14, 18, 19). The observed thresholds (NLR = 25, CAR = 5.5, FAR = 21) were higher than those reported in less severely ill populations, reflecting the extreme inflammatory and metabolic burden in ICU patients (14, 18, 19). FAR showed weaker prognostic performance, consistent with previous observations in other critical illnesses. These findings suggest that CAR and NLR may serve as practical early indicators of mortality risk, particularly in critically ill COVID-19 patients (2, 6, 20-24). Elevated values may indicate a need for immunomodulatory therapy, while lower values could guide supportive or antiviral interventions (21-24). However, due to the retrospective design, limited sample size, and absence of certain covariates such as mechanical ventilation or comprehensive comorbidity data, these associations should not be interpreted as fully independent of other clinical factors.

Although elevated NLR and CAR may reflect the severity of inflammation, their use to guide therapeutic interventions such as corticosteroids or tocilizumab remains speculative. No interventional data currently support treatment decisions based on these biomarkers, and prospective trials are needed to assess any potential predictive or therapeutic role. Beyond COVID-19, ratio biomarkers have shown utility across diverse conditions. In cardiovascular diseases, they help assess inflammation and vascular risk (5). In oncology, they monitor immune responses and disease progression (24). In autoimmune and chronic illnesses, they reflect systemic inflammatory and metabolic status (4-6, 13-18). Their simplicity, rapid availability, and cost-effectiveness make them practical for early risk stratification, personalized decision-making, and monitoring disease evolution (2, 6, 21, 24).

Comparison with previous studies highlights context-specific differences. For example, postoperative ICU patients had CAR cut-offs of ~1.75 - 1.58 for predicting short- and long-term mortality (25). In contrast, our critically ill COVID-19 cohort required a higher CAR threshold (5.5), likely due to more severe systemic inflammation and metabolic stress (14, 18, 26). Similarly, FAR cut-offs in chronic heart failure were reported at 9.06 (14), whereas we observed 21 in severe COVID-19 sepsis. NLR thresholds also differed; in general, COVID-19 populations, values above 3 indicated severe disease (25, 26), but our ICU cohort required NLR > 25 to identify high-risk individuals (14, 18).

Overall, ratio biomarkers provide a simple, rapid, and accessible complement to traditional diagnostics. They integrate multiple aspects of pathophysiology—systemic inflammation, immune response, and nutritional status—allowing early risk assessment, informed therapeutic decisions, and personalized care (21-24, 27-30). Their use complements—but does not replace—comprehensive clinical evaluation and advanced diagnostics.

Several pharmacological strategies aimed at modulating the host inflammatory response in COVID-19 have been explored in the literature, emphasizing that targeting specific cytokine pathways may influence disease progression without yet being validated for routine therapeutic guidance. For example, inhibitors of key pro-inflammatory cytokines such as IL-6 have been discussed in the context of severe COVID-19 due to their potential to attenuate the cytokine release syndrome that underlies critical illness, although evidence remains mixed and dependent on concurrent interventions like corticosteroids (31). Furthermore, blockade of IL-1 signalling has been proposed as a mechanistic approach to mitigate hyperinflammation; observational and cohort studies suggest IL-1 receptor antagonists may reduce systemic inflammation and need for mechanical ventilation in selected patients, yet prospective clinical validation is still needed (32). A recent study by Adamescu *et al*. further underscores the central role of cytokines IL-6 and IL-1 in COVID-19 disease progression, reporting that elevated IL-6 is significantly associated with more severe disease, and suggesting that therapies targeting these mediators could be promising in patients with high cytokine burden or specific comorbid conditions, although this remains to be formally proven in interventional studies (33). These findings complement our focus on inflammation-based biomarkers by showing biologically plausible links between systemic immuno-inflammatory activation and clinical outcomes, but also highlight that therapeutic use of such pathways requires careful evaluation in well-designed trials. This context supports our position that although inflammation-based biomarkers may reflect immune activity and systemic stress, their use for guiding specific therapies (*e.g.*, corticosteroids, tocilizumab) remains speculative without interventional trial evidence (34).

Study limitations

This study has several limitations that should be considered when interpreting the results. It was designed as a retrospective, single-centre analysis with a relatively small sample size, which may restrict the generalisability of the findings. Because the study population included only critically ill COVID-19 patients with sepsis, the results may not reflect outcomes in milder or non-COVID cases. Further prospective, multicentre research with larger cohorts is needed to confirm these associations and to refine the optimal biomarker thresholds for broader clinical application.

Conclusions

In critically ill COVID-19 patients with sepsis, NLR and CAR were associated with 28-day mortality, with CAR showing the strongest effect among the markers studied. FAR demonstrated limited prognostic value. Male patients had higher mortality and more variable inflammatory responses, highlighting sex-based differences. Ratio biomarkers integrate inflammation, immune function, and nutritional status, offering practical guidance for early risk stratification and individualized therapy. Their simplicity, rapid availability, and broad applicability make them valuable tools in routine critical care, particularly in urgent or resource-limited settings. By supporting timely identification of high-risk patients and guiding therapeutic decisions, these markers enhance clinical management without replacing advanced diagnostics. Their use may contribute to more precise, patient-centred care and improved outcomes.

