Association of haematological biomarkers with severity of COVID-19 pneumonia

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Abstract

Background: Coronavirus disease 2019 (COVID-19) was first reported in Wuhan, China in December 2019. It is caused by SARS-CoV-2, a beta coronavirus. In this study, we assessed the association of biomarkers such as neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) and lymphocyte monocyte ratio (LMR) with the severity of COVID-19 in patients. Methods: This retrospective observational study was carried out at a tertiary care hospital of the sub-Himalayan region of Uttarakhand over a period of six months from May to October 2020. A total of 350 patients with confirmed RT-PCR COVID-19 infection were included in the study. Detailed clinical, demographic and biochemical data of each patient was obtained from the hospital record section after permission from the Institute Ethical Committee. NLR, PLR and LMR ratios were calculated and compared with the outcomes in each patient. The patients were subdivided into two sub-groups: those with saturation less than 94% and those with saturation more than 94%. The patients were categorised as mild (with SpO₂ of > 94%) and moderate-severe (with SpO₂ of ≤94%) based on oxygen saturation. Results: A total of 350 patients with Covid-19 pneumonia were enrolled in the study. The mean age of the patients with oxygen saturation of ≤94% was 54.91 ± 13.29 years, which was comparable to the other group. Absolute neutrophil count (ANC) and NLR were significantly higher in patients with a saturation of < 94%. However, LMR and PLR were significantly lower in the group with saturation of <94%. Thus, a significant association was found between haematological inflammatory ratios and the severity of COVID-19 infection. Conclusion: NLR, LMR and PLR ratios can be utilised as point of care markers to assess severity in patients with COVID-19 pneumonia.

Keywords: Association of NLR, LMR, PLR, severity of COVID-19

Introduction

COVID-19 infection has emerged as a global pandemic. It was detected in Wuhan, China in December 2019. Since then, it has rapidly spread to almost all the countries of the world, taking a heavy toll on human life.[1,2] As per the worldometer, on 2nd March, 2021, there were approximately 11.12 million cases with 157385 reported deaths due to COVID-19 infection in India. Kerala and Maharashtra, which are the two worst-hit Indian states, continue to report a high daily positivity rate.[3]

The common signs and symptoms of the disease include fever, breathlessness, cough, loose stools, headache and fever. The presentation of the patients spans from mild to severe form of the disease and a more catastrophic form as acute respiratory distress syndrome (ARDS). Besides respiratory system involvement, neurological, cardiovascular, renal and hepatic complications of SARS-CoV-2 infection have also been reported.

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The gold standard diagnostic modality of COVID-19 infection is real-time–polymerase chain reaction (RT-PCR). However, it is time-consuming. Thus, there is an urgent need to analyse serum biomarkers of inflammation, which can have both diagnostic and prognostic implications. Haematological biomarkers such as total leucocyte count (TLC), neutrophil-lymphocyte ratio (NLR) and lymphocyte-monocyte ratio (LMR) have been individually studied as prognostic markers and to predict severity in patients with COVID-19 infection.\cite{9,10}

As in patients with severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), there is dysregulated host response leading to cytokine storm in patients with COVID-19 infection. Robust inflammatory response coupled with weak adaptive immunity contributes to multi-organ involvement in COVID-19 infection. In addition, NLR has been assessed in patients with COVID-19 pneumonia with oxygen saturation of ≤94% and >94%. Several case series have observed a significant relationship between NLR and mortality in patients with COVID-19 infection.\cite{11} Few studies have also highlighted platelet-lymphocyte ratio (PLR) and LMR as inflammatory markers.\cite{12} In this study, we assessed the association of all the three markers—NLR, LMR and PLR—with the severity of COVID-19 patients.

**Materials and Methods**

The retrospective study was carried out at the Emergency Medicine Department of a tertiary care hospital of Uttarakhand over a period of six months. A total of 350 RT-PCR-confirmed cases of COVID-19 infection were enrolled in the study. Detailed demographic (age, sex), clinical, haematological and biochemical parameters, co-morbidity history (diabetes, hypertension, asthma, COPD and ischaemic heart disease), CT findings and CT score were noted for each patient from the hospital record section. The study was conducted after obtaining approval from the Institutional Ethical Committee dated 12-12-2020.

