Clinical Medicine and Health Research Journal (CMHRJ)
Volume 03, Issue 05, September - October, 2023
Page No. 626-631,

Research Article

Hemogram Parameters and Hemogram-Derived Ratios in Covid-19 Severity

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Received: 15 September, 2023 Accepted: 18 October, 2023 Published: 24 October 2023

Abstract:

Background: Understanding the hematological manifestations of the COVID-19, is of paramount importance in terms of patient management and prognosis.

Aim: To review the fundamental hemogram parameters and their clinical significance.

Methods: This is a retrospective, cross-sectional, and observational investigation. Hemogram findings of the participants within 30 days following the onset of symptoms were analyzed. Participants were categorized into moderate and severe groups based on the assessment of disease severity.

Results: Both erythrocyte sedimentation rate and C-reactive protein are considerably elevated in both groups, with higher levels observed in the severe group compared to the moderate group. The percentage of neutrophils, is elevated above normal in both groups, with the severe group demonstrating higher values. The statistical difference between the groups is significant.

Conclusion: Hemogram-derived ratios would be beneficial to include them in common laboratory practices.

Keywords: Severity of COVID-19, hemogram parameters, hemogram-derived ratios.

1. Introduction

The COVID-19 pandemic, induced by the novel coronavirus SARS-CoV-2, has posed significant challenges to global healthcare systems. Understanding the hematological manifestations of the disease, as reflected in hemogram values, is of paramount importance in terms of patient management and prognosis (1).

Hemogram parameters encompassing various metrics offer valuable insights into the pathophysiology and severity of COVID-19. Given that the disease primarily targets the respiratory system, it can also exert systemic effects, including hematological alterations (2).

Hemogram values constitute an integral component in evaluating the clinical course and severity of COVID-19. Monitoring these parameters can assist in risk stratification, early intervention, and informed decision-making. As our comprehension of COVID-19 continues to evolve, ongoing research remains crucial for enhancing our understanding of hematological findings and their clinical significance in this pandemic (3).

Lymphocyte counts notably decrease, particularly in severe cases of COVID-19. Lymphopenia is regarded as a significant marker of immune dysregulation and an indicator of disease severity. A high neutrophil-to-lymphocyte ratio is associated with an increased risk of severe illness and poor prognosis, reflecting the balance between innate and acquired immune responses (4). Thrombocytopenia (a low platelet count) has been observed in some COVID-19 patients, especially in those with severe disease. Platelet dysfunction can contribute to a prothrombotic state (5). Although not specific to COVID-19, monitoring hemoglobin and hematocrit levels is necessary to assess the overall health status of patients, especially those with comorbidities. Red cell distribution width, which is associated with a worse prognosis in COVID-19 patients, can be used as an indicator of systemic inflammation and impaired oxygenation (6).

Identifying patients at risk of developing severe illness in COVID-19 cases is imperative (7). To achieve this goal, it is crucial to identify accurate, simple, and cost-effective prognostic tools for patient classification (8). Common laboratory parameters and inflammatory markers, along with their variations, have been reported in COVID-19 patients (9,10) but their relationship with disease severity is still under investigation (11).

The purpose of this article is to review the fundamental hemogram parameters frequently observed in COVID-19 patients and their clinical significance.

2. Materyal and Metot

2.1 Study Population

The study included 1000 individuals diagnosed with COVID-19 by seeking care at a tertiary healthcare center as the third-tier of referral. Those who did not meet the criteria were excluded from the study, resulting in a study cohort comprising 950 participants.

2.2 Exclusion Criteria

- Chronic respiratory disease,
- Individuals under the age of 18,
- Those who have not had their COVID-19 diagnosis confirmed by Real time-Polymerized Chain Reaction (Rt-PCR),
- Those with incomplete laboratory data have been excluded from the study.

