

# Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio Can Predict the Severity in COVID-19 Patients from Ethiopia: A Retrospective Study

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**Background:** Coronaviruses are a broad family of pathogens that can cause mild to severe respiratory illnesses. Due to a strong inflammatory response and a weak immunological response, viral pneumonia inflammation, like Coronavirus Disease 2019 (COVID-19), displays an unbalanced immune response. Therefore, circulating biomarkers of inflammation and the immune system can serve as reliable predictors of a patient's prognosis for COVID-19. Hematological ratios are reliable markers of inflammation that are frequently utilized in pneumonia, primarily in viral infections with low cost in developing countries.

**Purpose:** To examine the neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), and platelet-to-lymphocyte ratio (PLR) in predicting the severity of COVID-19 patients.

**Methods:** An institutional-based retrospective study was done on 105 hospitalized COVID-19 patients at the University of Gondar comprehensive specialized referral hospital, Northwest Ethiopia. The laboratory evaluations that were gathered, evaluated, and reported on included the total leucocyte count (TLC), absolute neutrophil count (ANC), absolute lymphocyte count (ALC), absolute monocyte count (AMC), NLR, LMR, and PLR. The Kruskal–Wallis test and Wilcoxon matched-pairs signed test were used to see whether there were any differences between the continuous variables. Receiver operating curve (ROC) analysis was used to determine the appropriate cut-off values for NLR, PLR, and LMR. *P*-value <0.05 was considered a statistically significant association.

**Results:** ANC, NLR, and PLR were highest in the critical group (*p* = 0.001), while this group had the least ALC and LMR (*p* = 0.001). We calculated the optimal cut-off values of the hematological ratios; NLR (8.4), LMR (1.4), and PLR (18.0). NLR had the highest specificity and sensitivity, at 83.8% and 80.4%, respectively.

**Conclusion:** Our research showed that NLR and PLR were good indicators of severity in COVID-19. However, our findings indicate that LMR is not a reliable predictor.

**Keywords:** COVID-19, NLR, LMR, PLR, Ethiopia

## Introduction

Coronaviruses are enveloped, non-segmented, positive-sense RNA viruses that are widely present in both humans and other mammals. They are members of the family Coronaviridae and the order Nidovirales.<sup>1</sup> The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak that started in Wuhan, China, in December 2019 quickly spread to people all over the world. The clinical signs of COVID-19 are complex, ranging from flu-like symptoms to multiple organ failure and death.<sup>2</sup>

As of July 12, 2022, the WHO had received reports of 554,290,112 confirmed cases of COVID-19 worldwide, including 6,351,801 fatalities. The most severely impacted regions were those in Western Pacific, North America, and Europe. However, with 9,156,483 confirmed cases, Africa had the fewest COVID-19 instances overall.<sup>3</sup> On March 13, 2020, the first confirmed case in Ethiopia was noted. Over 275,000 confirmed cases and 4290 fatalities had been reported as of June 23, 2021.<sup>4</sup>

Despite the wide variety of COVID-19 symptoms, fever, cough, and myalgia were the most frequently seen signs at the beginning of the illness.<sup>2</sup>

An unbalanced immune response is observed in viral pneumonia inflammation, such as COVID-19, as a result of a strong inflammatory response and a subpar immunological response.<sup>5</sup> As a result, circulating biomarkers of inflammation and the immune system can serve as reliable predictors of the prognosis for COVID-19 patients.<sup>6</sup> For the prognosis of patients with viral pneumonia, the white blood cell (WBC) count, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), and serum C-reactive protein (CRP) levels were studied as predictors.<sup>7-9</sup> Hematological ratios are valuable, affordable prognostic markers that can be widely examined in developing nations with respectable significance in viral pneumonia, particularly COVID-19.<sup>9</sup>

In COVID-19 patients and patients with viral pneumonia, the neutrophil-to-lymphocyte ratio (NLR) has been shown to be a useful diagnostic tool and prognostic predictor. When compared to people with non-severe cases of COVID-19, patients with severe cases usually have lower leukocyte counts, smaller proportions of monocytes, eosinophils, and basophils, as well as higher NLR.<sup>7,9,10</sup> Although it is most useful for managing COVID-19 patients, especially in developing countries, not many studies have been done in Africa, primarily Ethiopia. More research is required to determine the appropriate NLR, LMR, and PLR values and their predictive value. In this retrospective investigation, the NLR, LMR, and PLR were assessed as prognostic indicators and inflammatory biomarkers in COVID-19 positive cases.