All the patients were subdivided into two groups, one with oxygen saturation of >94% (mild group) and the other with oxygen saturation of ≤94% (moderate-severe group). NLR, plasma-lymphocyte ratio (PLR) and LMR were calculated in all the patients and were compared in both groups. The clinico-demographic, biochemical, haematological and outcomes of all the patients were compared for both groups. Clinical and haematological parameters of alive and expired patients were also compared.

The data was collected after taking permission from the institute’s ethical committee and research cell.

**Statistical analysis**

Statistical analysis was performed by the SPSS program for Windows, version 17.0 (SPSS, Chicago, Illinois). Continuous variables are presented as mean ± SD, and categorical variables are presented as absolute numbers and percentages. Data were checked for normality before statistical analysis. Normally distributed continuous variables were compared using the unpaired t-test, whereas the Mann–Whitney U test was used for variables not normally distributed. Categorical variables were analysed using either the Chi-square test or Fisher’s exact test. Kaplan–Meier survival analysis was used to estimate the mortality of study patients as admission was based on SpO₂ (>94% or ≤94%). For all statistical tests, a P value of <0.05 was taken to indicate a statistically significant difference.

**Results**

As shown in Table 1, a retrospective analysis of 350 patients with COVID-19 pneumonia was done in this study. They were subdivided into two groups: one with oxygen saturation of ≤94% (80, 22.8%) and the other with oxygen saturation of >94% (270, 77.1%). Of these, 263 (75.1%) were males and 87 (24.8%) were females. There was no statistically significant difference in gender and age in both groups. The mean age of the patients with oxygen saturation of ≤94% was 54.91 ± 13.2 years, which was almost similar to the mean age in the other group. Mean diastolic blood pressure (72.6 ± 11.58 mm of Hg) was significantly lower in the group of patients with SpO₂ ≤94%. Similarly, Glasgow Coma Scale (GCS) was significantly lower in the former group. Mean heart rate (100.31 ± 16.5 beats/min) and respiratory rate (25.4 ± 2.48 per min) were higher in the group with SpO₂ ≤94%. Among the co-morbidities, hypertension (99, 28.2%) and diabetes mellitus (125, 35.7%) were the most common. Hypertension was significantly more common in the group with oxygen saturation of ≤94%.