2.3 Study Design and Participants

Our study is a retrospective and, cross-sectional investigation. The study data were obtained from hospital records. Laboratory findings of the participants within 30 days following the onset of symptoms were analyzed. Additionally, demographic characteristics, the presence of chronic diseases, and data related to molecular and radiological analyses were examined, sourced from electronic medical records. In accordance with the guidelines of the World Health Organization (WHO), the COVID-19 diagnoses of the participants were confirmed using Rt-PCR (12). Chest radiography was employed for the detection of inflammation, while radiological findings were utilized to differentiate pneumonia. Current guidelines on the severity of COVID-19 were consulted to make determinations. Participants were categorized into moderate and severe groups based on the assessment of disease severity (12).

2.4 Groups

The participants were grouped according to demographic characteristics, such as gender (female-male) and age categories (young-elderly or elderly-very elderly). Elderly status was determined in accordance with the criteria set forth by the WHO, with a threshold age of 74 years established. Two distinct groups were subsequently delineated: those aged up to 75 years and those aged 75 years and older. The severity of COVID-19 disease is divided into five groups in terms of clinical symptoms, laboratory and radiographic abnormalities, hemodynamics and organ functions. The severity of COVID-19 disease is divided into five groups in terms of clinical symptoms, laboratory and radiographic abnormalities, hemodynamics and organ functions. These are:

- Asymptomatic or presymptomatic infection,
- Mild,
- Moderate,
- Severe,
- Critical illness (12).

In our study, participants in the symptomatic or presymptomatic infection, mild and moderate groups were combined to create the "moderate" group. Similarly, severe and critical groups are grouped together as "severe".

2.5 Measurements

Our research encompasses the analysis of hemogram parameters, hemogram-derived ratios, activated partial thromboplastin time (aPTT), International Normalized Ratio (INR), C-reactive protein (CRP) and erytrocyte sedimantation rate (ESR). The aPTT values are given in seconds, INR values in minutes, CRP values in milligrams per deciliter (mg/dL) and ESR values in millimeters per hour (mm/h).

2.5.1 The hemogram parameters subjected to analysis are enumerated below.

- Hemoglobin (Hb)
- Hematocrit (Hct)
- Red Blood Cell Count (RBC)
- Mean Corpuscular Volume (MCV)
- Mean Corpuscular Hemoglobin (MCH)
- Mean Corpuscular Hemoglobin Concentration (MCHC)
- Red Cell Distribution Width (RDW)
- White Blood Cell (WBC)
- Platelet Count (PLT)
- Mean Platelet Volume (MPV)
- Lymphocyte, Monocyte, Neutrophil, Eosinophil, and Basophil among all WBC (respectively referred to as LYM, MON, NEUT, EOS, and BAS).

2.5.2 Hemogram-derived ratios included in the analysis are listed below.

- Percentages of Lymphocytes, Monocytes, Neutrophils, Eosinophils, and Basophils among all WBC (respectively referred to as LYM%, MON%, NEUT%, EOS%, and BAS%).

2.6 Ethics

The institution where the research was conducted has obtained ethical approval from the ethics committee. All procedures related to the research are in accordance with the Helsinki Declaration.

2.7 Statistical Analysis

In the analysis of our data, the software package SPSS 25.0 for Windows (SPSS Inc, Chicago, Illinois, USA) and Microsoft Excel (Microsoft Corporation, USA) were employed. The distribution of the data was assessed using the Kolmogorov-Smirnov test. Categorical variables were analyzed using the chi-squared test, and these variables were presented in both numerical and percentage formats. Parametric continuous variables were presented in terms of mean and standard deviation. Independent samples t-tests were employed to analyze these variables.

3. Results

In our study, there were 544 female and 406 male participants. Among the participants, 508 were aged 75 and above, while 442 participants were below 75 years of age, falling into the young-elderly category. Pneumonia was detected in 617 participants, with 254 of them classified as severe cases. Among the participants, 532 had chronic illnesses, and out of these, 231 were categorized as severe cases. The demographic characteristics of the participants, along with the presence of pneumonia and chronic illnesses, were compared in terms of the severity of COVID-19. Accordingly, statistically significant differences were found among groups in terms of gender, age, the presence of pneumonia, and the presence of chronic

illnesses (Table 1).