## Patients and Methods

After screening all the COVID-19 patient charts, the study comprised 105 eligible patients with COVID-19 who were hospitalized at the University of Gondar Comprehensive Specialized Hospital in Northwest Ethiopia between July and August 2021. The patient charts were excluded due to a lack of data on the hematological test, age, gender, and results of the SARS-CoV-2 RNA test. According to the WHO, throat swab specimens from every patient included in this retrospective analysis exhibited positive real-time PCR results for SARS-CoV-2 RNA.

## Data of the Patients

Clinical data from all eligible patients, including age, gender, diabetes, hypertension, chronic chest disease, and cardiovascular disease, were collected in accordance with the Helsinki Declaration and after approval from the School of Biomedical and Laboratory Sciences research ethics council (RF. No/SBMLS/2905/2021).

## Laboratory Investigations Included

Total leukocyte count (TLC), hemoglobin (HB) level, total platelet count, absolute lymphocyte count (ALC), absolute monocyte count (AMC), absolute neutrophil count (ANC), NLR, LMR, and PLR were all extracted.

The following categories of disease severity were used to group patients:<sup>11</sup>

1. Patients who meet any of the following criteria are considered critical: shock, organ damage requiring monitoring and care in an intensive care unit, or respiratory failure requiring artificial ventilation.
2. Severe: patients with SpO<sub>2</sub> <94% in room air, respiratory rate >30 breaths per minute, lung infiltrates >50%, or a ratio of arterial partial oxygen pressure to inspired oxygen fraction (PaO<sub>2</sub>/FiO<sub>2</sub>) <300 mmHg.
3. Patients who did not have a critical or severe illness fall under the category of non-severe patients.

## Statistical Analysis

Using STATA version 17, data management and analysis were carried out. For quantitative variables, the normality test was initially employed (Kolmogorov v Smirnov). When continuous variables were provided at their median values

(interquartile range), the Kruskal–Wallis test and Wilcoxon-matched-pairs signed test were employed to evaluate whether there were any differences between them. The categorical variables were reported as percentages of totals, and the Fisher's exact test and the chi-square test were used to compare them. For the continuous NLR, PLR, and LMR, receiver operating curve (ROC) analysis was utilized to establish the ideal cut-off values.  $P$ -value  $<0.05$  was considered a statistically significant association.

## Results

### Characteristics of the Study Participants

The study's population was divided into three groups: non-severe (7.6%), severe (24.1%), and critical (77.4%). The critical group had older patients than the severe group and non-severe group did, although there was no statistically significant difference between the two ( $p = 0.6135$ ). In all groups, male patients predominated.

Though not statistically significant ( $p = 0.608$ ), the critical group had the highest hemoglobin (HB) level compared to the other groups, with a median (IQR), of 14 (5–125). Although the lowest platelet count was also found in the non-severe group, it was not statistically significant ( $p=0.716$ ). With a statistically significant difference ( $p=0.001$ ), the NLR and PLR were highest in the critical group, followed by the non-severe group. The LMR was inversely related to severity ( $p=0.001$ ).

In comparing associated co-morbidities, the critical group was more associated with Malaria versus the non-severe and severe groups ( $p<0.047$ ).

Most of the non-severe group recovered (85.7%) and discharged home. The death was more in the critical (28.8%) and severe (20%) groups (Table 1).