| Table 1: Demographic, clinical and hospital stay variables of patients with COVID-19 pneumonia with oxygen saturation of more than and less than 94% |
| Variables | SpO₂ <94% (n=80) | SpO₂ >94% (n=270) | P  |
| Age (1 year) | 54.91±13.29 | 55.75±15.54 | 0.663 |
| Sex | | | |
| F | 16 (20%) | 71 (26.3%) | 0.252 |
| M | 64 (80%) | 199 (73.1%) | |
| Systolic Blood Pressure (SBP) | 124.61±19.02 | 126.99±19.35 | 0.337 |
| Diastolic Blood Pressure (DBP) | 72.6±11.58 | 76.05±13.76 | 0.042 |
| Mean Arterial Pressure (MAP) | 89.9±12.3 | 94.5±29.4 | 0.177 |
| Heart Rate (HR) | 100.31±16.5 | 92.7±14.1 | <0.001 |
| Respiratory rate (RR) | 25.4±2.48 | 19.2±2.3 | <0.001 |
| GCS | 13.46±2.9 | 14.3±2.2 | 0.005 |
| Haemoglobin (HB) | 16.91±19.3 | 12.15±3.08 | 0.001 |
| Hypertension | 33 (41.2) | 66 (24.4) | 0.003 |
| Ischaemic Heart Disease (IHD) | 18 (22.4) | 36 (13.3) | 0.06 |
| Diabetes mellitus | 29 (36.2) | 96 (35.5) | 0.6 |
| Asthma | 3 (3.7) | 8 (2.9%) | 0.8 |
| COPD | 6 (7.5) | 11 (4.0%) | 0.7 |
| Referred | 4 (5%) | 3 (1.1%) | 0.027 |
| Mortality | 36 (45%) | 115 (42.6%) | 0.027 |
| Discharged | 32 (40%) | 139 (51.5%) | 0.027 |
| Length of Stay | 13.15±9.24 | 11.21±7.11 | 0.142 |
other co-morbidities were ischaemic heart disease (54, 15.4%), asthma (11, 3.1%) and COPD (17, 4.8%). Mortality (36, 45%) was higher in the group with $\text{SpO}_2$ of $\leq 94\%$. Length of stay was not significantly longer in the group with $\text{SpO}_2$ of $\leq 94\%$. In the mild group, significantly more patients were discharged as compared to the severe group. Among the haematological parameters, TLC (12.71 $\pm$ 17.8/cumm) were significantly higher in the group with $\text{SpO}_2$ of $\leq 94\%$. NLR was significantly higher in the group with $\text{SpO}_2$ of $\leq 94\%$ [Table 2]. Lymphocyte-monocyte ratio (LMR) (1.48 $\pm$ 0.9) and platelet-lymphocyte ratio (PLR) (406.13 $\pm$ 251.1) were significantly lower in the group with $\text{SpO}_2$ of $\leq 94\%$. No significant association was observed with the other biochemical parameters [Table 3]. Table 4 shows the association of various parameters with mortality in patients with COVID-19 pneumonia. Age (65.23 $\pm$ 13.7 years), respiratory rate (33.7 $\pm$ 2.3 per min), absolute neutrophil count (ANC) (14618.2) and NLR (14.29) were significantly higher in the group who succumbed to death [Figure 1].

Discussion

The COVID-19 pandemic, first detected in December 2019, has spread exponentially all over the world. Although the mortality of COVID-19 infection is only 2.5%, it poses a humongous challenge to identify and initiate timely management in these patients. The common clinical characteristics of the infection are fever, cough and breathlessness.

The gold standard diagnostic modality of COVID-19 infection is RT-PCR test. In our study, the majority of the patients were more than 50 years of age. However, there was no statistically significant difference in age in the two subgroups. As per the previous studies, age is found to be significantly associated with mortality in patients with COVID-19 pneumonia.

The geriatric population has been found to be vulnerable to severe form of the disease due to co-existent co-morbidities as well as weak immune system. In our study, patients with COVID-19 pneumonia who succumbed to death belonged to a higher age group as compared to patients who were discharged in stable condition. In this study, diastolic blood pressure was significantly lower in the group with $\text{SpO}_2$ of $\leq 94\%$. Both heart rate and respiratory rate were significantly higher in the moderate-severe group. Both the parameters have been identified by previous studies as prognostic and mortality markers in COVID-19 pneumonia patients. Hypertension, followed by diabetes mellitus, was found to be the most common co-morbidities in patients with severe COVID-19 infection. However, hypertension was significantly more common in patients with $\text{SpO}_2$ of $\leq 94\%$. Similar results were observed by studies conducted by Mertz et al.

Chronic conditions such as cardiovascular diseases, hypertension, diabetes mellitus and chronic obstructive pulmonary diseases can have been found to have a significant impact not only on mortality but also on prognostic parameters in viral infections such as SARS-COV-2, MERS and SARS.

Lately, researchers have highlighted the significant role of multiple ratios such as NLR, LMR and PLR in many chronic inflammatory conditions. These ratios can be used as diagnostic and prognostic predictors of severity in patients with recently emerged COVID-19 infection. The NLR, PLR and LMR ratios can be utilised as low-cost diagnostic and prognostic biomarkers in COVID-19 patients.

