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Research Article

Clinical Significance of Hematological Ratios in Assessing Covid-19 Severity

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Abstract

Background: Hematological indices have been increasingly investigated as potential biomarkers for predicting COVID-19 severity. Identifying reliable, cost-effective, and accessible indicators can aid in early risk stratification and optimized patient management.

Objectives: This study aimed to evaluate the clinical significance of hematological ratios, including the Neutrophil-to-Lymphocyte Ratio (NLR), Lymphocyte-to-Monocyte Ratio (LMR), Platelet-to-Lymphocyte Ratio (PLR), Lymphocyte-to-CRP Ratio (LCR), Absolute Neutrophil Count (ANC), and Absolute Lymphocyte Count (ALC) in assessing COVID-19 severity.

Methods: A cross-sectional study was conducted over one year at the Department of Laboratory Medicine, BSMMU, Dhaka, including 165 RT-PCR-confirmed COVID-19 patients categorized into mild, moderate, severe, and critical cases. Hematological parameters were analyzed, and their diagnostic performance was evaluated using Receiver Operating Characteristic (ROC) curve analysis. Results: Among all indices, ANC had the highest predictive value (AUC=0.702, $p<0.001$), followed by ALC (AUC=0.624, $p=0.006$). NLR (AUC=0.550, $p=0.013$) showed a strong correlation with severity ($R^2=0.414$), reinforcing its clinical utility. In contrast, LMR and PLR exhibited weak associations ($p=0.378$ and $p=0.009$, respectively). LCR showed an inverse relationship with severity (AUC = 0.275, $p<0.001$), reflecting the inflammatory burden in critical cases.

Conclusion: This study identifies ANC, NLR, and LCR as significant hematological markers for predicting COVID-19 severity, with ANC showing the highest diagnostic accuracy. These readily available indices can serve as cost-effective tools for early risk stratification and aid in clinical decision-making. Further large-scale studies are recommended to establish standardized cut-off values for broader clinical application.

Key words: covid-19; hematological indices; neutrophil-to-lymphocyte ratio; absolute neutrophil count; disease severity; biomarkers

Introduction

The coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has posed unprecedented challenges to global healthcare systems since its emergence1. Characterized by a wide clinical spectrum, COVID-19 can present as an asymptomatic or mild illness in some individuals, while in others, it may lead to severe pneumonia, acute respiratory distress syndrome (ARDS), multi-organ dysfunction, and even death. The unpredictable disease course necessitates early identification of patients at risk of severe progression to enable timely medical intervention and optimized resource allocation2. Therefore, identifying reliable, accessible, and cost-effective biomarkers for assessing COVID-19 severity has become a critical area of research. Haematological parameters have gained increasing attention as potential

indicators of disease severity in COVID-19 patients. These parameters reflect the immune response and systemic inflammatory burden, both of which play crucial roles in the pathogenesis of COVID-193,4. Among various haematological markers, composite ratios such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR) have emerged as useful indicators of disease progression. These ratios provide insight into the balance between innate immune activation and adaptive immune suppression, which is a hallmark of severe COVID-195. Neutrophils are key mediators of the innate immune response and contribute to the hyperinflammatory state observed in severe COVID-19 cases, while lymphocytes play a crucial role in viral clearance and immune regulation. A high NLR reflects both neutrophilia and lymphopenia, conditions frequently associated with poor prognosis in COVID-19 patients. Similarly, elevated PLR has been linked to excessive inflammatory and thrombotic activity, which is a common complication in severe cases. On the other hand, the monocyte-to-lymphocyte ratio (MLR) may provide additional prognostic information, as monocytes are involved in the cytokine storm that exacerbates lung injury and systemic inflammation6-8. Several studies have demonstrated that increased haematological ratios correlate with disease severity, intensive care unit (ICU) admission, the need for mechanical ventilation, and mortality in COVID-19 patients. Given the simplicity and accessibility of routine blood tests, haematological ratios can serve as cost-effective, rapid, and widely available biomarkers for risk stratification. However, despite their clinical relevance, there remains a need for further validation in diverse patient populations and healthcare settings to establish standardized cut-off values and improve their predictive accuracy6-10. This study aims to evaluate the clinical significance of haematological ratios in assessing the severity of COVID-19. By analysing haematological data from hospitalized COVID-19 patients, we seek to determine the correlation between these ratios and disease progression. Understanding the prognostic value of these ratios may help guide clinical decision-making, improve early risk assessment, and contribute to better management strategies for COVID-19 patients, ultimately reducing morbidity and mortality associated with the disease.