The hematological values such as total leukocyte count (TLC), hemoglobin (HB) level, total platelet count, absolute lymphocyte count (ALC), absolute monocyte count (AMC), absolute neutrophil count (ANC), NLR, LMR, and PLR both at admission and at discharge were tested. Except for absolute lymphocyte count (ALC) ( $p = 0.069$ ), all showed significant difference in median value. The total platelet count at patient admission 201 (5–528) was increased to 228 (4–531) at discharge ( $p = 0.027$ ), total leukocyte count (TLC) from 7 (3.4–33) to 9 (1.3–19) ( $p = 0.005$ ), and absolute lymphocyte count (ALC) from 1 (0.07–301) to 2 (0.5–39) ( $p = 0.002$ ). Hemoglobin (HB) level at patient admission 14 (4–12.5) was decreased to 13 (6–17) at discharge ( $p = 0.002$ ), absolute neutrophil count (ANC) from 9 (24–97) to 8 (1–95) ( $p = 0.004$ ), absolute monocyte count (AMC) from 6 (1–208) to 5 (1–21) ( $p = 0.001$ ), NLR from 14 (0.4–47) to 9 (0.01–43) ( $p = 0.001$ ), and PLR from 27 (0.18–232) to 26 (0.94–101) ( $p = 0.044$ ) (Table 2).

### ROC Curve to Detect Optimal Cut-Off Values of the Hematological Ratios

We investigated the ideal cut-off values for NLR, LMR, and PLR, determined by ROC analysis and shown in (Figure 1). NLR, LMR, and PLR had areas under the curves (AUC) of 0.874, 0.279, and 0.861, respectively. LMR's AUC was less than 0.50, which precluded its usage as a potential diagnostic biomarker for further investigation. The NLR (8.4) and PLR cut-off levels were ideal (180). NLR was shown to have higher sensitivity and specificity, with respective values of 80.4% and 83.8% (Figure 1).

## Discussion

A variety of infections are approached using the total blood count test, which has the advantages of being available and very informative. According to studies, white blood cells (WBC) and peripheral blood lymphocytes may be slightly lower at the early stages of COVID-19 disease, however this is influenced by the prognosis of the condition.<sup>12</sup> Hematological ratios and other coagulation tests can be used to evaluate the severity and prognosis of COVID-19 diseases. The severity and prognosis of COVID-19 diseases can be assessed by hematological ratios and other coagulation assays. There is evidence that, in addition to hematological ratios, rising D-dimer and thrombin levels also have predictive relevance because all SARS-CoV-2 genetic variants have a significant potential for thrombogenic, especially in elderly patients.<sup>13</sup>

**Table 1** Characteristics of COVID-19 Patients at the University of Gondar Comprehensive Specialized Referral Hospital, Northwest Ethiopia

Variant	Group			P value
	Non-Severe n=7 (6.5%)	Severe n=26 (24.1%)	Critical n=77 (69.4%)	
Age/years	46 (24–78)	46 (21–87)	60 (21–97)	0.615*
<b>Sex</b>				
Male n (%)	5 (71.4)	20 (80)	41 (57)	0.092**
Female n (%)	2 (28.6)	5 (20)	32 (43)	
<b>CBC median (range)</b>				
HB (g/dL)	13.4 (7–19)	13 (4–18)	14 (5–125)	0.608*
Platelets (×10 <sup>9</sup> /L)	187 (59–292)	185 (5–528)	204 (10–519)	0.716*
TLC (×10 <sup>9</sup> /L)	9 (2–26)	6 (2–25)	7 (1–33)	0.283*
ANC (×10 <sup>9</sup> /L)	7 (57–87)	8 (48–94)	9 (24–97)	0.001*
ALC (×10 <sup>9</sup> /L)	16 (10–24)	16 (4–36)	5 (1–55)	0.001*
AMC (×10 <sup>9</sup> /L)	6 (2–15)	8 (1–208)	6 (0.3–79)	0.281*
NLR	5 (3–9)	5 (1–23)	17 (0.4–47)	0.001*
LMR	4 (1–7)	2 (1–301)	1 (1–20)	0.001*
PLR	19 (5–70)	14 (1–79)	33 (1–101)	0.001*
<b>Co-morbidities</b>				
Malaria n (%)	2 (29)	1 (4)	4 (5)	0.047**
COPD n (%)	0 (00)	1 (4)	2 (3)	0.849**
CKD n (%)	0 (00)	1 (4)	0 (00)	0.199**
CHF n (%)	0 (00)	1 (4)	2 (3)	0.085**
DM n (%)	0 (00)	6 (24)	16 (23)	0.361**
HIV n (%)	0 (00)	0 (00)	4 (6)	0.402**
TB n (%)	1 (14)	2 (8)	4 (6)	0.641**
Leishmaniasis n (%)	0 (00)	0 (00)	1 (1.4)	0.801**
Hepatitis n (%)	1 (14)	0 (00)	1 (1.4)	0.184**
<b>Outcome</b>				
Recovery n (%)	6 (85.7)	20 (80)	52 (71.2)	0.532**
Death n (%)	1 (14.3)	5 (20)	21 (28.8)	

Notes: \*Kruskal–Wallis test. \*\*Chi square test. Bold is significant *p* value; *P* value is significant if <0.05.

