



## **Immuno-Haematological Markers to Predict Outcome in COVID -19 Hospitalized Patients**

<sup>1</sup>Dr. Anurag Yadav, Department of Biochemistry, Assistant Professor, MNR Medical Collage & Hospital, Sangareddy, Telangana, India

<sup>2</sup>Dr. Nanda Kumar LG, Department of Physiology, Professor, MNR Medical College & Hospital, Sangareddy, Telangana, India

<sup>3</sup>Dr. Golla Anmol Manaswini Yadav, Department of General Medicine, Junior Resident, Malla Reddy Institute of Medical Sciences, Hyderabad, Telangana, India

<sup>4</sup>Dr. Karveri Karewad, Department of Physiology, Assistant Professor, MNR Medical College & Hospital, Sangareddy, Telangana, India

<sup>5</sup>Dr. Srivats N Yadav, MBBS Graduate, Osmania Medical College, Hyderabad, Telangana, India

**Citation of this Article:** Dr. Anurag Yadav, Dr. Nanda Kumar LG, Dr. Golla Anmol Manaswini Yadav, Dr. Karveri Karewad, Dr. Srivats N Yadav, “Immuno-Haematological Markers to Predict Outcome in COVID -19 Hospitalized Patients,” IJMSAR – April – 2022, Vol. – 5, Issue - 2, Page No. 17-22.

**Copyright:** © 2022, Dr. Anurag Yadav, et al. This is an open access journal and article distributed under the terms of the creative commons attribution noncommercial License. This allows others to remix, tweak, and build upon the work non commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

**Corresponding Author:** Dr. Anurag Yadav, Department of Biochemistry, Assistant Professor, MNR Medical Collage & Hospital, Sangareddy, Telangana, India

**Type of Publication:** Original Research Article

**Conflicts of Interest:** Nil

### **Abstract**

#### **Objective**

Study aimed to assess haematological markers as prognostic indicators in COVID-19 patients to predict outcome.

#### **Material and Methods**

A Retrospective study of COVID-19 patients admitted at MNR Medical College & Hospital, Sangareddy was conducted from August 2020 to June 2021. Total Leukocyte count (TLC), Neutrophil-to-lymphocyte ratio (NLR), derived NLR ratio (d-NLR)

and platelet-to-lymphocyte ratio (PLR) were calculated and correlated with outcome. These parameters were compared with other inflammatory markers using ROC analysis.

#### **Results**

310 patients of 426 fulfilled the inclusion criteria (Male-205, Female-105). There is a significant higher mean of NLR in patients with death (14.46±5.84) compared to patients recovered (8.43±4.33), similarly the dNLR was higher in death

(8.06±2.34) compared to recovered (4.97±1.49). A significant positive strength of association between the NLR and dNLR with the ESR, CRP, CORADS score and CT severity score in the patients. The ROC analysis showed the NLR (AUC=0.777) and dNLR (0.799) a better marker to predict the outcome.

### **Conclusion**

In COVID-19, immuno-haematological markers such as NLR, dNLR, and PLR were found to be a convenient and cost-effective technique for predicting clinical outcome in hospitalised patients, and they correlated with other inflammatory markers. As a result, these markers serve as superior indications for risk categorization and management.

### **Keywords**

COVID -19, dNLR, Haematological markers, NLR, PLR.

### **Introduction**

SARS-CoV-2 commonly causes pneumonia and acute respiratory distress syndrome (ARDS) in adults, although it is increasingly recognised as a multisystem illness.<sup>1</sup> The global health infrastructure has been stressed as a result of the COVID-19 epidemic, emphasising the significance of cost-effective biomarkers.<sup>2,3</sup> The analysis of haematological indicators during hospitalisation, as well as their relevant criteria, may be important tools for doctors in identifying patients at risk of developing serious illness early.<sup>4</sup>

