Section: General Medicine

Original Research Article

SIGNIFICANCE OF NEUTROPHIL TO LYMPHOCYTE RATIO AND PLATELET TO LYMPHOCYTE RATIO FOR PREDICTING CLINICAL OUTCOME AND SEVERITY IN COVID-19 PATIENTS ADMITTED IN IN A TERTIARY CARE HOSPITAL

Mohammad Shan Ansari[1], Raju H Badiger[2], Harsha G[3], Kruthik G[4]

[1]Senior Resident, Department of General Medicine, AIIMS, New Delhi, India
[2]Professor, Department of General Medicine, JNMC, Belagavi, Karnataka, India
[3]3rd Year PG Resident, Department of General Medicine, Safdarjung Hospital, New Delhi, India
[4]Senior Resident, Apollo Hospital, Mysuru, Karnataka, India

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Corresponding Author:
Dr. Raju H Badiger,
Email: vishwasbadiger14@gmail.com

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Abstract

Background: The coronavirus disease-2019 (COVID-19) has a very diverse presenting spectrum, ranging from no symptoms to severe illness. Even though there is an extensive list of predictors of disease severity, neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are more appropriate due to their affordability and simplicity. So, this study was planned to assess their significance for predicting clinical outcome and severity of the disease. **Materials and Methods:** The present study was a hospital based observational cross-sectional study carried on the COVID-19 patients. A detailed demographic and clinical history of the patients was assessed along with basic laboratory analysis. Further, NLR and PLR were calculated in accordance with the CBC results. Patients were divided into severe and mild cases based on clinical picture and test results. The data was analysed using SPSS v21 and for all the tests the value of p less than 5% (0.05) was considered significant. **Result:** The present study included 135 COVID-19 patients with mean age of 58.20±15.20yrs and range of 24-102years. The majority of the patients were from the age group of 40-59years. The study's male to female ratio was 3.21:1, indicating a preponderance of men. Maximum of the patients presented to the hospital had breathlessness and diabetes mellitus. NLR and PLR were higher in COVID-19 patients and both ratios could forecast the severity of the disease and were able to discern the disease's outcome. The majority of the patients exhibited PLR between 10-20 and NLR between 5-10. **Conclusion:** COVID-19 is a fast spreading virus with a wide range of clinical indications. In present study, the much elevated NLR and PLR values show that these markers have a high predictive value for both worsening clinical outcomes and disease progression. The metrics NLR and PLR are readily measured, available, reasonably priced, and dependable. So can be utilized for ongoing monitoring, which may aid in forecasting the course of COVID-19 treatment.

INTRODUCTION

Wuhan, China, in December 2019, experienced an unexplained pneumonia,[1] identified as Corona virus or COVID-19 by World Health Organization (WHO).[2] The WHO has proclaimed COVID-19 to be a pandemic.[3] Over 1.7 million people have died and over 79 million individuals have been infected globally.[3,4] Acute respiratory distress syndrome (ARDS) has been brought on by this recently discovered virus.[5] The presenting spectrum of COVID-19 is diverse, ranging from no symptoms to severe illness necessitating critical care.[5,6] According to data, 4.3% of patients died and 26% of patients required intensive care unit (ICU) care.[7] More than 14% of those infected, experienced severe disease with dyspnea, tachypnea, and desaturation that required hospitalization and oxygen supplementation.[8] The majority of infections are either asymptomatic or show mild to moderate symptoms such as fever, exhaustion, and dry cough. Therefore, in order to slow or stop the disease's course, it is imperative to investigate potential risk factors for the severity of COVID-19. Manifested risk factors for severe sickness include male sex, obesity, heart failure, and advanced age,[9] abnormal immune-inflammatory response may also be a significant component in the course of the disease.[10]