Abbreviations: ALC, absolute lymphocyte count; AMC, absolute monocyte count; ANC, absolute neutrophil count; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; DM, diabetes mellitus; HB, haemoglobin; HIV, human immune virus; LMR, lymphocyte-to-monocyte ratio; n, number; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; TB, tuberculosis; TLC, total leukocyte count.

Our study found that patients in the critical group had the lowest lymphocyte counts and the highest neutrophil counts, which could be explained by the fact that co-morbidity and secondary bacterial infections are common in critical cases, as previously supported by a sizable conceptual.<sup>14</sup> According to a study from the Nigerian COVID-19 research,

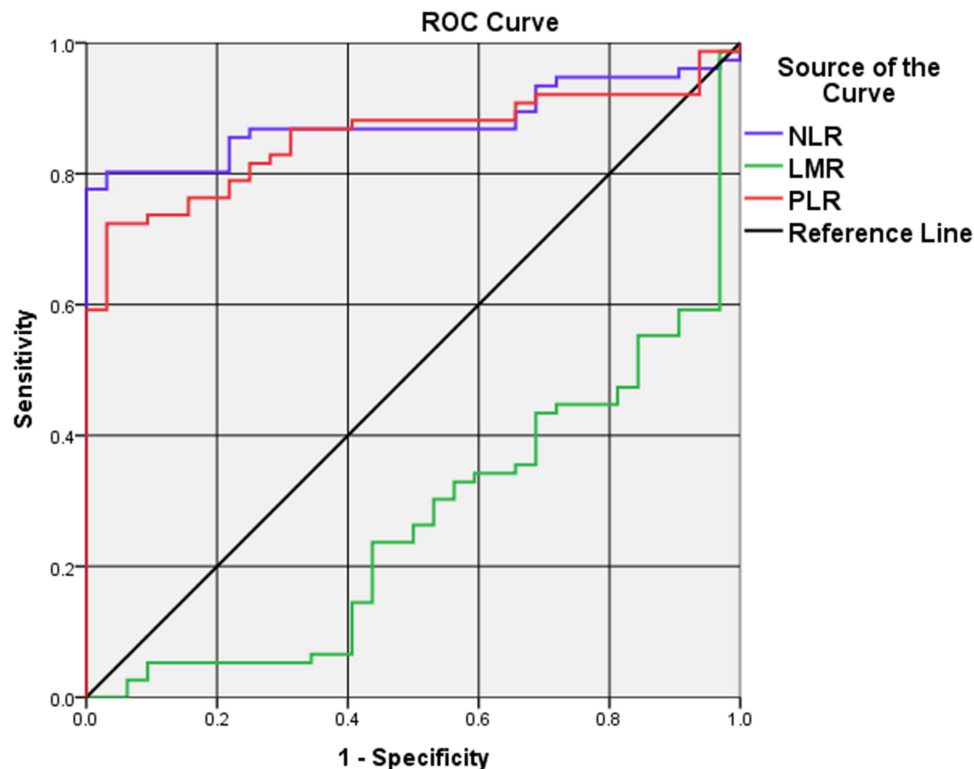
**Table 2** Comparison of Hematological Parameters of COVID-19 Patients at the University of Gondar Comprehensive Specialized Referral Hospital, Northwest Ethiopia, During Admission and at Discharge