COVID-19 infection starts as an inflammatory condition and can develop to cytotoxic storm and death. Because of the serious nature of the disease, which includes severe pneumonia, acute respiratory distress syndrome, and multi-organ failure, patients may be hospitalised for an extended period of time with poor overall results.<sup>5</sup> Certain studies have focused on haematological features such as neutrophil lymphocyte

ratio (NLR), platelet lymphocyte ratio (PLR), red cell distribution width, and others, suggesting that they may be utilised as a guide and predict prognosis in COVID-19 patients.<sup>6,7</sup>

A timely and correct diagnosis has far-reaching consequences for the patient, the healthcare facility, and public health and administrative employees. In the present epidemic, healthcare services are failing to satisfy the increased demands of an infected population that is fast growing. The efficient use of existing resources is critical to save the greatest number of lives. Clinical evaluation is essential, but laboratory indicators, or biomarkers, can give additional, objective information that can have a major influence on many aspects of patient management.

Indian being a developing country with resource restriction, it is difficult for the patients to undergo the expensive testing procedures frequently during the admission. It is also burden on the economy of the country as many of the COVID health centres are operated by the government at nil or minimal cost for the patients. Study aimed to assess haematological markers as prognostic indicators in COVID-19 patients to predict outcome.

### **Material and Methods**

This Observational study was conducted at MNR Medical College & Hospital, Sangareddy, Telangana between August 2020 to June 2021 among the patients with COVID 19 infection.

All patients with rapid antigen and RT-PCR positive for COVID-19, admitted to the hospital were included in the study. Patients with age < 18yrs, pregnant females, haematological disorders, on Renal replacement therapy, malignancies and Immunodeficiency states like HIV, organ transplant, chronic steroid use and on any immunomodulators were

excluded from study. All the data were collected after obtaining the institutional ethics clearance from the committee and consent was obtained from all the participants included in the study.

All the clinical data, haematological and radiological parameters were obtained from the medical records. Total Leukocyte Count (TLC), Neutrophil-to-Lymphocyte Ratio (NLR), derived NLR ratio (d-NLR, neutrophil count divided by the result of WBC count minus neutrophil count) and Platelet-to-Lymphocyte Ratio (PLR) were calculated and correlated with outcome. These parameters were compared with other inflammatory markers like Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP) to further strengthen their validation as prognostic markers.

Statistical analysis: Data obtained was entered in Excel sheet. Continuous variables i.e., NLR, dNLR, PLR, ESR, CRP, CORADS and CTSS were expressed as means  $\pm$  S.D. Categorical variables were summarized as frequencies and percentages. Correlation of continuous variables was done using Pearson correlation coefficient. The Diagnostic ability of study parameters were derived using Receiver Operator Curve (ROC). Statistical analyses were performed using SPSS v21. A p-value of  $<0.05$  was considered statistically significant and

## **Results**

Total of 310 patients fulfilled the inclusion criteria with male preponderance (Male 198, Female 105). The mean haemoglobin was  $14.65 \pm 3.65$  gm/dl and  $13.98 \pm 3.55$  in recovered and death groups. Despite the mean Total Leukocyte count was normal in both recovered and death group, i.e.,  $9652 \pm 1265$  cells/cumm and  $10653 \pm 1432$  cells/cumm respectively, the mean Absolute Neutrophil count was significantly higher in

death group (Recovered- $5878.0 \pm 2980.3$ , Death -  $10140 \pm 3957$ ,  $p < 0.05$ ). (Table 1)

There is a significant higher mean of NLR ( $14.46 \pm 5.84$ ) and dNLR ( $8.06 \pm 2.34$ ) in patients with death compared to NLR ( $8.43 \pm 4.33$ ) and dNLR ( $4.97 \pm 1.49$ ) in recovered patients However; we did not find the significant mean difference of PLR. (Table 1) .There was significant positive strength of association between the NLR and dNLR with the ESR, CRP, CORADS score and CT severity score in the patients. (Table 2)

The Receiver operator curve (ROC) analysis showed the NLR (Area under curve = 0.777) and dNLR (Area under curve = 0.799) a better marker to predict the outcome. (Fig 1)

## **Discussion**

Leukocytes, particularly neutrophils, constitute the initial line of defence against infection in the body.<sup>8</sup> COVID-19 patients have a number of laboratory abnormalities, including neutrophilia and lymphopenia, which are linked to illness severity and prognosis.<sup>9</sup> This study looked at the efficacy of immune-haematological indicators in predicting disease severity and compared it to other inflammatory markers and radiological severity in predicting outcome.

