ORIGINAL ARTICLE

An Emerging Marker Predicting The Severity of Covid-19: Neutrophil-Lymphocyte Count Ratio

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ABSTRACT

Objective: To assess the efficacy of neutrophil-lymphocyte count ratio in predicting the severity of covid-19

Materials and Methods: The patients with positive results for COVID-19 were shifted to COVID ITC, CMH, Multan. The clinical histories of confirmed patients of COVID-19 during February 2020 to May 2021 were reviewed. The patients were divided into 4 classes, mild, common, severe, and fatal, according to guidelines of COVID-19 i.e., trial version 7. Data was collected regarding age, sex, smoking history, temperature, epidemiological history, clinical symptoms, and laboratory findings of all included patients including NLCR.

Results: The mean NLCR of Mild and Severe Group was 2.77±1.23 and 20.31±4.45, respectively, (p=0.000). (Table. II). The area under the curves of NLCR was larger than neut, suggesting the optimal performance of NLCR with cut-off value 5.89. The sensitivity and specificity of NLCR was 85% and 95%, respectively. (Table. III).

Conclusion: It can be concluded that an increase in NLCR levels can indicate that the covid-19 disease is moving towards exacerbation. NLCR can be recommended as a novel and highly sensitive and specific indicator for severity prediction in Covid-19 patients.

Keywords: Emerging, Marker, Severity, Covid-19, Neutrophils, Lymphocytes, Ratio

INTRODUCTION

In Wuhan, China a number of cases of pneumonia with unknown causes were detected during 2019 by the end of December. The official name of this deadly disease is "COVID-19" according to World Health Organization (WHO).[1] The virus was named by the International Committee on Taxonomy of Viruses (ICTV) as SARS-CoV-2 that stands for severe acute respiratory syndrome coronavirus-2.[2] The routes of transmission of this virus are through respiratory droplets and touch to the infection person/surface.[3–5] Due to easy spreading of the virus, the epidemic spread in other areas of China as well as in the world.[6] This disease, COVID-19 has been constituted in the international concern as public health emergency. Due to more understanding of the disease and experience in the diagnosis and therapy of COVID-19, inflammatory changes in the lungs were confirmed to be the major indication for COVID-19.[7] But, the clinical features, pathogenesis, and pathological changes are still not clear, mainly for patients with long duration of disease, co-morbidities, complicated conditions, and high death rate. Hence, for increasing cure rate and decreasing the clinical morbidity, the early diagnosis of the severe patients is or great importance. In our study, the main focus was age, gender, epidemiological history, smoking history, laboratory indicators of COVID-19 patients, clinical symptoms, in combination with peripheral blood neutrophil to lymphocyte count ratio (NLCR) to explore a suitable, efficient, and practical clinical marker that can forecast severity of COVID-19 in the early phase.

MATERIALS AND METHODS

The patients with symptoms of COVID-19 were admitted and isolated in hospital in Multan Punjab. The samples of throat swabs and blood were collected and sent immediately after collection to the COVID ITC, CMH, Multan. The real-time fluorescence polymerase chain reaction (RT-PCR) or genetic sequence testing were used for preventive testing of COVID-19. One positive result of the above methods of laboratory was used for the diagnosis of COVID-19. The patients with positive results for COVID-19 were shifted to COVID ITC, CMH, Multan. The clinical histories of confirmed patients of COVID-19 during February 2020 to May 2021 were reviewed. The patients were divided into 4 classes, mild, common, severe, and fatal, according to guidelines of COVID-19 i.e., trial version 7.[8]

Covid-19 was classified into different clinical types on the basis of following criteria: patients with no sign of pneumonia on CT chest and with mild symptoms were termed as Mild Type, patients with respiratory symptoms with fever and CT chest showing signs of pneumonia were called as Common Type, patients with respiratory distress i.e., respiratory rate more than 30 breaths per minute or oxygen saturation in blood less than 93% ($SpO_2 < 93\%$) in resting position or SpO_2/FiO_2 less than or equal to 300mmHg were known as Severe type and similarly patients with need for mechanical ventilation due to respiratory failure or other organ failures requiring ICU admission were termed as Fatal type. Mild and common types were grouped into one group i.e., mild group while severe and fatal types were grouped into one group i.e., Severe group. Data was collected regarding age, sex, smoking history, temperature, epidemiological history, clinical symptoms, and laboratory findings of all included patients including NLCR.

All the data collected was statistically analyzed using computer software SPSS version 23. Normally distributed data was analyzed using independent t-test and Mann-Whitney U test. P value of less than or equal to 0.05 was considered as statistically significant.

RESULTS

In this study, n=250 (71.4%) patients included in Mild Group and n=100 (28.6%) patients included in Severe Group. The mean age of Severe Group was greater than the mean age of Mild Group, it suggested that the older age patients had higher risks to suffer severe COVID-19, (p=0.000). There were more females in Severe Group, but the difference was insignificant, (p=0.128). Smoking was also insignificant effect on severity of COVID-19, (P=0.171). There were more complications in Severe Group, (p=0.000). (Table. I).

