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Neutrophil to lymphocyte ratio patterns and the severity of COVID-19: A cross-sectional study

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Short Communication

Abstract

BACKGROUND: The neutrophil-to-lymphocyte ratio (NLR), obtained from a peripheral blood sample, is considered an indicator of subclinical inflammation. The aim of this study was to determine the NLR pattern in the deceased and survivor patients with coronavirus disease 2019 (COVID-19) during hospitalization.

METHODS: This was a cross-sectional analytical study that was performed in Tohid Hospital in Sanandaj, Iran, from March to July 2021. In our study, 30 patients had received the treatments for COVID-19 and did not need to be admitted to the intensive care unit (ICU). They were discharged from the hospital and considered "Group A". Besides, 21 patients who were admitted to the ICU but were discharged were considered "Group B". Finally, 40 patients with COVID-19 who were hospitalized in the ICU and died were considered "Group C". Complete blood count (CBC) test was performed for all patients at 3 different times (at the time of admission, mid-hospitalization, and the last day of hospitalization). In the end, the data were analyzed by one-way analysis of variance (ANOVA) and the Kruskal-Wallis H test.

RESULTS: 91 patients were included in this study. The NLR index during hospitalization in Group C was significantly higher than in Group B and in Group B was significantly higher than in Group A. On the other hand, in Group C, the NLR was significantly increased at three consecutive times during hospitalization; however, in Group B and Group A, at the end of hospitalization, this ratio was lower than in mid-hospitalization.

CONCLUSION: The NLR was an important indicator in predicting patients' prognoses. Pulmonary inflammation in patients with COVID-19 will be accompanied dominantly by neutrophils; thus, the NLR parameter could be important in the progress of the clinical status.

KEYWORDS: COVID-19; SARS-CoV-2; Prognosis; Neutrophil-to-Lymphocyte Ratio; Hematological Parameters

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Introduction

Coronavirus is a single-stranded ribonucleic acid (RNA) virus that can affect the lungs, liver, and nervous system.[1] The disease was first identified in Wuhan, China, and spread rapidly around the world, leading to a global epidemic.[2] The symptoms of the disease are different such as fever, dyspnea, cough, weakness, and lethargy.[3] Several studies have shown that shortness of breath, high respiratory rate, low saturation of oxygen, old age, male gender, and the presence of multiple comorbidities are related to the severity of the disease.[4] In the study by Rose et al., it was concluded that a high level of the neutrophil-to-lymphocyte ratio (NLR) was significantly

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associated with the severity of disease, adverse outcome, and mortality. On the other hand, they concluded that the NLR increased during hospitalization in non-survivors; however, the NLR decreased during hospitalization in the survivors.[5] As a subclinical inflammation parameter, the NLR is considered based on dividing the number of neutrophils by the number of lymphocytes in peripheral blood samples. The NLR is an inflammatory marker predicting the prognosis of several diseases such as tuberculosis (TB).[6] Inflammation plays a key role in the development of coronavirus disease 2019 (COVID-19) and is probably an important factor in its prognosis. We expect inflammatory markers to increase in these patients.[7] One of the cheap and affordable inflammatory indicators is NLR. High NLR can indicate deterioration and prognosis of the disease.[6,8]

We want to answer this question: what is the pattern of NLR during hospitalization in patients with COVID-19 with different outcomes?

Methods

This was a cross-sectional analytical study. This study was performed in Tohid Hospital in Sanandaj as the center of COVID-19 in Kurdistan Province in the west of Iran, in March-July 2021. The study population included patients with COVID-19 in this hospital with positive polymerase chain reaction (PCR) tests with pulmonary involvement. The information of 91 patients including complete blood count (CBC) test, the history of underlying medical disease, age, and gender was collected. Then the patients were divided into three groups (Group A, Group B, and Group C) based on the severity of the disease. Finally, the relationship between the NLR index and the severity of the disease was evaluated in these groups.

30 patients with COVID-19 who were discharged from the hospital after one week without needing to be admitted to the intensive care unit (ICU) were considered "Group A". Besides, 21 patients who were admitted to the ICU but were discharged (rescued) after one week of hospitalization were considered "Group B", and 40 patients with COVID-19 who were hospitalized in the ICU and died were considered "Group C". Convenience sampling was done. The groups were matched for age, sex, and history of underlying medical disease. Exclusion criteria included informed dissatisfaction to participate in the study, outpatient treatment before hospitalization, and hospitalization for less than 7 days. At the beginning of hospitalization (in the emergency department), a CBC test was performed for all patients and the patients were followed up until they were discharged from the hospital or died. The information obtained from the tests at three different times (at the time of admission, mid-hospitalization, and the last day before discharge or death) was recorded in the checklist.