In the current investigation, the inflammatory parameters revealed a substantial difference between patients who recovered and those who died. In the current study, we discovered a significantly greater mean of NLR and dNLR among patients with the poorest prognosis compared to those who lived and were discharged. In terms of correlation, the dNLR was shown to have a much stronger positive association with the CT severity score than the NLR, PLR, and ESR. The dNLR appears to be superior than the NLR in terms of correlation with CT severity score and

outcome in COVID-19 patients. In agreement with the current study, Yang H et al.<sup>10</sup> determined that the dynamic measures, lymphocyte count, neutrophil count, Lymphocyte Monocyte Ratio (LMR), and NLR, substantially varied and helped distinguish between non-severe and severe groups. Ramesh J et al.<sup>5</sup> conducted a retrospective analysis on 154 severe COVID-19 patients (diabetic subset-57) and determined cut-offs for TLC-8950 cells/cumm, ANC-7679 cells/cumm, NLR-5.14, and dNLR-3.44 that were substantially linked with death.

### **Conclusion**

In COVID-19, immuno-haematological indicators such as NLR, dNLR, and PLR were shown to be a convenient and cost-effective technique for predicting clinical outcome in hospitalised patients, and they correlated with other inflammatory markers. As a result, NLR, dNLR, and PLR serve as cost-effective risk categorization and management markers, improving outcomes even in the background of normal leukocyte counts.

### **Reference**

1. Samprathi M, Jayashree M. Biomarkers in COVID-19: An Up-To-Date Review. *Front Pediatr* 2021;8:1-12.
2. Martin A, Markhvida M, Hallegatte S, Walsh B. Socio-Economic Impacts of COVID-19 on Household Consumption and Poverty. *Econ disasters Clim Chang* 2020;4:453-79.
3. Nicola M, Alsafi Z, Sohrabi C, Kerwan A, Al-Jabir A, Iosifidis C, et al. The socio-economic implications of the coronavirus pandemic (COVID-19): A review. *Int J Surg* 2020;78:185-93.
4. Liao D, Zhou F, Luo L, Xu M, Wang H, Xia J, et al. Haematological characteristics and risk factors in the classification and prognosis evaluation of

- COVID-19: a retrospective cohort study. *Lancet Haematol* 2020;7:e671-8
5. Ramesh J, Reddy SLS, Rajesh M, Varghese J. Evaluation of simple and cost-effective immuno-haematological markers to predict outcome in hospitalized severe COVID-19 patients, with a focus on diabetes mellitus - A retrospective study in Andhra Pradesh, India. *Diabetes Metab Syndr* 2021;15:739-45.
6. Seyit M, Avci E, Nar R, Senol H, Yilmaz A, Ozen M, et al. Neutrophil to lymphocyte ratio, lymphocyte to monocyte ratio and platelet to lymphocyte ratio to predict the severity of COVID-19. *Am J Emerg Med* 2021;40:110-4.
7. Wang C, Zhang H, Cao X, Deng R, Ye Y, Fu Z, et al. Red cell distribution width (RDW): a prognostic indicator of severe COVID-19. *Ann Transl Med* 2020;8:1230.
8. Li Y, Wang W, Yang F, Xu Y, Feng C, Zhao Y. The regulatory roles of neutrophils in adaptive immunity. *Cell Commun Signal* 2019;17:1-11.
9. Henry B, Cheruiyot I, Vikse J, Mutua V, Kipkorir V, Benoit J, et al. Lymphopenia and neutrophilia at admission predicts severity and mortality in patients with COVID-19: a meta-analysis. *Acta Biomed* 2020;91:1-19.
10. Yang H, Xu Y, Li Z, Yan L, Wang J, Liao P. The Clinical Implication of Dynamic Hematological Parameters in COVID-19: A Retrospective Study in Chongqing China. *Int J Gen Med* 2021;14:4073-80

