Original Research Article

Predictive accuracy and diagnostic significance of NLR (Neutrophil Lymphocyte Ratio) and D-dimer in COVID-19 patients

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Abstract

Background: COVID-19 is a highly infectious disease that wreaks havoc on the world's healthcare systems. To recognize severe patients, simple and quick risk classification procedures are required. D-Dimer and Neutrophil-Lymphocyte Count Ratio (NLR) as a prognostic utility has shown promising results in patients with COVID-19.**Objectives:** To evaluate the utility of multi-test using D-Dimer and NLR in patients with COVID-19.**Methods:** Two hundred and twenty-seven confirmed cases with COVID-19 infection treated at the study center were studied prospectively. Age, sex, total leukocyte count, neutrophil, lymphocyte, and D-dimer were estimated. NLR was calculated using the values of neutrophils and lymphocytes. Correlation between NLR, D-Dimer was obtained using the Pearson correlation coefficient. **Results:** COVID-19 was more prevalent in the age group of 51-60 years [54 (23.68%)] followed by 61-70 years [53 (23.25%)] and 41-50 years [51 (22.37%)]. Mean age of study cohort was 53.34±14.68 years. COVID-19 was more prevalent in males [156 (68.42%)]. A positive correlation was obtained between age (r=0.319, P<0.001), total count ((r=0.621, P<0.001), neutrophil (r=0.801, P<0.001) and D-Dimer (r=0.426, P<0.001) with NLR whereas negative correlation was observed with lymphocyte (r=-0.805, P<0.001) for NLR. **Conclusion:** Multi-tests of D-Dimer and NLR were more beneficial than single tests in treating patients with COVID-19 infection.

Keywords: pneumonia, SARS-CoV2 viruses, Neutrophil-Lymphocyte Count Ratio, D-Dimer

Introduction

Several instances of pneumonia of unclear cause were recorded in Wuhan, Hubei province, China, in early December 2019[1]. The Chinese Center for Disease Control and Prevention (CDC) discovered a novel beta-coronavirus from a patient's throat swab sample using high-throughput sequencing on January 7, 2020.[2].The sickness has been dubbed the 2019-novel coronavirus disease (COVID-19) by the World Health Organization because it mimics the severe acute respiratory syndrome coronavirus (SARS-CoV) (WHO)[3,4].The high pathogenicity of SARS-CoV2 viruses has yet to be fully elucidated. Infectious disorders are complicated by inflammation. Inflammation has a vital role in the evolution of viral pneumonia, notably in cases of coronavirus disease 2019 (COVID-19). Patients with pulmonary inflammation have been demonstrated to have higher levels of pro-inflammatory cytokines in their blood. WBC count, neutrophil count, lymphocyte count, neutrophil/lymphocyte ratio (NLR), and platelet/lymphocyte ratio (PLR) are all indicators of systemic inflammation. These markers can help predict the prognosis and follow-up of viral pneumonia patients[5-7].NLR is a beneficial, quick, and low-cost biomarker whose importance has been demonstrated in bacterial pneumonia and viral infections.[8].Thus, we wondered that whether NLR might be a potential predictor for the critical illness of COVID-19. Hence, the present study we evaluated the predictive accuracy and diagnostic significance of NLR and D-dimer in COVID-19 patients.

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Methods

This study was a retrospective single-center study, which included 227 patients with COVID-19 infection treated at the study center from the study duration. Institutional Ethics Committee approval was obtained before starting the study (approval no: GMERC/MCG/IEC (HR)/Approval/2962/2021; Date 15 April 2021).Confirmed cases of COVID-19 (those were positive for the SARS-CoV-2 PCR test), which was diagnosed based on the new coronavirus pneumonia diagnosis and a treatment plan developed by the Indian Council of Medical Research Delhi, were included. Those with primary infection by the influenza virus, parainfluenza virus, adenovirus, respiratory syncytial virus, rhinovirus, human metapneumovirus, SARS coronavirus, mycoplasma, chlamydia, and bacteria were excluded. Demographic details, including age and sex, were recorded. In laboratory parameters, total leukocyte count, neutrophil, lymphocyte, and D-dimer were estimated. NLR was calculated using the values of neutrophils and lymphocytes.

All the data analysis was performed using IBM SPSS ver. Software. Cross tabulation and frequency distribution were performed to prepare the tables. PRISM software was used to prepare graphs. Quantitative data were expressed as mean and standard deviation, and categorical data were expressed as numbers and percentages. One-way ANOVA was used to compare the means. Pearson correlation was performed to obtain the correlation between the variables. Multiple regression analysis was performed to obtain the odds ratio. The level of significance was assessed at 5%.

Results

COVID-19 was more prevalent in the age group of 51-60 years [54 (23.68%)] followed by 61-70 years [53 (23.25%)] and 41-50 years [51 (22.37%)].Mean age of study cohort was 53.34±14.68 years. COVID-19 was more prevalent in males [156 (68.42%)] than females [72 (31.58%)].

Table 1: Descriptive analysis of study cohort

Parameter	Minimum	Maximum	Mean	Std. Deviation
Age	14	83	53.18	14.904
Total Count	2400	47600	9914.47	6755.759
Neutrophil	36	93	68.52	14.352
Lymphocyte	3	54	23.38	12.676
NLR	.7	31.0	4.809	4.3343
D-dimer	.00	15.02	1.8092	2.85016

No significant difference was obtained in NLR between males (4.731±4.3) and females (4.978±4.2) (p=0.691).