![Figure 1: Kaplan–Meier curves for mortality in COVID-19 patients grouped into two groups based on $\text{SpO}_2$ (>94% or $\leq$94%) at admission. ($\text{SpO}_2$: Peripheral venous blood oxygen saturation value)](https://example.com/figure1.png)

### Table 2: Haematological variables of patients with COVID-19 pneumonia with oxygen saturation greater than and less than 94%

| Variables                  | $\text{SpO}_2 \leq 94\%$       | $\text{SpO}_2 >94\%$       | $P$      |
|----------------------------|-------------------------------|----------------------------|---------|
| HB                         | 16.91 $\pm$ 19.39             | 12.15 $\pm$ 3.08           | 0.001   |
| RBC Count                  | 4.27 $\pm$ 1.01               | 4.06 $\pm$ 1.06            | 0.126   |
| TLC                        | 12.71 $\pm$ 4.78              | 9.90 $\pm$ 5.00            | <0.001  |
| Absolute neutrophil count  | 11817.66 $\pm$ 4797.57        | 8107.37 $\pm$ 3981.2       | <0.001  |
| Absolute lymphocyte count  | 675.8 $\pm$ 519.8             | 917.5 $\pm$ 727.6          | 0.029   |
| Absolute monocyte count    | 659.4 $\pm$ 500.3             | 4.96 $\pm$ 373.5           | 0.044   |
| Neutrophil-lymphocyte ratio| 25.7 $\pm$ 17.8               | 15.4 $\pm$ 14.7            | <0.01   |
| Lymphocyte-monocyte ratio  | 1.48 $\pm$ 0.9                | 3.9 $\pm$ 14.7             | 0.001   |
| Platelet-lymphocyte ratio  | 406.13 $\pm$ 251.1            | 433.28 $\pm$ 695.6         | 0.006   |
| PT INR                     | 1.25 $\pm$ 0.72               | 1.05 $\pm$ 0.24            | 0.005   |
In the present study, the ANC and NLR ratio were significantly higher in the group with oxygen saturation of ≤94% and in the patients who expired. Thus, the NLR ratio should be integrated with the prognostic nomograph in patients with COVID-19 pneumonia. Shang et al. studied the role of NLR, CRP and platelets as predictors of disease severity and emphasised NLR as the determinant of COVID-19 pneumonia severity. A Chinese study has highlighted that NLR cut-off value of >3.3 in COVID-19 pneumonia is associated with poor prognosis and lower survival rate. NLR has also been studied as a marker of endothelial dysfunction and is significantly associated with cardiovascular mortality. The endothelial dysfunction leads to viral alveolar damage in patients with COVID-19 infection. SARS-CoV-2 utilises angiotensin-converting enzyme-2 (ACE-2) receptor to enter the cells. This ACE-2 is expressed in multiple organs including endothelial cells.

The patients with multiple co-morbidities such as hypertension and diabetes have pre-existing endothelial dysfunction. Thus, these patients are more vulnerable to the severe form of the disease. Endothelial damage triggers the inflammatory cascade stimulating activation of complement and increasing endothelial permeability, resulting in cytokine storm.

There is an increase in NLR in the severe form of the disease. The values of both baseline NLR and peak values of NLR can be compared to assess the severity of the disease. Hence, NLR can be used as a cost-effective and easily measurable biomarker of COVID-19 disease severity.

NLR ratio has been assessed as a useful marker in various oncological diseases, autoimmune disorders and bacterial pneumonias. However, the ratio has been rarely reported in patients with viral pneumonia. Elevated NLR and leucopenia have been reported as independent risk factors in patients with COVID-19 pneumonia. Some studies have also reported eosinophilia and leucopenia as prognostic variables in patients with COVID-19 pneumonia. Clearly, these biomarkers can aid in ruling out other causes of respiratory infections and undifferentiated fevers.

Summary

1. Higher levels of ANC and neutrophil-lymphocyte ratio are associated with increased severity of COVID-19 infection.
2. Lower levels of LMR and PLR are associated with increased disease severity in patients with COVID-19 pneumonia.