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In addition to reducing patient mortality and severity, early clinical detection and treatment of COVID-19 may also assist stop the virus's transmission. Despite all the precautions, it is still difficult to diagnose COVID-19 patients at an early stage and to estimate its severity and fatality. Numerous methods, like as hemogram and biochemical analysis, are being employed to help in the early diagnosis and prognosis of COVID-19. White blood cell count (WBC count), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and even some biochemical markers like c-reactive protein (CRP) and lactate dehydrogenase (LDH) have been used independently to predict prognosis in systemic inflammatory conditions.[11] Both NLR and PLR could be employed as prognostic variables for the disease. Even though there is an extensive list of predictors of severe COVID-19 illness, these markers are more appropriate for low-resource establishments and third-world nations due to their affordability and simplicity. The management and consequently the course of the disease depend critically on the prompt detection of these markers. Up until recently, there was limited research demonstrating that high NLR could be a predictor of COVID-19 patients' severity and unfavorable fate.[12,13] Research has demonstrated that individuals with severe Covid-19 infection had different CBC findings—such as neutrophilia, lymphopenia, and thrombocytopenia—than those with non-severe Covid-19 infection. At presentation, patients with severe COVID-19 had greater neutrophil counts, lower lymphocyte percentages, and higher lymphocyte counts, all of which suggested a high viral load and weakened immune systems. It has been verified that lymphopenia is a symptom of severe COVID-19.[5,14] According to several research, NLR and PLR are higher in patients with severity. Till now, very limited research has been done to compare NLR and PLR in predicting the disease outcome and severity. So, this study was planned to compare the clinical characteristics, NLR, and PLR, and to connect the same with the severity of COVID-19 infection.

MATERIALS AND METHODS

The present study was a hospital based observational cross sectional study carried on the COVID-19 patients admitted at KLE's Dr. Prabhakar Kore Hospital and MRC, Belagavi for a period of around one year. A total of 135 patients diagnosed with COVID-19, who were willing to participate with age above 18years were enrolled in the study. Patients diagnosed with tuberculosis, neoplasms and age below 18years were excluded from the study. Ethical clearance was obtained from the Institutional Ethical Committee and informed consent was taken from all the participants. The participants were diagnosed COVID-19 positive by a specialist on the basis of the real time reverse transcriptase polymerase chain reaction (RT-PCR) report and chest computed tomography (CT) report. A detailed demographic and clinical history of the patients was assessed and documented. Following the standard aseptic protocol, venous blood was drawn from the patient and sent for basic laboratory analysis like complete blood counts including neutrophil count; lymphocyte count platelets count, PT/INR renal function tests. Further, NLR and PLR were calculated in accordance with the CBC results. Patients were divided into severe and mild cases based on the clinical picture and test results of the patients. Between non-severe and severe patients, data on epidemiology, symptoms, signs, laboratory tests, chest computed tomography (CT) scans, and available treatments were gathered and compared.

Mean and standard deviation for the continuous quantitative variables were calculated and comparison was done using Student's unpaired t-test. The pre and post treatment measures were compared using student's paired t test. Discrete variables were represented by median. The categorical data were expressed in terms of rates, ratios and percentages. The association between the outcome, clinical and demographic characteristics were tested using Chi-square test, test of proportion or Fisher's exact test. For discrete variables non-parametric tests were used. For all the tests the value of p less than 5% (0.05) was considered significant and all the data was analysed using SPSS v21.

RESULTS

In the present study, the mean age of patients was found to be 58.20±15.20yrs with the range of 24-102years. As depicted in table 1, the majority of the patients were from the age group of 40-59years followed by 60-79years, 20-39years and >80years with 54(40.00%), 53(39.26%), 17(12.59%) and 11(8.14%) patients respectively.

[Figure 1] shows that, there was male preponderance with 103(76.3%) and female 32(23.70%) with male to female ratio of 3.21:1.

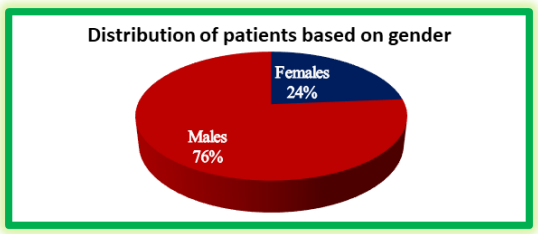

Figure 1: Distribution of patients based on gender

[Table 2] shows the symptoms presented by the patients at the time of hospital visit. Maximum of the patients suffered breathlessness with 107(79.26%) cases followed by cough, fever and myalgias with 88(65.18%), 79(58.52%) and 17(12.59%) cases. Other symptoms like altered sensation, abdomen pain, chest pain, drowsiness, vomiting, facial swelling, headache, hemoptysis, loss of appetite, restlessness and right eye swelling from 5days were

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observed in 14(10.37%) patients. None of the symptoms were seen in 3(2.22%) patients.

[Figure 2] illustrates the associated co-morbidities observed in the COVID-19 patients of our study. Mainly patients had diabetes mellitus followed by hypertension, chronic kidney disease, ischemic heart disease, thyroid disorder and asthma in 59(43.70%), 56(41.48%), 9(6.66%), 5(3.70%), 3(2.22%) and 2(1.48%) patients respectively.