Finally, the data were entered into SPSS statistical software (version 23, IBM Corporation, Armonk, NY, USA), and the normality of quantitative data was checked by the Kolmogorov-Smirnov test. Data were analyzed by one-way analysis of variance (ANOVA) and the Kruskal-Wallis H test. This study was approved by the Ethics Committee of Kurdistan University of Medical Sciences (IR.MUK.REC.1400.048).

Results

In the present study, 91 patients were included in the study, of which 52 (57.1%) were women and 39 (42.9%) were men.

According to table 1, there was no significant relationship between gender and underlying disease history between the 3 groups ($P > 0.05$).

The mean and standard deviation (SD) of the age of the patients in groups A, B, and C were 15.6 ± 60.8, 14.5 ± 63.4, and 18.5 ± 57.4, respectively. On the other hand, the mean and SD of hospitalization in the 3 groups (A, B, and C) were 6.9 ± 1.1, 13.7 ± 7.8, and 13.6 ± 6.6 days, respectively.

Table 1. Sex and underlying medical disease in 3 groups of patients

		Outcome			Total	P
		Group A	Group B	Group C		
Sex	Women	11 (21.2)	22 (42.3)	19 (36.5)	52 (100)	0.70
	Men	10 (25.6)	18 (46.2)	11 (28.2)	39 (100)	
Underlying medical disease	No	4 (21.1)	8 (42.1)	7 (36.8)	19 (100)	0.90
	Yes	17 (23.6)	32 (44.4)	23 (31.9)	72 (100)	

Data are presented as number and percent

According to the one-way ANOVA test, the NLR of patients in three different groups and at 3 different times are shown in table 2.

According to table 2, the NLR in the Group C and in all three times was significantly higher than the Group B, and in the Group B was higher than the Group A ($P < 0.001$).

According to figures 1 and 2, the NLR index during hospitalization in Group C was significantly higher than in Group B and in Group B was significantly higher than in group A. On the other hand, the NLR in Group C was significantly increased at three times of hospitalization, and at the end of hospitalization, the NLR index in the Group A and Group B was lower than mid-hospitalization.

Discussion

The NLR is considered based on dividing the number of neutrophils by the number of lymphocytes in peripheral blood samples and is an inflammatory marker predicting the prognosis of several diseases.[6] Inflammation plays a key role in the development of COVID-19 and its prognosis.[7] During this study, we want to know what is the pattern of NLR during hospitalization in patients with COVID-19 with different outcomes.

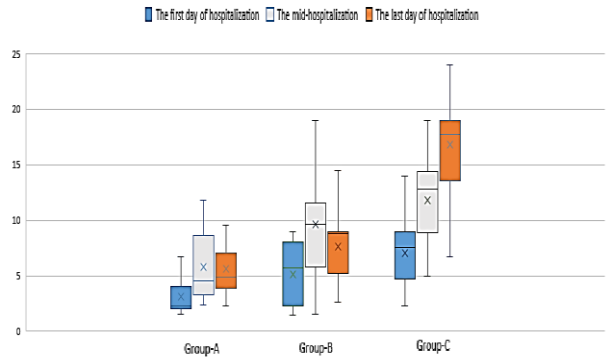

Figure 1. The trend of the neutrophil-to-lymphocyte ratio (NLR) at three different times of hospitalization in three groups of patients with coronavirus disease 2019 (COVID-19) (box and whisker plot)

Table 2. The neutrophil-to-lymphocyte ratio (NLR) in patients with coronavirus disease 2019 (COVID-19) in three different times (at the time of admission, in the middle of hospitalization, and on the last day before discharge or death) in three groups of patients

		N	Mean ± SD	Standard error	95% CI for mean		P
					Lower bound	Upper bound	
The NLR of the first day of hospitalization	Group A	30	3.3 ± 1.8	0.3	2.7	4.0	< 0.001*
	Group B	21	5.8 ± 4.1	0.9	3.9	7.6	
	Group C	40	9.0 ± 7.9	1.2	6.5	11.5	
The NLR of mid hospitalization	Group A	30	5.6 ± 3.4	0.6	4.3	6.9	< 0.001**
	Group B	21	10.7 ± 7.2	1.5	7.4	14.0	
	Group C	40	14.3 ± 8.9	1.4	11.4	17.2	
The NLR of the last day of hospitalization	Group A	30	6.0 ± 3.4	0.6	4.8	7.3	< 0.001*
	Group B	21	9.0 ± 5.2	1.1	6.7	11.4	
	Group C	40	18.7 ± 11.0	1.7	15.1	22.2	

*Kruskal–Wallis H test; **One-way analysis of variance (ANOVA)
CI: Confidence interval; NLR: Neutrophil-to-lymphocyte ratio; SD: Standard deviation

