



Research Article

Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio as Prognostic Biomarkers of Mortality in Severe Covid-19 Patients: An Observational Study

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Abstract

Background: Since January 2020, there has been more than 420 thousand deaths in India. This study aims to determine the utility of Neutrophil-to-lymphocyte ratio (NLR) and Platelet-to-Lymphocyte ratio (PLR) as a marker of mortality in hospitalized COVID-19 patients.

Methods: In a retrospective study, we collected data from 73 hospitalized patients who were diagnosed with Covid-19 in HDU, Midnapore Medical College and Hospital. Patients were categorized into survivor group and death group based on the outcome.

Results: There was a significant positive correlation of NLR ($p < 0.001$) and PLR ($p = 0.025$) with COVID-19 deaths. The calculated AUC using ROC for NLR and PLR was 0.728 and 0.744 respectively, which is highly suggestive of NLR and PLR as a marker in determining mortality in severe COVID-19 infection.

Conclusion: NLR and PLR can be used as a convenient, rapidly available and cost-effective prognostic biomarker in severe covid-19 patients.

Keywords: COVID-19, Neutrophil-to-Lymphocyte ratio (NLR), Platelet-to-Lymphocyte ratio (PLR), Prognostic marker

Introduction

In late December 2019 and January 2020, a novel CoV (2019-nCoV) was isolated from clusters of patients with pneumonia of unknown cause in Wuhan, Hubei Province, China [1]. The illness likely to have been caused by this CoV was named “novel coronavirus-infected pneumonia” (NCIP). The COVID-19 has then rapidly spread to all over the world [2]. On January 2020, the World Health Organization (WHO) declared the emergence of the novel coronavirus a public health emergency of international concern [3].

On January 2020, the first confirmed case of COVID-19 infection was reported in India [4]. As of July 2021, there has been more than 30 million COVID-19 cases and 420 thousand deaths in India [5]. More importantly, the explosive nature of the second wave has put the health infrastructure under pressure, making hospitalization possible for only more severe patients, which could also explain the higher mortality among the hospitalized patients [6]. So it is imperative to find a convenient and objective index to detect critical patients at an early stage to effectively allocate med-

ical resources and divert attention to patients with poorer prognosis.

There has been reports of neutrophilia and lymphopenia in hospitalized COVID-19 patients [7,8]. Many studies regarding immune-inflammatory parameters in COVID-19 infection concluded that neutrophil/lymphocyte ratio is associated with the progression of the infection and thus can be considered as an independent marker for poor clinical outcomes in COVID-19 infection [9-12]. There has been studies which demonstrated the elevated platelet/lymphocyte ratio as a prognostic indicator of severity in COVID-19 patients [13,14].

Our study aims to review the prognostic value of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) to determine the mortality in severe COVID-19 infection.

Methodology

This was a retrospective, single-centred and observational study conducted at HDU, Midnapore Medical College and Hospital, Peschim Medinipur,

West Bengal, India from 1st July, 2021 to 21st July, 2021. Written informed consent was waived by the Institutional Research Committee of Midnapore Medical College and Hospital.

We included adult patients (>18 years old) with confirmed severe COVID-19 (diagnosed using RT-PCR assay) infection. Severe COVID-19 was defined as patients that met any of the following criteria: (i) Respiratory rate > 30/min (ii) SpO₂ < 90% on room air. Patients who were referred for hematological ailments were excluded from the study. We screened a total of 80 patients and 73 patients were found to be eligible and enrolled in the study and they were segregated into 2 groups based on the clinical outcome: Survivor group (n=29) and Death group (n=44).

Clinical data includes demographic information (age, gender, time of admission, time of discharge, comorbidities), medical history, laboratory tests (routine blood tests) and outcome (survival or death at hospital discharge). We collected the complete results of these tests and calculated for Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR).

Statistical Analysis

Data were coded and analyzed using Statistical Package for Social Sciences (SPSS) version 28. Data was summarized using mean and standard deviation in quantitative data and using frequency for categorical data. Pearson test was used for linear correlation and Spearman test for rank correlation. Z test was used for the area under Receiver Operating Characteristic (ROC) curve comparison. P-values of less than 0.05 were considered as statistically significant.