The mean of WBC was found to be higher in Severe Group than Mild Group 10.74±3.63 (10^9/L) and 4.94±0.92 (10^9/L), respectively, (p=0.000). Neutrophil count and neut (%) was also noted higher in Severe Group than that of Mild Group, (p<0.001). Lymphocyte count in Mild and Severe Groups was 1.61±0.52 (10^9/L) and 0.67±0.41 (10^9/L), (p=0.000). While, the lymphocyte ratio was noted higher in Mild Group than Severe Group, 35.36±5.46 % and 9.74±3.11 %, respectively, (p=0.000). The mean NLCR of Mild and Severe Group was 2.77±1.23 and 20.31±4.45, respectively, (p=0.000). (Table. II).

The area under the curves of NLCR was larger than neut, suggesting the optimal performance of NLCR with cut-off value 5.89. The sensitivity and specificity of NLCR was 85% and 95%, respectively. (Table. III).

Table. I Demographic and baseline variables of the study groups

Variable	Mild Group n=250 (71.4%)	Severe Group n=100 (28.6%)	P-value
Age (years)	41.63±10.94	59.56±9.44	0.000
Gender			
Male	n=130 (52.0%)	n=43 (43.0%)	0.128
Female	n=120 (48.0%)	n=57 (57.0%)	
Smokers	n=42 (16.8%)	n=11 (11.0%)	0.171
Complications	n=78 (31.2%)	n=62 (62.0%)	0.000

Table. II Laboratory indicators of the study groups

Variable	Mild Group n=250 (71.4%)	Severe Group n=100 (28.6%)	P-value
WBC (10^9/L)	4.94±0.92	10.74±3.63	0.000
Neutrophil count (10^9/L)	3.47±0.62	10.51±4.42	0.000
Neut (%)	62.93±12.37	86.74±8.87	0.000
Lymphocyte count (10^9/L)	1.61±0.52	0.67±0.41	0.000
Lymphocyte ratio (%)	35.36±5.46	9.74±3.11	0.000
NLCR	2.77±1.23	20.31±4.45	0.000

Table. III Markers the predicting the severity of COVID-19

Variable	Sensitivity	Specificity	Area under the curve	Cut-off value
NLCR	85%	95%	0.921	5.89
Neut (%)	81%	96%	0.901	77.85

DISCUSSION

Covid-19 has spreaded all over the world. The reported source of infection of Covid-19 is a patient infected with SARS-cov-2, and it is a type of virus which had the potential to spread from asymptomatic patients to almost anyone as no one has the immunity to this virus.[8] In this study we assessed age distribution in covid-19 patients with respect to severity of disease and results show that elderly patients had more severe disease as compared to their younger counterparts.[9-11] The mean and standard deviation of the age among mild and severe covid patients was 41.63±10.94 and 59.56±9.44 years respectively, showing severer disease among elderly. This suggests that management of elderly patients should be focused more as they are more prone to develop severe disease.

The results also showed that lymphocyte count as well as lymphocyte ratio decreased with the increase in the severity of the covid-19 disease. On the other hand, neutrophil count, neutrophil ratio and WBC (white blood cell count) increased with increase in the severity of the covid-19 disease. The difference in levels of lymphocyte, WBC and neutrophil count and lymphocyte and neutrophil ratios was significant among the two groups i.e., mild, and severe patients. This shows that as a result of different stressful events occurring during the inflammatory response of the body to covid-19, the physiological response of the cells of inflammation was characterized by the decrease in the lymphocyte count and increase in the neutrophil count.[12] These indicators differed among mild and severe patients and therefore might indicate poor prognosis in patients with severe Covid-19 disease. Thus, early detection of severity of the covid-19 disease possesses great value in terms of preventing morbidity and increasing the cure rate.

The main focus of our study was to analyze the laboratory indicators i.e., NLCR among all covid-19 patients irrespective of the severity of the disease. Ratio of neutrophil count and lymphocyte count in the peripheral blood is known as NLCR. Neutrophils are primarily involved in the innate immunity while lymphocytes are involved in the adaptive immunity. When combined in the form of NLCR, they are mainly found in serum of the patients with acute inflammation indicating systemic inflammation. Thus, when compared to the sensitivity of lymphocyte count and neutrophil count separately, NLCR is more sensitive in terms of predicting the severity of the covid-19 disease. NLCR has already been used previously in prediction of outcome in patients with severe pneumonia and mortality associated with it.[13-15] The results suggest that elevation in the values of NLCR was associated with poor prognosis as well as increased risk of mortality in covid-19 patients. The current study suggests that NLCR and neutrophil ratio are better in terms of predicting the severity of the covid-19 disease. Moreover, NLCR can be considered as an optimal marker of severity as it has a sensitivity and specificity of 85% and 95% respectively for prediction of severity of covid-19.

Thus, it can be suggested that dynamic monitoring of neutrophil and lymphocyte ratio levels of serum are of utmost importance in order to evaluate the efficacy and condition of the covid-19 patient. Moreover, NLCR has a benefit of being economical and convenient biomarker of inflammation. Thus, NLCR can easily be recommended as early predicting marker of covid-19 for evaluation of severity of the disease.

CONCLUSION

It can be concluded that an increase in NLCR levels can indicate that the covid-19 disease is moving towards exacerbation. Therefore, it is necessary to dynamically monitor these levels which can contribute to evaluation of the severity of the disease. NLCR can be recommended as a novel and highly sensitive and specific indicator for severity prediction in Covid-19 patients.

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