Table 1. Comparison of Moderate and Severe COVID-19 Cases in Terms of Various Variables.

Variables		Moderate		Severe		p
		n	%	n	%	
Gender	**Male**	278	55,4	266	59,9	**0,04**
	Female	227	44,6	179	40,1	
Age	**<75**	307	41,9	105	33,8	**0,02**
	≥75	333	52,1	205	66,2	
Pneumonia	**Yes**	325	38,1	108	29,7	**<0,01**
	No	363	61,9	254	70,3	
Chronic Disease	**Yes**	253	45,5	165	41,6	**0,03**
	No	301	54,5	231	58,4	

Moderate and severe cases of COVID-19 have been compared in terms of hemogram values. According to this comparison, the MCHC value is within normal limits in moderate cases, while in severe COVID-19 cases, it is lower than the normal range. aPTT values are found to be within normal limits in moderate cases, whereas in severe cases, they are elevated beyond the normal range. Both ESR and CRP are considerably elevated in both groups, with higher levels observed in the severe group compared to the moderate group. The differences between the groups are statistically significant in these parameters. A similar pattern is observed in the neutrophil count, where levels are above normal in both groups, with the severe group exhibiting higher levels than the moderate group. Statistically, there is a significant difference between the groups in terms of neutrophil count. Other values are within normal limits in both groups, and there is no statistically significant difference between the groups in these parameters.

Table 2. Comparison of Moderate and Severe COVID-19 Cases in Terms of Hemogram Values.

Variables (Normal Values)	Moderate (Mean±SD)	Severe (Mean±SD)	p
Hb (14-18)	10,44±1,7	9,90±1,3	0,61
Hct (41-53)	34,42±3,3	32,55±2,6	0,74
RBC (4.5-5.9)	3,32±0,5	3,21±0,9	0,76
MCV (80-92)	89,12±9,2	84,12±6,2	0,45
MCH (28-33)	28,87±3,2	28,23±2,6	0,80
MCHC (32-36)	33,29±2,8	31,66±4,2	0,68
RDW (11-16)	14,04±2,7	16,02±1,6	0,55
WBC (4.5-11)	9,22±5,2	11,39±6,2	0,59
PLT (130-400)	199,81±38,2	184,92±26,5	0,66
MPV (9-13)	12,10±2,2	11,09±1,8	0,71
aPTT (22-36)	28,8±1,3	29,3±2,1	0,52
INR (0.8-1.2)	1.11±0,3	1.39±0,4	0,09
ESR (0-20)	35,3±4,8	50,2o±8,0	**0,02**
CRP (<3)	29,3±10,2	54,45±12,8	**0,01**
LYM (0.9 - 5.2)	0.97±0,2	1.17±0,5	0,08
MON (0.1-0.9)	0.47±0,0	0.38±0,0	0,08
NEUT (1.8-7.9)	6.51±2,8	13.59±4,3	**0,01**
EOS (0,0-0,8)	0.13±0,0	0.15±0,0	0,3
BAS (0,0-0.2)	0,01±0,0	0,01±0,0	0,8

The hemogram-derived ratios in moderate and severe COVID-19 cases have been compared. According to this analysis, the NEUT% value is elevated above normal in both groups, with the severe group demonstrating higher values than the moderate group. The statistical difference between the groups is significant. Other parameters fall within normal limits. The values in the severe group are higher than those in the moderate group, but there is no statistically significant difference between the two groups.

Table 3. Comparison of Moderate and Severe COVID-19 Cases in Terms of Hemogram-Derived Ratios.