Results

A total of 73 patients were enrolled in the study, out of whom 29 patients were in the Survivor group and 44 patients in the Death group. The average age of the patients in the survivor group was 50.21 ± 2.77 (47-53 years) with 22 males and 7 females and the average age in the death group was 55.86 ± 2.45 (53-58 years) with 24 males and 20 females. The differences in age and gender between the two groups were not found to be statistically significant.

Table 1: Correlation of comorbidities in the 2 groups

COMORBIDITIES	SURVIVOR GROUP (n=29)	DEATH GROUP (n=44)	P value
Diabetes	3	12	0.082
Hypertension	8	15	0.239
Hypothyroidism	1	5	0.231
Seizure disorder	1	1	0.248

As presented in Table 1, the difference in the prevalence of diabetes, hypertension and other comorbidities between the 2 groups was not statistically significant (p > 0.05).

The formula used for calculations are:

1. NLR = Absolute number of neutrophils/Absolute number of lymphocytes.
2. PLR = Absolute platelet count/Absolute number of lymphocytes.

However, correlation analysis showed that NLR and PLR had a significant correlation with the clinical outcome as shown in Table 2 (p<0.05).

Table 2: Mean Laboratory results in the 2 groups

BLOOD TESTS	SURVIVOR GROUP (n=29)	DEATH GROUP (n=44)	P value
NLR	4.76 ± 3.491	7.59 ± 3.712	<0.001
PLR	77.23 ± 16.44	108.5 ± 6.66	0.025

The receiver operating characteristic (ROC) curves of the NLR and PLR for predicting mortality in COVID-19 patients are presented in Figure 1. The PLR had a higher area under the curve (AUC) of 0.744 compared to AUC of NLR of 0.728, which shows that the PLR is a better predictor of mortality than NLR.

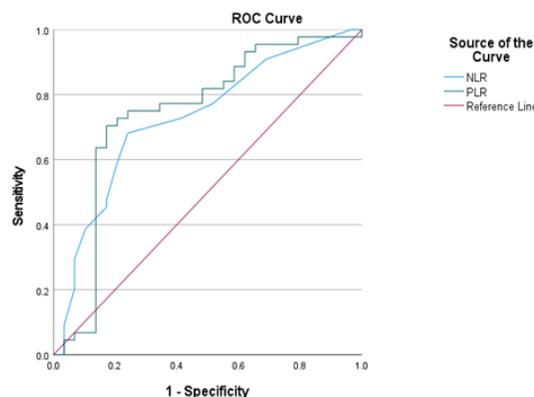


Figure 1: NLR and PLR prediction of COVID-19 deaths

Discussion

We infer from the results of the study that there was a significant difference in NLR and PLR between survivor group and death group COVID-19 patients with death group patients tending to have significantly higher NLR and PLR.

These findings are consistent with Imran et al., Wang et al., Ye et al., which concluded the association of higher NLR with poor prognosis in COVID-19 infection [9,11,12]. Our results also bolster the studies of Qu et al., Simadibrata et al., suggesting that the change in the novel biomarker PLR could reflect the disease progression and prognosis of COVID-19 patients [13,14].

The pathogenesis of COVID-19 has not been completely understood. Many studies have shown that the increased amounts of proinflammatory cytokines in serum was associated with extensive lung damage in SARS patients and suggests that the cytokine storm was associated with disease severity [8]. There has been reports of pronounced lymphopenia and neutrophilia in COVID-19 patients [12,15]. Broad range of cytokines are associated with pro-megakaryopoietic activity. In addition, the proinflammatory cytokine IL-6 has been shown to enhance hepatic Tpo expression, contributing to platelet production. These findings in peripheral blood suggested a role of dysregulated immune responses in the pathogenesis of COVID-19 which is associated with high mortality [16,17].

Our study also has limitations being a single-centered and retrospective study with a small sample, so further studies addressing these issues are warranted to validate our data.

Hence, we conclude that NLR and PLR may serve as a convenient, cost-effective and readily available prognostic biomarker in severe COVID-19 infection. These markers allow the clinicians to stratify patients into differ-

ent prognostic categories at an early stage and institute active and effective treatment that would help to curb the mortality rate.

Disclosure

The authors report no conflicts of interest for this work.

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