

Original Article

The Predictive Value of Hematologic Parameters and Inflammatory Rates at Admission on the Need for Hospitalization in COVID-19 Patients Over 65 Years of Age

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ABSTRACT

Objective: The COVID-19 pandemic has led to high mortality and morbidity rates, especially in individuals over 65 years of age. The aim of this study was to evaluate the prognostic value of hematologic parameters, inflammatory rates and chronic diseases at the time of admission in COVID-19 patients over 65 years of age in predicting the need for hospitalization.

Materials and Methods: A total of 1392 patients aged ≥ 65 years admitted to the emergency department with a diagnosis of COVID-19 were included in our retrospective study. Ratios such as neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), and hematological parameters were analyzed. In addition, comorbidity status and the need for hospitalization were assessed.

Results: NLR (≥ 4.8) and PLR (≥ 165) were significantly higher in patients requiring hospitalization ($p < 0.001$). Low lymphocyte levels ($< 1.0 \times 10^9/L$) were found to be another important parameter predicting the need for hospitalization. According to ROC analysis, the area under the curve (AUC) for NLR was 0.762, 0.724 for PLR and 0.728 for chronic renal failure (CRF). Comorbidities such as malignancy, hypertension and chronic renal failure were also observed to increase the need for hospitalization ($p < 0.01$).

Conclusion: Our study shows that inflammatory markers such as NLR and PLR are powerful tools for predicting the need for hospitalization in COVID-19 patients over 65 years of age with a history of CRF and malignancy. Integrating these parameters into clinical applications and using them in early diagnosis and intervention processes can make a significant contribution to the management of elderly individuals. Our findings provide data to guide the development of clinical decision support systems.

Keywords: COVID-19, geriatric patient, pandemic



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INTRODUCTION

Coronaviruses are enveloped RNA viruses that cause significant disease in humans and mammals. Towards the end of 2019, a previously unknown coronavirus (SARS-CoV-2) was discovered in Wuhan, China, among a group of patients experiencing symptoms such as persistent cough, high fever, difficulty breathing, and extreme fatigue [1]. This new coronavirus spread rapidly and became a global pandemic, affecting millions of people worldwide [2].

Older age, in particular, is a significant risk factor for the severe progression of COVID-19 infection. Geriatric patients are more prone to severe forms of the disease because of age-associated immune system changes and accompanying chronic diseases [3]. In this age group, the disease has a more severe course and hospitalization rates and mortality increase significantly [4].

Various laboratory parameters are utilized for early diagnosis and prognosis prediction of COVID-19. Hematological parameters and inflammatory markers play a crucial role in assessing disease severity and forecasting the clinical progression [1]. In the advanced age group, the prognostic significance of the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and other inflammatory markers becomes more important [2].

This study aimed to evaluate the significance of chronic diseases, hematological parameters, and inflammatory ratios at the time of admission in predicting hospitalization requirements for COVID-19 patients aged 65 and above. We also aimed to determine the factors that may be effective on mortality in this age group.

MATERIALS AND METHODS

Study Design and Participants

This study was conducted between March 15, 2020 and June 15, 2020 in the Emergency Department COVID-19 outpatient clinic of a tertiary care hospital. It consisted of patients over the age of 65 who came to the Emergency Department COVID-19 outpatient clinic of a tertiary care hospital and were diagnosed with COVID-19 for the first time with PCR. Ethical approval for the study was granted by our hospital's ethics committee. (ethics committee no: 2020/07.151). The demographic data of the cases, chronic diseases, emergency presentation, hemogram parameters upon presentation to the emergency department, whether they were hospitalized in the ward or intensive care unit, and patient outcome were examined separately and collected retrospectively. In our hospital, patients who routinely come to the emergency department are hospitalized if their CURB-65 score is two

or higher and/or CO-RADS (COVID-19 Reporting and Data System) is 3 or higher. Patients were categorized into two groups: those who required hospitalization and those who did not. Patients over the age of 65, diagnosed with COVID-19 with PCR and those with complete data were enrolled in the study. Patients younger than 65 years of age, those without a PCR-confirmed COVID-19 diagnosis, and those with incomplete data for the analyzed parameters were excluded from the study. The research adhered to the principles outlined in the Declaration of Helsinki. Patient consent was not required due to the retrospective design.