Table 4: Difference between clinico-demographic and biochemical profile patients with COVID-19 pneumonia alive and died

| Variables Demographic | Alive (n=199) (50.8%) | Dead (n=151) (43.1%) | P |
|------------------------|------------------------|------------------------|--------|
| Age                    | 52.3±15.56             | 65.23±13.73            | <0.001 |
| Sex                    |                        |                        |        |
| F                      | 41 (23.03)             | 42 (27.8)              | 0.320  |
| M                      | 137 (76.9)             | 109 (72.1)             |        |
| SBP                    | 125.15±12.9            | 126.64±20.97           | 0.487  |
| DBP                    | 75.66±12.9             | 74.8±13.96             | 0.602  |
| MAP                    | 94.4±34.5              | 92.13±14.7             | 0.45   |
| HR                     | 93.8±14.9              | 96.04±14.9             | 0.185  |
| R.R                    | 23.13±2.39             | 23.7±2.37              | 0.028  |
| Oxygen saturation      | 94.8±4.47              | 44.2±2.54              | <0.001 |
| GCS                    | 14.4±1.95              | 13.6±2.9               | 0.011  |
| HB                     | 13.1±8.2               | 13.00±11.9             | 0.908  |
| RBC                    | 4.17±1.00              | 3.96±1.09              | 0.079  |
| TLC                    | 10.32±5               | 10.88±5.29             | 0.378  |
| ANC/MM³                | 8480.6 (5124.6-11825.12) | 14618.2 (8179.6-15671.3) | 0.002 |
| NLR                    | 10.91 (5.418-20.8)     | 14.29 (5.514-24.81)    | 0.014  |
| LMR                    | 1.6 (1.163-2.8)        | 1.6/(1.155-2.88)       | 0.947  |
| PLR                    | 228.8/(129.20-401.838) | 35.7 (125.53-409.65)   | 0.855  |

Table 3:Biochemical variables of patients with covid-19 pneumonia with oxygen saturation more and less than 94%

| Variables | SpO₂ <94% | SpO₂ >94% | P |
|-----------|-----------|-----------|---|
| SGPT (U/L) | 73.03±71.3 | 85.08±21.9 | 0.989 |
| SGPT (U/L) | 78.82±54.09 | 84.4±124.7 | 0.683 |
| CREAT (mg/dl) | 2.25±288 | 1.9±1.9 | 0.669 |
| BUN (mg/dl) | 75±56 | 64.4±48.5 | 0.121 |
| K+ (Potassium) | 4.87±0.99 | 4.86±0.78 | 0.878 |
3. Haematological biomarkers can be used as severity risk indicators in the quick assessment of patients with COVID-19 infection.

**Conclusion**

NLR, LMR and PLR ratios can be used as cheap and readily available biomarkers to assess severity in patients with COVID-19 infection. The focus of this study is early detection of COVID-19 infection and stratifying it as severe and non-severe using these ratios.