Variant			
CBC Median (Range)	During admission	During Discharge	P value
HB (g/dL)	14 (4–12.5)	13 (6–17)	<b>0.002***</b>
Platelets ( $\times 10^9/L$ )	201 (5–528)	228 (4–531)	<b>0.027***</b>
TLC ( $\times 10^9/L$ )	7 (3–33)	9 (1–19)	<b>0.005***</b>
ANC ( $\times 10^9/L$ )	9 (24–97)	8 (1–95)	<b>0.004***</b>
ALC ( $\times 10^9/L$ )	6 (2–55)	9 (2–79)	0.069***
AMC ( $\times 10^9/L$ )	6 (1–208)	5 (1–21)	<b>0.001***</b>
NLR	14 (1–47)	9 (1–43)	<b>0.001***</b>
LMR	1 (1–301)	2 (1–39)	<b>0.002***</b>
PLR	27 (1–232)	26 (1–101)	<b>0.044***</b>

**Notes:** \*\*\*Wilcoxon-matched-pairs signed test. Bold is significant p value; P value is significant if <0.05.

**Abbreviations:** ALC, absolute lymphocyte count; AMC, absolute monocyte count; ANC, absolute neutrophil count; HB, haemoglobin; LMR, lymphocyte-to-monocyte ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; TLC, total leukocyte count.

low or aberrant lymphocyte counts were also replicated by COVID-19 non-survival patients, which is consistent with our findings.<sup>15</sup> The ability of the virus to infect lymphocytes, to kill lymphatic organs like the thymus and spleen,<sup>16</sup> to disrupt the levels of interleukin (IL)-6 and other inflammatory cytokines may result in lymphocyte apoptosis (particularly T-cell



**Figure 1** ROC curve was used to study the optimal cut off values of different haematological ratios; NLR (8.4) and PLR (18). Specificity: NLR (83.8%) and PLR (22.6%). The sensitivity of the NLR (80.4%) and the PLR (77.7%).

**Abbreviations:** LMR, lymphocyte monocyte ratio; NLR, neutrophil lymphocyte ratio; PLR, platelet lymphocyte ratio.

apoptosis),<sup>17,18</sup> and the inhibition of lymphocyte proliferation by lactic acid are just a few of the theories used to explain lymphopenia in COVID-19 patients.<sup>19</sup>

High monocyte counts are another hematological characteristic that was seen in the severe group, even though there is no statistically significant distinction ( $p = 0.281$ ). Similarly, the studies observed no statistically significant variation in the number of monocytes between healthy people and COVID-19 patients.<sup>20,21</sup> Monocytes promote inflammation by producing cytokines and activating lymphocytes. Studies found a link between cytokine storms and excessively active monocytes/macrophages in COVID-19 patients with acute respiratory distress syndrome (ARDS).<sup>12,22,23</sup>

Despite the fact that there was no statistically significant difference in the number of monocytes between healthy individuals and COVID-19 patients, the team led by Zhang et al discovered that there was a difference in the shape and function of monocytes between COVID-19 patients and healthy individuals. They discovered that people with COVID-19 have bigger monocytes that can secrete IL-6, IL-10, and TNF in addition to the markers CD11b+, CD14+, CD16+, CD68+, CD80+, CD163+, and CD206+.<sup>20</sup>

We concentrated on the importance of the hematological ratios NLR, LMR, and PLR in the current investigation. Our results supported earlier research that revealed elevated NLR predicts worse outcomes in COVID-19 patients and that patients with high NLR receive more attention than patients with low NLR.<sup>9,21,24</sup> It should be highlighted that NLR was one of the most researched markers that was connected to the severity of COVID-19.<sup>25-27</sup> The antibody-dependent cell-mediated cell (ADCC), which can directly kill the virus, is stimulated by the massive amounts of reactive oxygen species that neutrophils generate.<sup>28</sup> One possible explanation for these observations is that. Additionally, among the several cytokines that neutrophils produce is circulating vascular endothelial growth factor (VEGF), which is markedly increased in COVID-19 patients.<sup>29,30</sup> Neutrophils can also be activated by a number of inflammatory substances, such as interleukin-6, tumor necrosis factor-alpha, granulocyte colony-stimulating factor, and interferon-gamma.<sup>31</sup> Viral infections, on the other hand, primarily affect lymphocytes, because chronic inflammation significantly reduces CD4+ T cells and boosts CD8+ suppressor T lymphocytes.<sup>32</sup> Thus, when compared to the severe and non-severe groups, the critical group had a greater NLR.