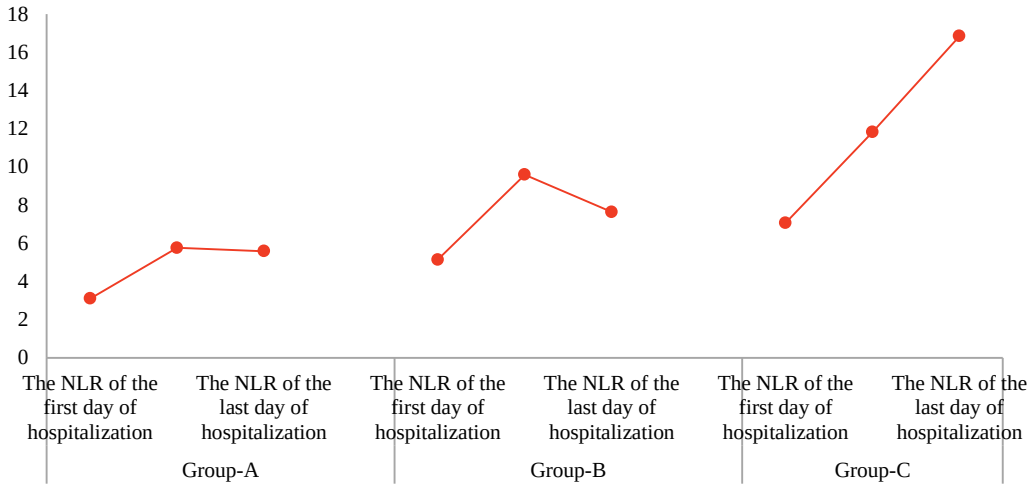

Figure 2. The trend of the neutrophil-to-lymphocyte ratio (NLR) at three different times of hospitalization in three groups of patients with coronavirus disease 2019 (COVID-19) (line with markers chart)

The inflammatory response activates the local innate immunity of the body to further protect against the entry of microorganisms.[9] The innate immune response to respiratory infection causes neutrophils to invade lung tissue, eventually leading to tissue damage, cytotoxicity, and vascular stasis.[10]

High circulating neutrophil levels lead to a decrease in systemic arginine.[11] Arginine produces nitric oxide (NO) and has known antiviral activity against RNA viruses such as severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2).[12]

In our study, patients who were admitted to the hospital with COVID-19 were followed up at 3 different times and the inflammatory index was examined during hospitalization. By doing a CBC test, we concluded that the NLR index during hospitalization in the non-survivor group (Group C) was significantly higher than in the survivor groups (Group A and Group B). On the other hand, in the non-survivor group (Group C), the NLR was significantly increased at 3 different times during the hospitalization.

The results of this study are similar to the results of other studies. For example, a retrospective study by Pirsalehi et al. showed that the NLR value which was greater than 6.5 might reflect the progression toward an adverse clinical outcome and a value of above 9 was leading to death. On the other hand, this ratio showed an increasing trend during hospitalization in their study.[13] This result was similar to our study.

In the study by Tatum et al., 125 patients with COVID-19 in Louisiana Hospital, United States (US), were reviewed and finally, it was concluded that the NLR value which was greater than 4.94 on the first day of admission was a predictor of intubation.[14] Moreover, in the literature study conducted by Chan and Rout, with a total of 3508 patients with COVID-19 in 20 studies, higher NLR was seen in the severe COVID-19 group [standardized mean difference (SMD): 2.8, 95% confidence interval (CI): 2.12-3.48].[15] On the other hand, in a cohort study conducted by Liu et al., 245 patients with COVID-19 were included in study and it was shown that NLR was an independent risk factor for nosocomial mortality in patients with COVID-19, especially men.[16]

Finally, a meta-analysis conducted by Lagunas-Rangel showed that high NLR was associated with severe COVID-19 (SMD: 2.4,

95% CI: 0.98-3.82).[17] It is similar to our results and explains the main purpose of our study too.

In the end, it must be said that one of the limitations of the present study was the small sample size. Therefore, conducting other studies with a bigger sample size than our study and doing changes in the types of the studies are recommended. Besides, researchers can use more criteria in the new future methods.

Conclusion

The results of this study showed that the NLR was an independent predictor of worse outcomes in patients with COVID-19. It may help identify high-risk individuals with COVID-19 infection at admission. Pulmonary inflammation in patients with COVID-19 will be accompanied dominantly by neutrophils; thus, the NLR parameter could be important in the progress of the clinical status. To determine the exact cut point for this index, a study with larger sample size is needed.

Conflict of Interests

Authors have no conflict of interests.

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