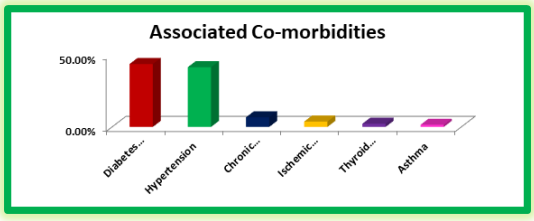

Figure 2: Distribution of patients based on the associated co-morbidities

[Table 3] depicts mean±SD and range of the parameters. Mean±SD of the duration of hospital stay, creatinine, bilirubin, SGOT, SGPT, SPO2, neutrophil, lymphocyte, platelet, NLR, PLR was observed as 6.62±6.52days, 1.93±3.01mg/dl, 0.63±0.51mg/dl, 57.35±40.80U/L, 65.45±161.75U/L, 76.66±31.16%, 84.71±9.35%, 10.10±7.71%, 358.95±284.42%, 14.98±11.61 and 35.54±36.89 and range was 0-42days, 0.41-21.74mg/dl, 0.14-3.32mgdl, 6.1-273U/L, 10-1265U/L, 0.5-100%, 57-97%, 2-34%, 90-690%, 1.71-48.5 and 0.09-185.5 respectively.

As visible from [Table 4] that NLR of many i.e. 48(35.56%) patients could not be recorded and the maximum patients i.e. 29(21.48%) had NLR around 5-10 followed by NLR <5, 30-35, 10-15, 15-20, 20-25 and ≥35 in 13(9.63%), 12(8.89%), 11(8.15%), 10(7.41%), 8(5.93%) and 4(2.96%) patients respectively. None of the patient had NLR between 25-30.

Further [Table 5] shows PLR of the patients. PLR also of many patients i.e. 51(37.78%) could not be recorded and the mainly patients i.e. 21(15.56%) had PLR between 10-20 followed by PLR of 0-10, 20-30, ≥90 and 30-40 with 17(12.59%), 16(11.85%), 8(5.93%) and 6(4.44%) patients respectively. 5(3.70%) cases had PLR between 60-70 and 70-80 followed by 2(1.48%) patients who had PLR from 40-50 and 50-60.

Table 1: Distribution of patients based on their age.

Age in years	n(%)
20-39	17(12.59%)
40-59	54(40.00%)
60-79	53(39.26%)
≥80	11(8.14%)

Table 2: Distribution of patients based on the symptoms

Symptoms	n(%)
Cough	88(65.18%)
Fever	79(58.52%)
Breathlessness	107(79.26%)
Myalgias	17(12.59%)
Loss of taste	1(0.74%)
Loss of smell	1(0.74%)
Others	14(10.37%)
Nil	3(2.22%)

Table 3: Mean and Range of the parameters of the study participants

Parameter	Mean±SD	Range
Duration of hospital stay (days)	6.62±6.52	0-42
Creatinine (mg/dl)	1.93±3.01	0.41-21.74
Bilirubin (mg/dl)	0.63±0.51	0.14-3.32
SGOT (U/L)	57.35±40.80	6.1-273
SGPT (U/L)	65.45±161.75	10-1265
SPO2 (%)	76.66±31.16	0.5-100
Neutrophil	84.71±9.35	57-97
Lymphocyte	10.10±7.71	2-34
Platelet	358.95±284.42	90-690
NLR	14.98±11.61	1.71-48.5
PLR	35.54±36.89	0.09-185.5

Table 4: Distribution of patients based on their NLR.

NLR	n(%)
<5	13(9.63%)
5-10	29(21.48%)
10-15	11(8.15%)
15-20	10(7.41%)
20-25	8(5.93%)
25-30	0(0.00%)
30-35	12(8.89%)
≥35	4(2.96%)

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NR	48(35.56%)

Table 5: Distribution of patients based on their PLR.