Methods

This cross-sectional study was conducted over a period of one year at the Department of Laboratory Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka. The study aimed to evaluate the clinical significance of hematological ratios in assessing COVID-19 severity. The study population consisted of RT-PCR-confirmed COVID-19 patients who were either admitted to the COVID unit or attended the fever clinic at BSMMU. Patients were selected using a non-randomized purposive sampling technique, ensuring inclusion based on eligibility criteria. The sample size was calculated using Buderer's formula, assuming a standard deviation (SD) of 3.98 and a 5% level of significance. Using this calculation, the required sample size was determined to be 162. The inclusion criteria comprised adult patients (≥18 years) of both sexes with RT-PCR-confirmed COVID-19, while patients who were critically ill (requiring mechanical ventilation), had hematological disorders, malignancies, or were unwilling to participate were excluded. Data collection included demographic variables, such as age, sex, and body mass index (BMI), along with information on comorbidities, including diabetes mellitus (DM), hypertension (HTN), chronic kidney disease (CKD), stroke, and cardiovascular diseases. Laboratory variables included complete blood count (CBC), inflammatory markers such as C-reactive protein (CRP), and serum ferritin. Patients were classified into mild, moderate, severe, and critical cases according to the National COVID-19 Management Guideline (9th version, Bangladesh). Following Institutional Review Board (IRB) approval, eligible patients were identified and provided with detailed information about the study. Informed written consent was obtained before blood sample collection. A total of 5.0 mL venous blood was drawn under aseptic precautions, using 0.5% chlorhexidine gluconate for disinfection. The blood was collected into two tubes: a violet-capped EDTA tube (2 mL) for CBC analysis and a red-colored plain tube (3 mL) for CRP and serum ferritin tests. The samples were processed at the Department of Laboratory Medicine, BSMMU, with CBC analyzed using the Sysmex 4000XN hematology analyzer (flow cytometry method), ESR by automated ESR analyzer (modified Westergren method), CRP by chemiluminescence immunoassay, and serum ferritin by automated photometry. Statistical analysis was conducted using SPSS version 26.0, with categorical variables expressed as frequencies and percentages, and continuous variables as mean ± SD. Comparative analyses were performed using Student's t-test (for normally distributed data) and Mann-Whitney U test (for non-normal data), while categorical data were analyzed using Chi-square (χ^2) tests. Correlation between hematological parameters and disease severity was assessed using Pearson's correlation coefficient, and receiver operating characteristic (ROC) curve analysis was conducted to determine diagnostic accuracy. A p-value <0.05 was considered statistically significant. Ethical considerations were maintained throughout the study. Approval was obtained from the Institutional Review Board (IRB) of BSMMU (Memo No. BSMMU/2021/9284), and confidentiality was ensured by assigning unique ID numbers to each participant. Universal safety precautions were followed, including the use of personal protective equipment (PPE) such as gloves, laboratory coats, and face shields, and proper disposal of biohazard waste. The study imposed no financial burden on participants, as funding was provided by the Research Grant Commission of BSMMU. The findings of this study aim to provide a cost-effective and accessible method for predicting COVID-19 severity using hematological ratios. The results are expected to enhance early risk stratification, improve patient management, and contribute to the overall understanding of COVID-19 pathophysiology, thereby aiding clinicians in making informed treatment decisions.