Statistical Analysis

Data analysis was conducted using IBM SPSS 27.0 (Armonk, NY: IBM Corp.) statistical package program. Descriptive statistical methods (frequency, percentage, mean, standard deviation, median, IQR) and Chi-Square (χ^2) test were employed for the comparison of qualitative data. Bonferroni correction was applied for multiple comparisons where differences were observed. The conformity of the data to normal distribution was assessed using the Kolmogorov-Smirnov test, skewness-kurtosis values, and graphical methods (histogram, Q-Q Plot, Stem and Leaf, Boxplot). In this study, the independent samples t-test and one-way ANOVA were used to compare normally distributed quantitative data between groups, while the Mann-Whitney U test was applied for non-normally distributed data. The relationships between variables were analyzed using Spearman's rho correlation test. A statistical significance level of $\alpha=0.05$ was considered.

RESULTS

A total of 1392 patients were enrolled in the study. The mean age of the patients was 76.8 ± 8.1 years and 58.3% ($n=811$) were female. While 72.8% ($n=1013$) of the patients were referred, 27.2% ($n=379$) were direct admissions. Of the patients admitted, 44.7% ($n=622$) were hospitalized, 52.2% ($n=727$) were followed up as outpatients, and 3.1% ($n=43$) were excluded. Table 1 presents the demographic and clinical characteristics of the patients.

When hematologic parameters of hospitalized and outpatients were compared, WBC (10.82 ± 5.94 vs. 8.76 ± 4.12 , $p < 0.001$), neutrophils (8.42 ± 5.32 vs. 6.14 ± 3.84 , $p < 0.001$), NLR (7.86 ± 6.42 vs. 4.12 ± 3.86 , $p < 0.001$), PLR (248.6 ± 156.4 vs. 186.4 ± 112.8 , $p < 0.001$) and MLR (0.82 ± 0.64 vs. 0.58 ± 0.42 , $p < 0.001$) were significantly higher in the inpatient group. Lymphocyte count was significantly lower in inpatients (1.42 ± 0.82 vs. 1.84 ± 0.92 , $p < 0.001$) (Table 2).

In the logistic regression analysis conducted to determine the factors influencing the need for hospitalization, the strongest predictors of hospitalization were NLR (OR: 1.32, 95% CI: 1.24-

Table 1. Demographic, clinical and hemogram parameters in geriatric patients

	n=1392 Mean±SD	%
Median (Min-Max)		
Gender*		
Female	811	58.3
Male	581	41.7
Age (year)**	76.8±8.1	80.0 (67.0–88.0)
Comorbidity*		
No	736	52.8
Yes	656	47.2
HT	306	22.0
CAD	263	18.9
DM	247	17.8
COPD	78	5.6
CKD	71	5.1
Others	176	12.7
History of malignancy		
Yes	165	11.8
No	1227	88.2
Method of arrival		
Referral	1013	72.8
Direct arrival	379	27.2
Method of exit		
Hospitalization	662	44.7
Discharge	727	52.2
Eksitus	43	3.1
WBC (×10 ³ /μL)	9.61±5.8	9.7 (7.3–16.0)
Neutrophile (×10 ³ /μL)	7.1±4.1	6.3 (4.3–9.1)
Lymphocyte (×10 ³ /μL)	1.81±2.1	3.0 (3.5–6.5)
Hemoglobine**	11.9±3.0	12.2 (10.0–14.1)
Thrombocyte (×10 ³ /μL)	79.8±110.4	282.0 (212–416)
NLR	5.89±2.2	6.3 (0.8–9.4)
PLR	217.9±90.1	259.1 (11.9–303.7)
MPV (fL)	10.6±1.2	10.4 (9.1–18.2)
MLR	0.82±0.64	0.9 (0.7–2.1)

Data are presented as mean±standard deviation, median and 25th–75th percentiles or n (%). HT: Hypertension; CAD: Coronary artery disease; DM: Diabetes; COPD: Chronic obstructive pulmonary disease; CKD: Chronic kidney disease; WBC: White blood cell; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; MLR: Monocyte-lymphocyte ratio; MPV: Mean platelet volume.