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Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics approval and consent to participate

Ethical approval was obtained from the Ethics Committee of the Institute for Pulmonary Diseases of Vojvodina (Protocol No. 9-II/3, February 24, 2022) and from the Ethics Committee of the Faculty of Medicine, University of Novi Sad (Protocol No. 01-39/190/1, May 13, 2022). The study was conducted in accordance with the Declaration of Helsinki and institutional ethical standards.

AI use disclosure

AI tools were used only for assistance in translating strictly specialized medical terms and phrases into English. The authors remain the sole creators of all study concepts, methodology, analyses, and interpretations, and take full responsibility for the content.

Conflict of interest

The authors declare no conflict of interest.

References

1. Ulloque-Badaracco JR, Mosquera-Rojas MD, Hernandez-Bustamante EA, Alarcón-Braga EA, Herrera-Añazco P, Benites-Zapata VA. Prognostic value of albumin-to-globulin ratio in COVID-19 patients: a systematic review and meta-analysis. Heliyon. 2022;8(5):e09457.
2. Alagbe A, Pedroso G, Oliveira B, Maia G, Costa E, Albuquerque D, et al. Association of lymphocyte counts, NLR and PLR with mortality in COVID-19 patients. Hematol Transfus Cell Ther. 2021;43:S508-S509.
3. Buonacera A, Stancanelli B, Colaci M, Malatino L. Neutrophil to lymphocyte ratio: an emerging marker of the relationships between the immune system and diseases. Int J Mol Sci. 2022;23(7):3636.
4. Birdal O. The relationship between C-reactive protein albumin ratio and long-term mortality in patients with acute coronary syndrome. Cureus. 2023;15(10):e47222.
5. Desai R, Fadah K, Srikanth S, Neha NFN, Jain A. Fibrinogen-albumin ratio predicting major adverse cardiovascular outcomes post-percutaneous coronary intervention: a systematic review and exploratory meta-analysis. Clin Cardiol. 2023;46(4):455-458.
6. Asperges E, Albi G, Zuccaro V, Sambo M, Pieri TC, Calia M, et al. Dynamic NLR and PLR in predicting COVID-19 severity: a retrospective cohort study. Infect Dis Ther. 2023;12(6):1625-1640.
7. Ulloque-Badaracco JR, Salas-Tello WI, Al-kassab-Córdova A, Alarcón-Braga EA, Benites-Zapata VA, Maguiña JL, et al. Prognostic value of neutrophil-to-lymphocyte ratio in COVID-19 patients: a systematic review and meta-analysis. Int J Clin Pract. 2021;75(11):e14596.
8. Tadesse Z, Bayissa AB, Diriba T, Chernet N, Tsegaye S, Tsega M. Neutrophil-to-lymphocyte ratio and cut-off values as predictor of severity and mortality in COVID-19 patients in Millennium COVID-19 Care Center, Addis Ababa, Ethiopia. Int J Gen Med. 2022;15:6739-6755.
9. Dymicka-Piekarska V, Dorf J, Milewska A, Łukaszyk M, Kosidło JW, Kamińska J, et al. Neutrophil/lymphocyte ratio (NLR) and lymphocyte/monocyte ratio (LMR) - risk of death inflammatory biomarkers in patients with COVID-19. J Inflamm Res. 2023;16:2209-2222.
10. Toori KU, Qureshi MA, Chaudhry A, Safdar MF. Neutrophil to lymphocyte ratio (NLR) in COVID-19: a cheap prognostic marker in a resource constraint setting. Pakistan J Med Sci. 2021;37(5):1435-1439.
11. Higaki A, Okayama H, Homma Y, Sano T, Kitai T, Yonetsu T, et al. Predictive value of neutrophil-to-lymphocyte ratio for the fatality of COVID-19 patients complicated with cardiovascular diseases and/or risk factors. Sci Rep. 2022;12(1):13606.
12. Colaneri M, Genovese C, Fassio F, Canuti M, Giacomelli A, Ridolfo AL, et al. Prognostic significance of NLR and PLR in COVID-19: a multi-cohort validation study. Infect Dis Ther. 2024;13(5):1147-1157.
13. Hendrikse NM, Llinares Garcia J, Vetter T, Humphreys AJ, Ehmann F. Biomarkers in medicines development— from discovery to regulatory qualification and beyond. Front Med. 2022;9:878942.
14. Yang S, Pi J, Ma W, Gu W, Zhang H, Xu A, et al. Prognostic value of the fibrinogen-to-albumin ratio (FAR) in patients with chronic heart failure across the different ejection fraction spectrum. Libyan J Med. 2024;19(1):2309757.
15. Ülker M, Domac SF, Demir M, Karacı R. The relationship of CRP/albumin ratio with etiology and prognosis in acute ischaemic stroke. Bosphorus Med J. 2022;9(4):209-215.
16. Feketea GM, Vlacha V. The diagnostic significance of usual biochemical parameters in coronavirus disease 19 (COVID-19): albumin to globulin ratio and CRP to albumin ratio. Front Med (Lausanne). 2020;7:566591.
17. Park JE, Chung KS, Song JH, Kim SY, Kim EY, Jung JY, et al. The C-reactive protein/albumin ratio