Results

This study included 165 RT-PCR-confirmed COVID-19 patients, categorized into mild (n=8), moderate (n=71), severe (n=77), and critical (n=9) cases, based on the National COVID-19 Management Guideline (Version 9.0, Bangladesh). Analysis of age distribution revealed that disease severity increased with age. The 50-59 years age group had the highest proportion of severe cases (33.8%), while 60-69 years comprised 77.8% of critical cases. The mean age of patients increased with disease severity, from 58.6 ± 16.7 years in mild cases to 61.7 ± 4.8 years in critical cases, although this association was not statistically significant (p=0.069). Comparison of hematological ratios among different severity groups demonstrated statistically significant differences in several markers. NLR (p=0.013) increased progressively with severity, from 2.9 ± 0.69 in mild cases to 11.6 ± 8.5 in critical cases. The scatter plot (Figure II) confirmed a strong positive correlation (R^2=0.414) between NLR and COVID-19 severity. In contrast, LMR did not show a significant difference between severity groups (p=0.378), with a weak correlation (R^2 =0.018) (Figure III), indicating limited predictive value. PLR (p=0.009) also showed an increasing trend with severity, from 16.5±14.6 in mild cases to 2914.7±4946.3 in critical cases, but the correlation remained weak (R^2=0.061), suggesting limited utility as a severity marker. Among inflammatory markers, LCR (p=0.007) was significantly lower in severe and critical cases, with critical cases showing the lowest mean value of 0.2±0.2, indicating an inverse relationship with severity. ANC (p<0.001) showed the strongest predictive power, increasing from 926,119±631,471 in mild cases to 2,976,456±1,654,719 in critical cases. ALC (p=0.004) was also significantly associated with severity, though with moderate predictive ability. The Receiver Operating Characteristic (ROC) curve analysis (Figure I) was used to evaluate the diagnostic performance of hematological indices in predicting COVID-19 severity. Among all parameters, ANC had the highest Area Under the Curve (AUC=0.702, p<0.001), demonstrating strong predictive accuracy. LCR had the lowest AUC (0.275, p<0.001), suggesting an inverse relationship with severity. NLR, PLR, and ALC showed moderate diagnostic accuracy, while LMR had the weakest predictive value. Age was associated with disease severity but did not reach statistical significance. Among the hematological indices, ANC emerged as the strongest predictor of COVID-19 severity, while NLR and LCR also demonstrated clinical significance. LMR and PLR, despite statistical significance, showed weaker predictive accuracy. These findings suggest that hematological markers, particularly ANC and NLR, can serve as useful and cost-effective indicators for early risk stratification in COVID-19 patients.

Age group (years)	COVID-19 Severity				p-value
	Mild (n=8)	Moderate (n=71)	Severe (n=77)	Critical (n=9)	
20-29	1(12.5%)	3(4.2%)	4(5.2%)	0(0.0%)	0.069[ns]
30-39	0(0.0%)	10(14.1%)	6(7.8%)	0(0.0%)	
40-49	1(12.5%)	15(21.1%)	18(23.4%)	0(0.0%)	
50-59	3(37.5%)	25(35.2%)	26(33.8%)	2(22.2%)	
60-69	0(0.0%)	9(12.7%)	14(18.2%)	7(77.8%)	
70-79	3(37.5%)	9(12.7%)	9(11.7%)	0(0.0%)	
Total	8(100.0%)	71(100.0%)	77(100.0%)	9(100.0%)	
Mean±SD	58.6±16.7	51.0±13.2	52.6±12.8	61.7±4.8	

Table I: Association of age with disease severity (n=165).

Hematological ratio	COVID-19 Severity				p-value
	Mild (n=8)	Moderate (n=71)	Severe (n=77)	Critical (n=9)	
NLR	2.9±0.69	5.9±4.5	7.02±6.8	11.6±8.5	0.013[s]
LMR	5.2±2.3	5.6±3.7	6.5±5.4	7.8±6.0	0.378[ns]
PLR	16.5±14.6	254.6±606.9	1140.2±3228	2914.7±4946.3	0.009[s]
LCR	1.9±1.8	1.1±2.2	0.4±0.9	0.2±0.2	0.007[s]
ANC	926119±631471	1110772±725634	1777565±1102436	2976456±1654719	<0.001[s]
ALC	246117±166599	249317±180770	418892±387875	475287±401138	0.004[s]

Table II: Comparison of hematological ratio with COVID-19 severity group (n=165).