Table 2. Comparison of hematologic parameters of discharged and hospitalized patients

Parameter	Hospitalized (n=622)	Discharged (n=727)	p
WBC (×10 ³ /μL)	10.82±5.94	8.76±4.12	<0.001*
Lymphocyte (×10 ³ /μL)	1.42±0.82	1.84±0.92	<0.001*
Neutrophile (×10 ³ /μL)	8.42±5.32	6.14±3.84	<0.001*
Thrombocyte (×10 ³ /μL)	246.8±112.4	252.4±108.6	0.286
MPV (fL)	10.6±1.2	10.4±1.1	0.142
NLR	7.86±6.42	4.12±3.86	<0.001*
PLR	248.6±156.4	186.4±112.8	<0.001*
MLR	0.82±0.64	0.58±0.42	<0.001*
MPR	0.046±0.018	0.044±0.016	0.064

WBC: White blood cell; MPV: Mean platelet volume; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; MLR: Monocyte-lymphocyte ratio; MPR: Platelet mean volume/platelet count ratio. *p<0.05.

1.41, p<0.001), chronic renal failure (CRF) (OR: 1.32, 95% CI: 1.21-1.56, p<0.001), PLR (OR: 1.24, 95% CI: 1.16-1.32, p<0.001) and WBC (OR: 1.18, 95% CI: 1.12-1.24, p<0.001). In the ROC analysis, having CRF (AUC: 0.728, sensitivity: 68.2%, specificity: 70.2%) and a history of Ca (AUC: 0.698, sensitivity: 58.2%, specificity: 68.2%), the optimal cut-off value for NLR was 5.2 (AUC: 0.762, sensitivity: 74.6%, specificity: 71.2%). The optimal cut-off value for PLR was determined as 215 (AUC: 0.724, sensitivity: 68.8%, specificity: 69.4%) (Table 3).

Table 3. The results logistical regression and ROC analysis of meaningful parameters in predicting hospitalization needs

Parameter	OR (%95 CI)	AUC	Cut-off	Sensitivity	Specificity
CRF	1.32 (1.21-1.56)	0.728		0.682	0.702
History of cancer	1.24 (1.08-1.35)	0.698		0.582	0.682
NLR	1.32 (1.24-1.41)	0.762	5.2	0.746	0.712
PLR	1.24 (1.16-1.32)	0.724	215	0.688	0.694
WBC	1.18 (1.12-1.24)	0.718	9.8	0.702	0.686
MLR	1.16 (1.08-1.24)	0.682	0.74	0.664	0.658
Lenfosit	0.82 (0.76-0.88)	0.642	1.6	0.624	0.612

OR: Odds ratio; AUC: The area under the curve CI: Confidence interval; CRF: Chronic renal failure; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; WBC: White blood cell; MLR: Monocyte-lymphocyte ratio. *p<0.05.

Platelet counts and MPV values showed no significant differences between the groups ($p>0.05$). Although MPV/platelet ratio was lower in hospitalized patients, this difference did not reach statistical significance ($p=0.064$). Eosinophil values also did not have a significant predictive value for the need for hospitalization ($p=0.128$).

DISCUSSION

The COVID-19 pandemic has created a great burden on healthcare systems with high mortality and complication rates, especially in elderly individuals. In our study, we evaluated the role of hematologic parameters, inflammatory ratios and chronic diseases at admission in predicting the need for hospitalization in COVID-19 patients over 65 years of age. We found that neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), CRF and history of malignancy were strong predictors of hospitalization.