LMR, which was noticed for having lower values in COVID-19 critical patients, is another attractive ratio even though there was no meaningful link. This finding has already been made in different study,<sup>26,33</sup> the LMR in the COVID-19 patients was considerably lower than in the healthy group.<sup>21</sup>

Our study's finding that the critical group had a higher PLR value is consistent with the findings of other studies that showed that patients with severe illnesses have greater PLR values than people who are not extremely ill.<sup>33</sup> In contrast, it is not possible for PLR to be a good predictor of death for COVID-19 patients, according to a study that examined at the predictive value of PLR in hospitalized COVID-19 patients.<sup>34</sup>

Using the ROC curve, the ideal thresholds for NLR, LMR, and PLR were calculated. In comparison to the other ratios, the NLR produced the greatest AUC value. It had an optimal cut-off value of 8.4, with 83.8% specificity and 80.4% sensitivity, and it was followed by PLR, which had an optimal cut-off value of 18.0, with 22.6% specificity and 77.7% sensitivity. Similarly, a previous studies showed that NLR had the highest AUC value with highest specificity and sensitivity.<sup>9,25</sup> Our results indicate that MLR may not be an accurate hematological ratio to employ as a predictor of COVID-19 severity, in contrast to NLR and PLR. Our study's conclusion that MLR could not be employed as a viable diagnostic biomarker because of its AUC being less than 0.50 was supported by the study of Aly et al.<sup>9</sup>

In this study, comparison of routine hematological values showed a significant increase of total platelet count ( $p = 0.027$ ), total leukocyte count (TLC) ( $p = 0.005$ ), and absolute lymphocyte count (ALC) ( $p = 0.002$ ) after hospitalization. In contrast, a significant decrease were showed in hemoglobin (HB) ( $p = 0.002$ ), absolute neutrophil count (ANC) ( $p = 0.004$ ), absolute monocyte count (AMC) ( $p = 0.001$ ), NLR ( $p = 0.001$ ), and PLR ( $p = 0.044$ ). A similar finding was reported by Javadi et al that after a week of admission to the hospital, a significant increase in WBC ( $P 0.001$ ) and platelets ( $P 0.001$ ) was shown among COVID-19 patients, and a significant decrease was reported in haemoglobin concentration ( $P 0.001$ ).<sup>35</sup>

The study does have certain limitations. The research was retrospective, single-centre and with a small sample size at beginning. Selection bias may have occurred since the patient charts were chosen only after a set of requirements were satisfied. Confounding factors may impact the value of the hematological ratios despite efforts to rule them out.

In conclusion, according to our analysis, NLR and PLR are good predictors of severity in COVID-19 and are promising markers that are rapid, affordable, and fascinating. However, our research shows that MLR is not a reliable indicator of severity in COVID-19.

## Data Sharing Statement

The manuscript contains all of the data that were produced and analyzed throughout this study.

## Ethical Acceptance

The School of Biomedical and Laboratory Sciences, College of Medicine and Health Sciences, University of Gondar, provided ethical approval under reference number SBMLS/2733. The written consent was permitted, and the investigation was also carried out in compliance with the Declaration of Helsinki's ethical guidelines for using human beings. All data was handled with strict confidentiality and was only used for this study. The research (a retrospective survey) involved no procedure for which written consent is generally required, and there was no danger of harm to participants, which was the reason for the waiver of written consent.

## Author Contributions

All of the authors have significantly contributed to this work, from its idea and design through its execution, data collection, analysis, and interpretation, as well as the writing, editing, and critical revision of the publication. The authors also agreed on the journal to which the article has been submitted, granted their final approval of the version to be published, and pledged to take responsibility for every part of the work.

## Disclosure

The authors declare that they have no conflicts of interest for this work.