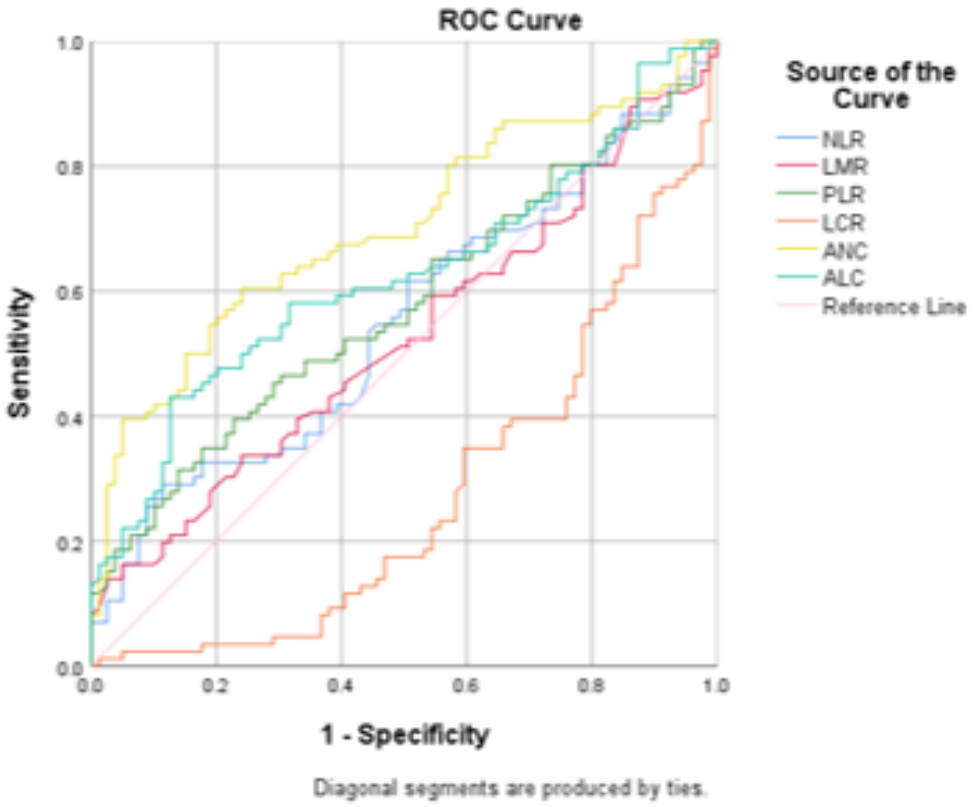

Figure 1: Receiver operating characteristic (ROC) curve is showing the relative diagnostic performances of NLR to detect the severity of COVID-19 patients.

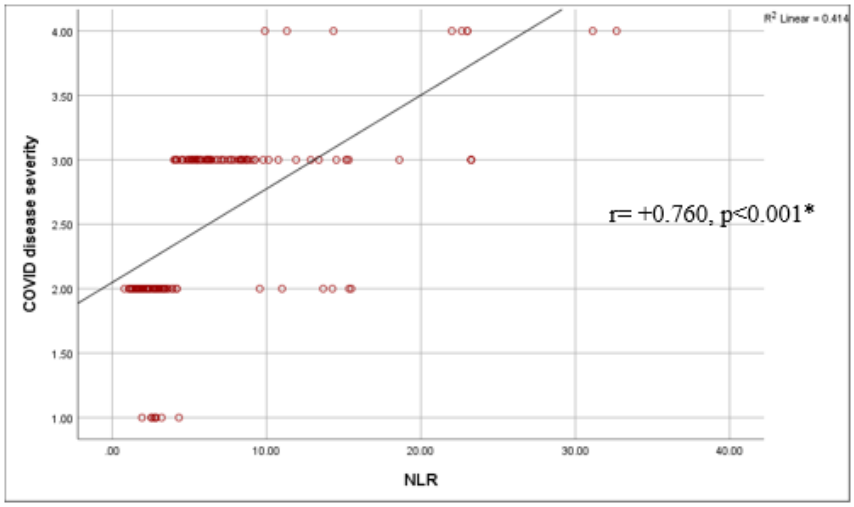

Figure II: Scatter diagram showing the spearman correlation of NLR with COVID disease severity (strong positive significant correlation).