PLR	n(%)
0-10	17(12.59%)
10-20	21(15.56%)
20-30	16(11.85%)
30-40	6(4.44%)
40-50	2(1.48%)
50-60	2(1.48%)
60-70	5(3.70%)
70-80	5(3.70%)
80-90	2(1.48%)
≥90	8(5.93%)
NR	51(37.78%)

DISCUSSION

The COVID-19 pandemic has raised many concerns in the modern era and jeopardized the security of public health around the world. Since COVID-19 has spread quickly over the world and no viable treatment has yet been found, medical practitioners are looking for an appropriate prognostic marker. Biomarkers that can shed light on the course, prognosis, and severity of the disease are crucial in such a situation. Therefore in this study, we have assessed the significance of NLR and PLR as prognostic markers in predicting COVID-19 patients' severity and mortality. In the present study, the mean age of patients was 58.20±15.20yrs, majority were in age of 50-80yrs. There was male preponderance with 76.3% and female 23.70% with male to female ratio of 3.21:1. This findings is supported by Singh Y et al,[15] and Erika Asperges et al,[16] as they also found male dominance and nearly same mean age but the study by Shaoping Huang et al,[17] is in disagreement with our study as mean age in their study was 44(30-61) years. The creatinine was 1.93mg/dl, bilirubin was 0.63mg/dl and SGOT and SGPT were in the normal range in our study with mean duration of hospital stay to be 6.62±6.52days. This study found that COVID-19 patients had a considerable thrombocytopenia, significantly higher neutrophil counts, and significantly reduced lymphocyte counts. Additionally, COVID-19 patients had considerably greater PLR and NLR. According to a study by Qu R et al., patients who experienced platelet peaks during therapy had lengthier average hospital stays than patients who did not.[10] A study by Seyit M. et al. also found a favourable relationship between hospital stay duration and NLR.[12] In present study, breathlessness, cough and fever were the most common symptoms presented by the patients. Demirkol ME et al., documented similar findings as of our study with fever, cough and dyspnea as the common symptoms.[18] The associated co-morbidities observed in the COVID-19 patients of our study were mainly diabetes mellitus and hypertension. This outcome is in harmony with the study by Huang S et al., as they observed that severe COVID-19 patients had more co morbidities like hypertension and diabetes than the non-severe patients.[19]

According to the severity of COVID-19 patients, our study showed greater mean levels of NLR and PLR in these patients. A study that found a substantial difference in PLR and NLR between patients classified as severe and those classified as non-severe strongly supports this finding, suggesting that measuring PLR and NLR could help identify high-risk individuals with COVID-19.[19] According to recent research, the NLR was higher in severe cases compared to non-severe cases.[20,21] In their study, Liu et al. also discovered that NLR was an independent risk factor for in-hospital mortality. They also suggested that identifying high-risk individuals might be facilitated by properly assessing NLR in COVID-19 patients.[20] Patients who were in critical condition also had a significantly higher NLR, according to a meta-analysis that merged data from five trials.[22] In a similar vein, Yang et al. also discovered that NLR serves as a good prognostic and predictive marker for COVID-19 patients.[23] Few other additional studies also demonstrated a link between NLR and illness severity agreeing with our findings.[21,23,24] In our research, patients with COVID-19 showed a marked thrombocytopenia. Additionally, we discovered that severe patients had higher PLR than non-severe patients. This result is consistent with the research conducted by Eslamijouybari M et al,[25] however, PLR in their study did not correlate with the severity of the condition, and no meaningful correlation was discovered between PLR and severity of the disease.[25] On plotting NLR and PLR from admission to post-discharge, four Chinese studies found trends that matched ours: patients with non-severe disease had constant, lower values, whereas patients with severe disease had higher, increasing values.[10,26-28] Simple to measure, widely available, affordable, and reliable, NLR and PLR are metrics whose ongoing monitoring may help in COVID-19 diagnosis and treatment.[29] Our research demonstrates that the prognosis and progress of the disease in COVID-19 patients may be predicted using this straightforward and readily available metric. In order to identify high risk COVID-19 patients, we should pay attention to these laboratory data as NLR

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and PLR may be readily computed based on a normal blood test upon arrival. We demonstrated that NLR and PLR can discriminate between COVID-19 patients with mild to moderate illness and those with severe symptoms.

CONCLUSION

COVID-19 is a fast spreading virus with a wide range of clinical indications. In present study, the number of comorbid conditions and the haematological parameters are connected to the severity of the disease. When compared to other indicators, the patients' mean NLR and PLR levels were higher. The much elevated NLR and PLR values at the time of admission show that these markers have a high predictive value for both worsening clinical outcomes and disease progression. So, our research demonstrates that NLR and PLR are able to differentiate between ventilation demand, death, and ICU admission, and that their trend corresponds with the degree of the illness. The metrics NLR and PLR are readily measured, available, reasonably priced, and dependable. They can be utilized for ongoing monitoring, which may aid in forecasting the course of COVID-19 treatment. Early patient stratification can be facilitated by it, allowing patients with greater NLR and PLR to get higher-level critical and supportive care.

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