## References

1. Richman DD, Whitley RJ, Hayden FG. *Clinical Virology*. John Wiley & Sons; 2020.
2. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497–506. doi:10.1016/S0140-6736(20)30183-5
3. WHO Coronavirus (COVID-19) dashboard. Available from: <https://covid19.who.int>. Accessed October 3, 2022.
4. Dires A, Gedamu S, Getachew Y. Perception of COVID-19 prevention methods efficacy and intention to use among patients with chronic disease in Dessie Town, Northeast Ethiopia: a multicentered cross-sectional study. *J Multidiscip Healthc*. 2021;14:1325–1339. doi:10.2147/JMDH.S313796
5. Xie B, Zhang J, Li Y, Yuan S, Shang Y. COVID-19: imbalanced immune responses and potential immunotherapies. *Front Immunol*. 2021;11:607583. doi:10.3389/fimmu.2020.607583
6. Sabbatinelli J, Matacchione G, Giuliani A, et al. Circulating biomarkers of inflammaging as potential predictors of COVID-19 severe outcomes. *Mech Ageing Dev*. 2022;204:111667. doi:10.1016/j.mad.2022.111667
7. Wu J, Wang X, Zhou M, et al. The value of lymphocyte-to-monocyte ratio and neutrophil-to-lymphocyte ratio in differentiating pneumonia from upper respiratory tract infection (URTI) in children: a cross-sectional study. *BMC Pediatr*. 2021;21(1):1–11. doi:10.1186/s12887-021-03018-y
8. Yang L, Gao C, Li F, et al. Monocyte-to-lymphocyte ratio is associated with 28-day mortality in patients with acute respiratory distress syndrome: a retrospective study. *J Intensive Care*. 2021;9(1):49. doi:10.1186/s40560-021-00564-6
9. Aly MM, Meshref TS, Abdelhameid MA, et al. Can hematological ratios predict outcome of COVID-19 patients? A multicentric study. *J Blood Med*. 2021;12:505–515. doi:10.2147/JBM.S316681
10. Sanjuna D, Singh N, Chandrakoshi G, Jain R, Jain A. Role of hematological parameters and biochemical markers as a predictor of severity of COVID-19 patients. *Asian J Med Sci*. 2022;13(7):21–27. doi:10.3126/ajms.v13i7.43970
11. Wei PF. Diagnosis and treatment protocol for novel coronavirus pneumonia (Trial Version 7). *Chin Med J*. 2020;133(9):1087–1095. doi:10.1097/CM9.0000000000000819
12. Fan BE, Chong VCL, Chan SSW, et al. Hematologic parameters in patients with COVID-19 infection. *Am J Hematol*. 2020;95(6):E131–4. doi:10.1002/ajh.25774
13. López Reboiro ML, Suárez Fuentetaja R, Gutiérrez López R, et al. Role of lupus anticoagulant and von Willebrand factor in chronic reactive endotheliitis in COVID-19. *J Infect*. 2021;82(6):e27–8. doi:10.1016/j.jinf.2021.03.006
14. Xu X, Yu C, Qu J, et al. Imaging and clinical features of patients with 2019 novel coronavirus SARS-CoV-2. *Eur J Nucl Med Mol Imaging*. 2020;47(5):1275–1280. doi:10.1007/s00259-020-04735-9
15. Ibrahim OR, Suleiman BM, Abdullahi SB, et al. Epidemiology of COVID-19 and predictors of outcome in Nigeria: a single-center study. *Am J Trop Med Hyg*. 2020;103(6):2376–2381. doi:10.4269/ajtmh.20-0759
16. Xu H, Zhong L, Deng J, et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. *Int J Oral Sci*. 2020;12(1):1–5. doi:10.1038/s41368-020-0074-x