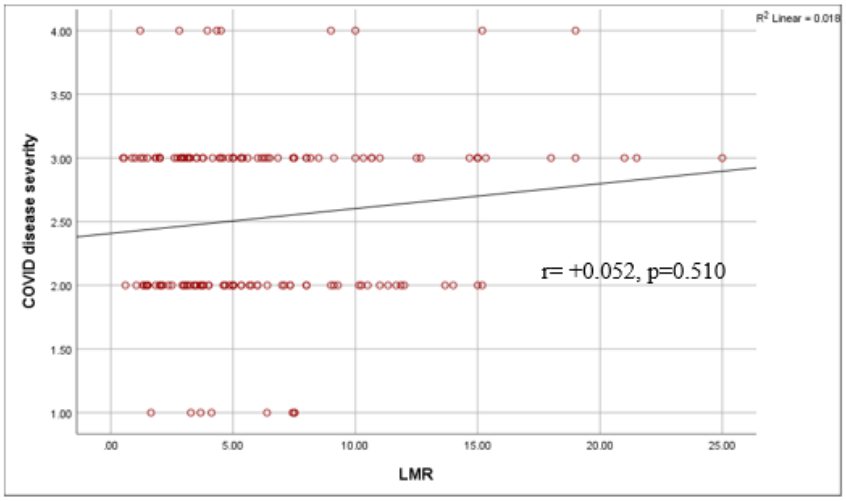

Figure III: Scatter diagram showing the spearman correlation of LMR with COVID disease severity (weak positive correlation).

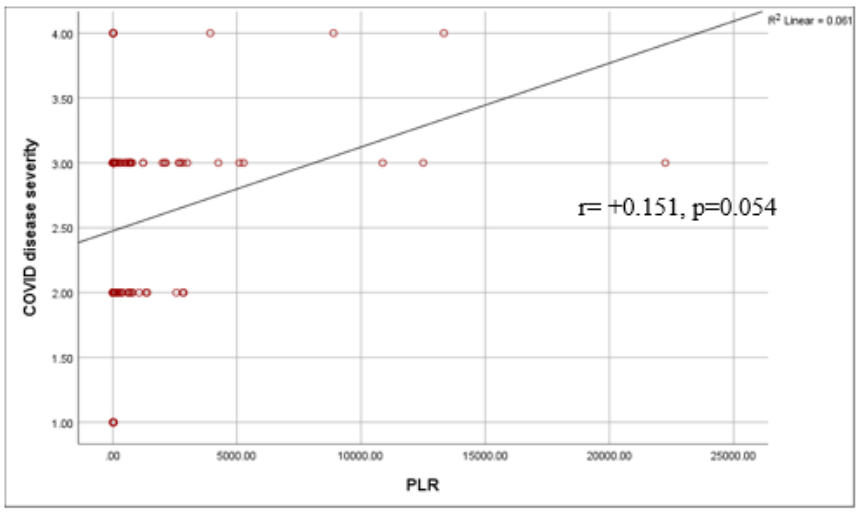

Figure III: Scatter diagram showing the spearman correlation of PLR with COVID disease severity (weak positive correlation).