Variables (Normal Values)	Moderate (Mean±SD)	Severe (Mean±SD)	p
LYM% (25-40)	11.7±1,2	12.2±2,5	0,65
MON% (3-8)	5,44±1,8	7,66±1,4	0,11
NEUT% (50-70)	76.8±11,2	89,6±14,3	**0,04**
EOS% (0-7)	2,32±0,8	3,44±1,1	0,56
BAS% (0-2)	0,12±0,0	0,15±0,0	0,09

4. Discussion

Of the 617 pneumonia cases detected in our study, 254 were classified as severe cases. Similarly, 231 of the 532 chronic diseases in the participant were classified as severe cases. These data and the demographic characteristics of the participants were compared in terms of the severity of COVID-19. Statistically significant differences were found between the groups in terms of gender, age, pneumonia and chronic disease. Moderate and severe Covid-19 cases were compared in terms of hemogram values. ESR and CRP values are significantly higher in both groups. The differences between groups are statistically significant. The neutrophil count is above normal in both groups and there is a statistically significant difference between the groups. Other values are within normal limits in both groups.

Hemogram-derived ratios were compared in moderate and severe Covid-19 cases. According to this analysis, the NEUT% value is above normal in both groups. It is higher in the severe group than in the moderate group. The statistical difference between the groups is significant. Other parameters are within normal limits.

COVID-19 pandemic has highlighted the crucial role of laboratory diagnostics in patient management. Among the various laboratory tests, a complete blood count with differential, commonly known as a hemogram, emerges as a valuable tool for assessing disease severity, monitoring progression, and guiding clinical decisions in COVID-19 patients. In COVID-19, early diagnosis and appropriate management are essential for improving patient outcomes. Hemogram parameters provide valuable insights into the host response to infection, inflammation, and hematological alterations associated with COVID-19 (13).

The total WBC count is a fundamental component of the hemogram and serves as an indicator of the immune response. In COVID-19, alterations in WBC counts are frequently observed. Leukopenia, characterized by decreased WBC count, may signify viral suppression of bone marrow function, while leukocytosis, an elevated count, often reflects a hyperinflammatory state. Monitoring WBC counts assists in assessing disease progression and the response to therapies (14).

Lymphopenia, a marked decrease in lymphocyte counts, is a hallmark of severe COVID-19. It primarily affects CD4+ and CD8+ T lymphocytes. Reduced lymphocyte subsets are associated with impaired antiviral immune responses. Monitoring lymphocyte subsets is crucial in identifying patients at risk for severe disease and guiding therapeutic interventions (15).

Changes in Hct levels are common in COVID-19 patients. Elevated Hct, also known as hemoconcentration, may indicate dehydration or a prothrombotic state, while decreased levels may suggest anemia or blood loss. Hematocrit values can guide fluid management and help assess the risk of thrombotic complications in COVID-19 (16).

Hemogram parameters are integral in the clinical assessment and management of COVID-19. They provide insights into the immune response, inflammatory state, and hematological changes associated with the disease. Regular monitoring of these parameters assists healthcare professionals in risk stratification, early detection of complications, and tailoring therapeutic strategies for COVID-19 patients. Hemogram values serve as invaluable tools in the comprehensive evaluation of COVID-19 patients and play a pivotal role in optimizing clinical outcomes during this ongoing pandemic (17).

Hemogram-derived ratios, which encompass various parameters derived from complete blood count analysis, have emerged as valuable tools in the evaluation of COVID-19 patients. Hemogram-derived ratios, such as the neutrophil-to-lymphocyte ratio, lymphocyte-to-monocyte ratio, platelet-to-lymphocyte ratio, and others, serve as readily available, cost-effective, and non-invasive markers that can aid in risk stratification, early detection of severe cases, and monitoring disease progression (3).

Neutrophil-to-Lymphocyte Ratio, calculated as the ratio of absolute neutrophil count to absolute lymphocyte count, has emerged as a robust prognostic marker in COVID-19. This ratio is associated with an exaggerated inflammatory response and is indicative of poor outcomes. It can serve as an early warning sign for severe disease and guide therapeutic interventions (18).

Lymphocyte-Monocyte Ratio, calculated as the ratio of the absolute number of lymphocytes to the absolute number of monocytes, reflects the balance between adaptive and innate immune responses. It decreases in severe COVID-19 cases. It is related to impaired immune response and increased risk of complications (19).