as a predictor of mortality in critically ill patients. J Clin Med. 2018;7(10):333.
18. Nalbant A, Kaya T, Varim C, Yaylaci S, Tamer A, Cinemre H. Can the neutrophil/lymphocyte ratio (NLR) have a role in the diagnosis of coronavirus 2019 disease (COVID-19)? Rev Assoc Med Bras. 2020;66(6):746-751.
19. Prozan L, Shusterman E, Ablin J, Mitelpunkt A, Weiss-Meilik A, Adler A, et al. Prognostic value of neutrophil-to-lymphocyte ratio in COVID-19 compared with influenza and respiratory syncytial virus infection. Sci Rep. 2021;11(1):21519.
20. Wang X, Hu Y, Luan H, Luo C, Kamila Kamili, Zheng T, et al. Predictive impact of fibrinogen-to-albumin ratio (FAR) for left ventricular dysfunction in acute coronary syndrome: a cross-sectional study. Eur J Med Res. 2023;28(1):68.
21. Carlos AF, Josephs KA. The role of clinical assessment in the era of biomarkers. Neurotherapeutics. 2023;20(4):1001-1018.
22. Urrechaga E. Reviewing the value of leukocytes cell population data (CPD) in the management of sepsis. Ann Transl Med. 2020;8(15):953.
23. Battaglini D, Lopes-Pacheco M, Castro-Faria-Neto HC, Pelosi P, Rocco PRM. Laboratory biomarkers for diagnosis and prognosis in COVID-19. Front Immunol. 2022;13:857573.
24. Mucherino S, Lorenzoni V, Triulzi I, Del Re M, Orlando V, Capuano A, et al. Cost-Effectiveness of Treatment Optimisation with Biomarkers for Immunotherapy in Solid Tumours: A Systematic Review. Cancers (Basel). 2024;16(5):995.
25. Oh TK, Ji E, Na HS, Min B, Jeon YT, Do SH, et al. C-reactive protein to albumin ratio predicts 30-day and 1-year mortality in postoperative patients after admission to the intensive care unit. J Clin Med. 2018;7(3):39.
26. Barya P, Narang S, Jain VK, Shrivastava R. Neutrophil-lymphocytic ratio (NLR) or albumin-globulin ratio (AGR) which one is a better predictor marker in assessment of severity of COVID-19 infection? Int J Med Biomed Stud. 2021;5(8):188-198.
27. Bakkerus L, Pickkers P. Personalized medicine in COVID-19. Intensive Care Med. 2022;48(11):1607-1610.
28. Liu WY, Chien CW, Tung TH. Healthcare practice strategies for integrating personalized medicine: management of COVID-19. World J Clin Cases. 2021;9(29):8647-8657.
29. AL-Taie A, Büyük AŞ, Sardas S. Considerations into pharmacogenomics of COVID-19 pharmacotherapy: hope, hype and reality. Pulm Pharmacol Ther. 2022;77:102172.
30. Wang LY, Cui JJ, OuYang QY, Zhan Y, Wang YM, Xu XY, et al. Complex analysis of the personalized pharmacotherapy in the management of COVID-19 patients and suggestions for applications of predictive, preventive, and personalized medicine attitude. EPMA J. 2021;12(3):307-324.
31. Maamar M, Artime A, Pariente E, Fierro P, Ruiz Y, Gutiérrez S, et al. Post-COVID-19 syndrome, low-grade inflammation and inflammatory markers: a cross-sectional study. Curr Med Res Opin. 2022;38(6):901-909.
32. Peng J, Fu M, Mei H, Zheng H, Liang G, She X, et al. Efficacy and secondary infection risk of tocilizumab, sarilumab and anakinra in COVID-19 patients: a systematic review and meta-analysis. Rev Med Virol. 2022; 32(3):e2295.
33. Adamescu AI, Tilișcan C, Stratan LM, Mihai N, Ganea OA, Miron VD, et al. The role of IL-6 and IL-1 in COVID-19 disease progression: the impact of gender-based differences, BMI variability and co-medications. Farmacia. 2025;73(2):308-316.
34. Lupaşcu RE, Ilie MI, Velescu BȘ, Udeanu DI, Sultana C, Ruță S, et al. COVID-19-Current therapeutical Approaches and future Perspectives. Processes. 2022;10(6):1053.