Discussion

The findings of this study demonstrate that Absolute Neutrophil Count (ANC), Neutrophil-to-Lymphocyte Ratio (NLR), and Lymphocyte-to-CRP Ratio (LCR) are significant hematological markers associated with COVID-19 severity. Among these, ANC showed the highest predictive accuracy (AUC= 0.702, p<0.001), indicating its strong potential as a severity predictor. This is consistent with previous studies that have reported elevated neutrophil counts in severe COVID-19 cases, contributing to hyperinflammation and cytokine storm, which ultimately lead to multi-organ

damage11. Similarly, NLR exhibited a strong positive correlation with disease severity (R^2 =0.414, p=0.013), which aligns with prior research findings. Different studies have also demonstrated that higher NLR values are associated with poor outcomes in COVID-19 patients, emphasizing its role as a reliable prognostic indicator12-15. The increase in NLR is driven by neutrophilia (a response to severe inflammation) and lymphopenia (reflecting immune suppression), both of which have been widely observed in critical COVID-19 cases. In contrast, Lymphocyte-to-Monocyte Ratio (LMR) and Platelet-to-Lymphocyte Ratio (PLR) showed weak correlations with disease severity (R^2=0.018 and R^2=0.061, respectively). This is in agreement with findings from other relevant studies16,17, who reported that while PLR might indicate inflammation, its diagnostic performance is weaker than NLR or ANC. Furthermore, LCR demonstrated an inverse relationship with severity (AUC=0.275, p<0.001), supporting the observations by other study18, where a lower LCR was linked to higher inflammation and poorer outcomes. Age was found to be associated with increasing disease severity in this study, with the highest proportion of critical cases observed in patients aged ≥60 years. Although this trend was not statistically significant (p=0.069), it is consistent with studies by other relevant studies19-21, who found that older age is a key risk factor for severe COVID-19 outcomes due to age-related immune dysfunction and comorbidities. However, our findings suggest that age alone may not be a sufficient predictor without considering hematological markers. Overall, these results reinforce that ANC, NLR, and LCR are useful hematological predictors of COVID-19 severity, with ANC showing the strongest diagnostic value. Compared to prior studies, our findings align with existing literature that supports NLR as a prognostic biomarker while also highlighting ANC as a superior predictor22,23. These hematological indices, being cost-effective and widely available, could serve as valuable tools for early risk stratification and clinical decision-making in COVID-19 management. However, further large-scale studies are necessary to validate these findings and establish standardized cut-off values for broader clinical application.

Conclusion

This study highlights the clinical significance of hematological ratios in assessing COVID-19 severity, with Absolute Neutrophil Count (ANC), Neutrophil-to-Lymphocyte Ratio (NLR), and Lymphocyte-to-CRP Ratio (LCR) emerging as key predictors. Among these, ANC demonstrated the strongest diagnostic accuracy, reinforcing its role as a reliable biomarker for identifying severe cases. NLR also showed a strong positive correlation with disease severity, consistent with prior studies emphasizing its prognostic value. Conversely, LMR and PLR exhibited weaker associations, suggesting they may not serve as independent predictors. The study also found that age was associated with increasing disease severity, particularly in patients aged ≥60 years, although this relationship was not statistically significant. This suggests that age alone may not be sufficient for risk assessment without considering hematological markers. Overall, these findings support the use of hematological indices, particularly ANC and NLR, as cost-effective, easily accessible tools for early risk stratification in COVID-19 patients. Integrating these markers into routine clinical assessment could help in identifying high-risk patients, guiding timely interventions, and improving patient management strategies. Future large-scale studies are recommended to establish standardized reference values and validate the clinical utility of these biomarkers across diverse populations

Author contributions

a. Conception and design: [SF]
b. Acquisition, analysis, and interpretation of data: [SF]
c. Manuscript drafting and revising it critically: [SF, SS]
d. Approval of the final version of the manuscript: [SF, SS, REM, RB, KF]
e. Guarantor accuracy and integrity of the work: [SF]

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Conflict of interest

All the authors declared no competing interests.

Ethical approval

The study was conducted following the Declaration of Helsinki as the cornerstone document on human research ethics. Before commencing the study, approval of this project was taken from the Institutional Review Board of Bangabandhu Sheikh Mujib Medical University (memo no BSMMU/2021/9284).

Data availability statement

The authors confirm that the data supporting the findings of this study are share upon request.

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