List of Tables and Figures

**Table 1:** Demographic, Haematological and Radiological data and their association with outcome

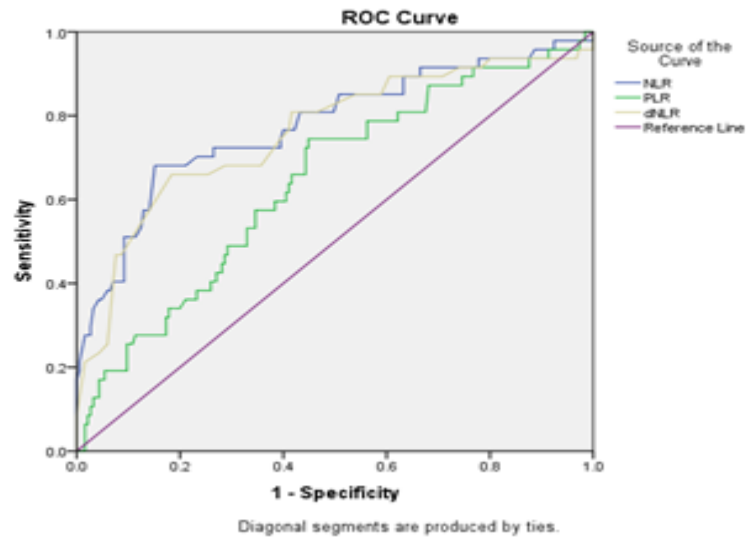
Variable	Recovered	Death	p-value
Age ( years)	47.01±13.4	51.4±15.3	0.093
Male	171	34	0.296
Female	82	23	
Hemoglobin (gm/dl)	14.55±3.65	13.98±3.55	0.123
Total Leukocyte Count (TLC) (cells /cumm)	9612±1265	10653±1432	0.142
Absolute Neutrophil Count (ANC)	5888.0±2980.3	10150±3957	0.05*
Lymphocyte Count (cells /cumm)	1083.39±608.0	928.93±614.6	0.214
Neutrophil Lymphocyte Ratio (NLR)	8.44±2.39	14.45±4.32	0.001**
Derived Neutrophil Lymphocyte ratio(dNLR)	4.96±1.49	8.05±2.34	0.001**
PLR	312.09±180.6	311.08±139.3	0.12
C-Reactive Protein(CRP) mg/L	9.22±3.11	15.21±3.42	0.05*
Erythrocyte Sedimentation Rate (ESR) (mm/1hr)	64.4±27.4	82.2±34.3	0.05*
CORADS	5.1±1.1	5.4±0.5	0.092
CT Severity Score(CTSS)	11.8±4.6	17.4±4.3	0.001**
*p<0.05 is considered statistically significant; **p<0.001 is considered statistically highly significant.			

Gm = gram, dL = decilitre, mm = millimeter, cumm = cubic millimeter, L= Litter.

**Table 2:** Correlation between Haematological and Radiological parameters

		CORADS	CTSS	ESR
Neutrophil Lymphocyte Ratio (NLR)	r	.053	.345**	.288
	Sig	.453	.000	.052
Platelet Lymphocyte Ratio (PLR)	r	-.010	.128	.031
	Sig	.888	.072	.750
Derived Neutrophil Lymphocyte ratio(dNLR)	r	.104	.846**	.505*
	Sig	.143	.000	.032
Erythrocyte Sedimentation Rate (ESR)	r	.286**	.336**	1
	Sig	.001	.000	
**p<0.001 is considered statistically highly significant.				

**Figure 1:** Receiver operator characteristic curve analysis of NLR, dNLR and PLR



Area Under the Curve	
Test Result Variable(s)	Area
NLR	.777
PLR	.642
dNLR	.799