17. Liao YC, Liang WG, Chen FW, Hsu JH, Yang JJ, MS Chang. IL-19 induces production of IL-6 and TNF-alpha and results in cell apoptosis through TNF-alpha. *J Immunol.* 2002;169(8):4288–4297. doi:10.4049/jimmunol.169.8.4288
18. Bassetti M, Vena A, Giacobbe DR. The novel Chinese coronavirus (2019-nCoV) infections: challenges for fighting the storm. *Eur J Clin Invest.* 2020;50(3):e13209. doi:10.1111/eci.13209
19. Fischer K, Hoffmann P, Voelkl S, et al. Inhibitory effect of tumor cell-derived lactic acid on human T cells. *Blood.* 2007;109(9):3812–3819. doi:10.1182/blood-2006-07-035972
20. Zhang D, Guo R, Lei L, et al. Frontline Science: COVID-19 infection induces readily detectable morphologic and inflammation-related phenotypic changes in peripheral blood monocytes. *J Leukoc Biol.* 2021;109(1):13–22. doi:10.1002/JLB.4HI0720-470R
21. Peng J, Qi D, Yuan G, et al. Diagnostic value of peripheral hematologic markers for coronavirus disease 2019 (COVID-19): a multicenter, cross-sectional study. *J Clin Lab Anal.* 2020;34(10):e23475. doi:10.1002/jcla.23475
22. Giamarellos-Bourboulis EJ, Netea MG, Rovina N, et al. Complex immune dysregulation in COVID-19 patients with severe respiratory failure. *Cell Host Microbe.* 2020;27(6):992–1000.e3. doi:10.1016/j.chom.2020.04.009
23. Merad M, Martin JC. Pathological inflammation in patients with COVID-19: a key role for monocytes and macrophages. *Nat Rev Immunol.* 2020;20(6):355–362. doi:10.1038/s41577-020-0331-4
24. Qin C, Zhou L, Hu Z, et al. Dysregulation of immune response in patients with COVID-19 in Wuhan, China. *Clin Infect Dis.* 2020;71(15):ciaa248. doi:10.1093/cid/ciaa248
25. Yang AP, Ping LJ, Qiang TW, Ming LH. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. *Int Immunopharmacol.* 2020;84:106504. doi:10.1016/j.intimp.2020.106504
26. Asghar MS, Khan NA, Haider Kazmi SJ, et al. Hematological parameters predicting severity and mortality in COVID-19 patients of Pakistan: a retrospective comparative analysis. *J Community Hosp Intern Med Perspect.* 2020;10(6):514–520. doi:10.1080/20009666.2020.1816276
27. Asghar MS, Haider Kazmi SJ, Ahmed Khan N, et al. Clinical profiles, characteristics, and outcomes of the first 100 admitted COVID-19 patients in Pakistan: a single-center retrospective study in a Tertiary Care Hospital of Karachi. *Cureus.* 2020;12(6):e8712. doi:10.7759/cureus.8712
28. 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(4):283–287. doi:10.1023/B:AGEN.0000029415.62384.ba
29. Sahebhasagh A, Nabavi SM, Kashani HRK, Abdollahian S, Habtemariam S, Rezabakhsh A. Anti-VEGF agents: as appealing targets in the setting of COVID-19 treatment in critically ill patients. *Int Immunopharmacol.* 2021;1(101):108257. doi:10.1016/j.intimp.2021.108257
30. Garcia LF. Immune response, inflammation, and the clinical spectrum of COVID-19. *Front Immunol.* 2020;11. doi:10.3389/fimmu.2020.01441
31. Scholl SM, Pallud C, Beuvon F, et al. Anti-colony-stimulating factor-1 antibody staining in primary breast adenocarcinomas correlates with marked inflammatory cell infiltrates and prognosis. *J Natl Cancer Inst.* 1994;86(2):120–126. doi:10.1093/jnci/86.2.120
32. Wan Z, Zhou Z, Liu Y, et al. Regulatory T cells and T helper 17 cells in viral infection. *Scand J Immunol.* 2020;91(5):e12873. doi:10.1111/sji.12873
33. Peng S, Patil N. Study correlating lymphocyte to monocyte ratio and platelet to lymphocyte ratio with the severity in COVID-19 patients: a cross sectional study. *Int J Adv Med.* 2021;8(2):201–206. doi:10.18203/2349-3933.ijam20210264
34. Wang X, Li X, Shang Y, et al. Ratios of neutrophil-to-lymphocyte and platelet-to-lymphocyte predict all-cause mortality in inpatients with coronavirus disease 2019 (COVID-19): a retrospective cohort study in a single medical centre. *Epidemiol Infect.* 2020;3:148.
35. Javadi A, Dabiri S, Meymandi MS, et al. Changes of routine hematological parameters in COVID-19 patients: correlation with imaging findings, RT-PCR and outcome. *Iran J Pathol.* 2022;17(1):37–47. doi:10.30699/ijp.2021.533645.2675

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