The degree of inflammation in patients with severe COVID-19 plays a key role in determining prognosis. The high WBC, neutrophil, NLR, PLR and MLR values found in the inpatients in our study are consistent with similar studies in the literature. Qin et al.^[5] reported that NLR reflects the severity of inflammation and is an effective tool in predicting poor prognosis. Similarly, Zhou et al.^[6] revealed that PLR reflects inflammatory burden in severe COVID-19 cases. Nile et al.^[7] emphasized that hematologic changes are linked to cytokine storm and predict poor prognosis. The fact that PLR value is also a strong predictive marker (cut-off: 215, sensitivity 68.8%, specificity 69.4%) shows the importance of changes in platelet and lymphocyte counts in reflecting disease severity. The cut-off value of 5.2 for NLR (sensitivity 74.6%, specificity 71.2%) demonstrates the power of this parameter to predict the need for hospitalization.

Lymphopenia is an important marker reflecting the weakness of the immune system against infection in COVID-19 patients. In our study, low lymphocyte levels were associated with inflammatory burden and increased the need for hospitalization. Sun et al.^[2] reported that low lymphocyte levels are an important factor in predicting mortality associated with COVID-19. In addition, lymphopenia is thought to be associated with immune dysregulation that worsens the course of infection^[7]. The fact that the MLR value was significantly higher in inpatients shows the importance of monocyte activation and the associated inflammatory response. In the study by Zhou et al.^[6], the role of monocytes in the pathogenesis of COVID-19 and their relationship with disease severity were examined in detail. In our study, the association of WBC elevation with the need for hospitalization (cut-off: $9.8 \times 10^3/\mu\text{L}$, sensitivity 70.2%, specificity 68.6%) is remarkable. Similarly, Wang et al.^[8] showed a correlation between leukocyte count and disease severity. The findings in

our study suggest that this parameter may also be helpful in clinical evaluation.

Comorbidities play a decisive role in disease prognosis in COVID-19 patients^[2,9]. The study by Huang et al.^[9] revealed that CRF significantly increased the mortality risk in COVID-19 patients^[10]. In addition, Wu et al.'s^[11] report, which included 72,314 patients, states that mortality increases with increasing comorbidity burden. In our study, we found that comorbidities such as malignancy, CRF and hypertension increased the need for hospitalization.

Early evaluation of inflammatory markers in COVID-19 patients is critical to improve prognosis and prevent complications. The NLR and PLR cut-off values determined in our study provide a valuable guide for risk assessment and patient triage. The study by Yang et al.^[10] shows that integrating such thresholds into clinical practice leads to improvements in patient management. Assessing inflammatory markers in the management of COVID-19 can strengthen not only individual patient management but also the overall capacity of health systems. Integration of markers such as NLR and PLR into routine clinical practice may enable more accurate prediction of prognosis and optimization of treatment processes^[12]. Future validation of these markers in different populations will make important contributions to the literature^[13].

The strengths of our study include the high number of patients, its focus on the elderly population and its detailed analysis for hospitalization, which has not been done before; however, the study has some limitations. First, the study was conducted with single-center data and the results may not be generalizable to the entire population. Second, some clinical data may not have been fully evaluated due to the retrospective design. Finally, long-term complications could not be evaluated because long-term follow-up data were not available.

CONCLUSION

The COVID-19 pandemic has placed a huge burden on healthcare systems with high mortality and morbidity rates, especially among the elderly. Our study provides valuable information in predicting the need for hospitalization of hematological parameters, inflammatory rates and chronic diseases in COVID-19 patients over 65 years of age. Especially easy-to-calculate parameters such as NLR and PLR may help in clinical decision-making. It would be useful to confirm these findings in future prospective, multicenter studies.

DECLARATIONS

Ethics Committee Approval: The Kanuni Sultan Suleyman Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 23.07.2020, number: 2020/07.151).

Author Contributions: Concept – BB; Design – BB, RY; Supervision – RY, HM; Data collection and/or processing – RY, MAO; Analysis and/or interpretation – MG, HM; Literature review – MAO, MG; Writing – BB, HM; Critical Review – BB, MAO, MG.

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