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**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med 2020;382:1199-207.
2. Hui DS, Azhar IE, Madani TA, Ntoumi F, Kock R, Dar O, et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health - The latest 2019 novel coronavirus outbreak in Wuhan, China. Int J Infect Dis 2020;91:264-6.
3. https://www.mohfw.gov.in/. [Last accessed on 2021 Mar 30].
4. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan. JAMA Intern Med 2020;180:934-43.
5. Ferrando C, Suarez-Sipmann F, Mellado-Artigas R, Hernandez M, Gea A, Arruoi E, et al. Clinical features, ventilatory management, and outcome of ARDS caused by COVID-19 are similar to other causes of ARDS. Intensive Care Med 2020;46:2200-11.
6. Azkur AK, Akdis M, Azkur D, Sokolowska M, van de Veen W, Bruggen MC, et al. Immune response to SARS-CoV-2 and mechanisms of immunopathological changes in COVID-19. Allergy 2020;75:1564-81.
7. Kong W, He Y, Bao H, Zhang W, Wang X. Diagnostic value of neutrophil-lymphocyte ratio for predicting the severity of acute pancreatitis: A meta-analysis. Dis Markers 2020;2020, Article ID 9731854, 9 pages.
8. 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.
9. Ying H-Q, Deng Q-Q, He B-S, Pan Y-Q, Wang F, Sun H-L, et al. The prognostic value of preoperative NLR, d-NLR, PLR and LMR for predicting clinical outcome in surgical colorectal cancer patients. Med Oncol 2014;31:305.
10. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020;382:727-33.
11. Xie J, Covassin N, Fan Z, Singh P, Gao W, Li G, et al. Association between hypoxemia and mortality in patients with COVID-19. Mayo Clin Proc 2020;95:1138-47.
12. Wong CKH, Wong JYH, Tang EHM, Au CH, Wai AKC. Clinical presentations, laboratory and radiological findings, and treatments for 11,028 COVID-19 patients: A systematic review and meta-analysis. Sci Rep 2020;10:19763.
13. Mertz D, Kim TH, Johnstone J, Lam P-P, Science M, Kuster SP, et al. Populations at risk for severe or complicated influenza illness: Systematic review and meta-analysis. BMJ 2013;347:f5061.
14. Badawi A, Ryoo SG. Prevalence of comorbidities in the Middle East respiratory syndrome coronavirus (MERS-CoV): A systematic review and meta-analysis. Int J Infect Dis 2016;49:129-33.
15. Yang AP, Liu JP, Tao WQ, Li HM. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. Int Immunopharmacol 2020;84:106504.
16. Epidemiology Working Group for NCIP Epidemic Response, Chinese Center for Disease Control and Prevention. [The epidemiological characteristics of an outbreak of 2019 novel coronavirus disease (COVID-19) in China]. Zhonghua Liu Xing Bing Xue Za Zhi 2020;41:145-51.
17. Martinez-Urbistondo D, Beltrán A, Beloqui O, Huerta A. The neutrophil-to-lymphocyte ratio as a marker of systemic endothelial dysfunction in symptomatic subjects. Nefrologia 2016;36:397-403.
18. Mehrz M, Desai SS, Kuy S, Henry TD, Patel AN. Cardiovascular disease, drug therapy, and mortality in Covid-19. N Engl J Med 2020;382:e102.
19. Gasparyan AY, Ayvazyan L, Mukanova U, Yessirkepov M, Kitas GD. The platelet-to-lymphocyte ratio as an inflammatory marker in rheumatic diseases. Ann Lab Med 2019;39:345-57.
20. Kusumanto YH, Dam WA, Hospers GAP, Meijer C, Mulder NH. Platelets and granulocytes, in particular the neutrophils, form important compartments for circulating vascular endothelial growth factor. Angiogenesis 2003;6:283-7.
21. Rabinovich H, Cohen R, Bruderman I, Steiner Z, Klajman A. Functional analysis of mononuclear cells infiltrating into tumors: Lysis of autologous human tumor cells by cultured infiltrating lymphocytes. Cancer Res 1987;47:173-7.
22. Saeed AM, Rosati LM, Narang A, Laheru DA, Ellsworth SG, Herman JM, et al. Elevated absolute monocyte count, absolute neutrophil count, and neutrophil-to-lymphocyte ratio as prognostic factors in locally advanced pancreatic cancer patients treated with stereotactic body radiation therapy. Int J Radiat Oncol Biol Phys 2015;93:E157.
23. Nam K-W, Kim TJ, Lee JS, Kwon H-M, Ko S-B, et al. High neutrophil-to-lymphocyte ratio predicts stroke-associated pneumonia. Stroke 2018;49:1886-92.
24. Liu J, Liu Y, Xiang P, Pu L, Xiong H, Li C, et al. Neutrophil-to-lymphocyte ratio predicts critical illness patients with 2019 coronavirus disease in the early stage. J Transl Med 2020;18:206.
25. Henry BM, de Oliveira MHS, Benoît S, Plebani M, Lippi G. Haematological, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019(COVID-19): A meta-analysis. Clin Chem Lab Med 2020;58:1021-8.
26. Gomez-Rial J, Rivera-Calle I, Salas A, Martínón Torres F. Role of monocyte/macrophages in Covid19 pathogens is: Implications for therapy. Infect Drug Resist 2020;13:2485-93.