Table 2: Comparing NLR between the different age groups.

Age group	Mean NLR	N	Std. Deviation	P-value
11-20	2.600	3	1.9975	<0.001
21-30	2.467	15	2.4055	
31-40	3.236	28	3.0109	
41-50	4.294	51	3.5323	
51-60	4.100	54	3.0318	
61-70	6.717	53	6.0482	
71-80	6.523	22	3.7033	
>80	10.600	2	9.8995	
Total	4.809	228	4.3343	

Table 3: Pearson correlation showing the association between NLR and other parameters.

		NLR
Age	Pearson Correlation co-efficient (r)	0.319
	Sig. (2-tailed)	<0.001
Total Count	Pearson Correlation co-efficient (r)	0.621
	Sig. (2-tailed)	<0.001
Neutrophil	Pearson Correlation co-efficient (r)	0.801
	Sig. (2-tailed)	<0.001
Lymphocyte	Pearson Correlation co-efficient (r)	-0.805
	Sig. (2-tailed)	<0.001
D-dimer	Pearson Correlation co-efficient (r)	0.426
	Sig. (2-tailed)	<0.001

Discussion

The number of people infected with COVID-19 is rapidly rising worldwide, putting a strain on healthcare systems, particularly ICU bed availability. As a result, early discovery of severe instances is critical for patient triage. While COVID-19 patients' clinical presentation, concomitant comorbidities, amount of radiographic infiltration, and blood oxygen saturation may signal the necessity for ICU admission, various laboratory indicators may aid in assessing disease severity[9].COVID-19 has an increased risk of severe disease and mortality in older persons, according to current studies. It is also well known that many diseases do not manifest themselves in older persons. In the present research, COVID-19 was more prevalent in 51-60 years, followed by 61-70 years. The mean age of patients with COVID-19 was 53.34±14.68 years. COVID-19 was more prevalent in males. In line with that, Unim et al. studied 3241 confirmed cases of COVID-19-related deaths and reported that Symptoms in older persons are often atypical, and they may be asymptomatic. This could cause a diagnostic and treatment lag, worsening COVID-19's prognosis. When evaluating people aged 65 and up suspected of having COVID-19, more care should be used[10].

The NLR is a rapid and easy-to-use marker of systemic inflammation that predicts prognosis in various clinical situations[11].In community-acquired pneumonia, NLR was recently reported to have more predictive potential than standard infection markers as CRP, white blood cell count, and neutrophil count[12].The overall number of leukocytes in peripheral blood is normal or decreases early in COVID-19, whereas the lymphocyte count decreases[13].However, how the lymphocyte count varies as the disease proceeds is unknown. In the present study, we evaluated the role of NLR and compared its association with demographic parameters. There was a significant positive correlation obtained between age and NLR. An increasing trend was noted with the growing age of COVID-19 patients. A rise in NLR indicates a gradual increase in neutrophils and a decrease in lymphocytes. An increase in neutrophils often suggests that the patient is suffering from a bacterial infection that is worsening. The loss of lymphocytes indicates a weakened immune system[11].These suggest that the infection has worsened and is tough to control. In general, COVID-19 individuals with elevated NLR should be monitored because they may have a bad prognosis or possibly be in danger of death.D-Dimer is a breakdown product formed during fibrin hydrolysis. It could reflect how infection affects coagulation in infectious disorders. According to previous research, an increase in D-dimer levels in patients with pneumonia indicates a hypercoagulable state of the blood and the existence of thrombosis[13]. The D-Dimer of COVID-19-infected critically ill individuals was significantly higher, with frequent clotting abnormalities and microthrombotic development in peripheral blood vessels[14].We explored not only the single D-Dimer value but its correlation with another biomarker NLR. A significant positive correlation was obtained between D-dimer and NLR. An increasing trend was noted with increasing D-dimer in COVID-19 patients.Tang et al., in a similar report, found that increased prothrombin time and D-dimer readings in severe COVID-19 patients may also be markers of a worse prognosis, explained by dysregulated coagulopathy[15].Furthermore, D-dimer levels are associated with disease severity and are a reliable predictive predictor for hospital mortality in COVID-19 patients admitted to the hospital. The increased D-dimer levels in SARS-COV-2 infection indicate a hyperfibrinolysis condition and a higher inflammatory burden. The optimal D-dimer level for predicting poor prognosis has been shown to range from > 1 mg/L [8] to > 2.14 mg/L[16].There were some limitations to the current study. A small number of patients only met the inclusion criteria. All laboratory values were gathered at admission, but there was no evaluation of follow-up data or linear changes connected to the patients' clinical status. Other biomarkers

such as IL-6 level, LDH, CK-MB, troponin, and procalcitonin were not investigated because we concentrated on the simplest and most cost-effective investigations.To conclude, due to greater D-Dimer and NLR values in perished patients than in the survival group, multi-tests of D-Dimer and NLR were more beneficial than single tests in treating patients with COVID-19 infection. To give a viable treatment for COVID-19 infection and lower mortality, more research is needed to determine the etiology of D-Dimer and NLR alterations.

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