Platelet-to-Lymphocyte Ratio calculated as the ratio of platelet count to lymphocyte count, has also demonstrated prognostic significance. It is associated with increased inflammation and is indicative of a more severe disease course. It can be particularly useful in identifying patients who may benefit from closer monitoring and aggressive management (20).

Various other ratios, such as the monocyte-to-lymphocyte ratio and the eosinophil-to-lymphocyte ratio, have shown promise in predicting disease severity and progression. These ratios offer additional insights into the inflammatory and immune status of COVID-19 patients.

The underlying mechanisms linking these ratios to COVID-19 pathogenesis involve dysregulated immune responses, cytokine storms, and endothelial dysfunction. Understanding these mechanisms can aid in tailoring treatment strategies (21).

Hemogram-derived ratios provide valuable insights into the inflammatory and immune status of COVID-19 patients. They offer a non-invasive and cost-effective means of risk stratification, early detection of severe cases, and monitoring disease progression. Integrating these ratios into clinical practice can enhance the management of COVID-19 patients and facilitate more timely interventions. However, further research is needed to validate their utility and establish standardized cutoff values for different populations and stages of the disease (21).

According to the results of a study, moderate disease was detected in 56.2% of the 500 participants, while severe disease was identified in 43.8% of them. Male participants predominated in both groups. The mean age in the moderate and severe groups was 56.9 and 62.1, respectively. There is a statistically significant difference in gender and age distribution between the two groups. Furthermore, there is a statistically significant difference in the number of participants with pneumonia detected among the groups (3). In our study, it is noteworthy that male participants predominate in both groups. Moreover, it is observed that in the severe group, there is a higher number of participants aged 75 and above. Furthermore, individuals with pneumonia and chronic diseases are predominantly present in the severe group. The distribution of all these variables has exhibited a statistically significant disparity between the moderate and severe groups.

COVID-19 is often detected as pneumonia. Chest x-ray, lung ultrasound and chest computed tomography are frequently used

in diagnosis. However, there are no proven data regarding the timing and selection of lung imaging. Bilateral multifocal alveolar opacities and pleural effusions are usually detected on chest x-ray. Radiological imaging is not a sensitive method for detecting this disease. Chest computed tomography is more sensitive than radiography but is not specific. No findings on radiographic imaging can completely rule out or rule out COVID-19 disease. The incidence of pneumonia increases with increasing disease severity (22).

This explains why pneumonia is more common in severe cases. Likewise, age and chronic disease are also effective in making COVID-19 more severe.

Inflammatory markers are used to predict the severity of inflammatory events. Serious clinical manifestations occur through the production of proinflammatory cytokines, which contribute to the development of lymphopenia, neutrophilia and thrombocytopenia, as well as inflammatory markers such as CRP. High CRP levels are associated with the severity of COVID-19. In our study, ESR and CRP values were found to be statistically significantly higher in the severe group compared to the moderate group. Our results are consistent with previous work (23–25).

In previous studies, some hemogram-derived ratios such as neutrophil-to-lymphocyte ratio (18), lymphocyte-monocyte ratio (19) and platelet-to-lymphocyte ratio (20) were found to be significant in evaluating the severity of COVID-19. The hemogram-derived ratios included in the analysis in our study are LYM%, MON%, NEUT%, EOS%, and BAS%. Of these, the only one found to be significant is NEUT%. Studies on the subject support the idea that neutrophils provide insight into the severity of CODID-19 (26,27).

5. Conclusion

The results obtained from our study showed that the percentages of "neutrophils among all WBC" parameter can be used as a potential marker in assessing the severity of COVID-19. In this way, a quick decision can be made about the severity of COVID-19. Hemogram-derived ratios are inexpensive parameters that can be easily calculated. Therefore, it would be beneficial to include them in common laboratory practices.

6. References

1. Shi Y, Wang G, Cai X-P, Deng J-W, Zheng L, Zhu H-H, et al. An overview of COVID-19. J Zhejiang Univ Sci B. 2020 May;21(5):343–60.
2. Avila E, Kahmann A, Alho C, Dorn M. Hemogram data as a tool for decision-making in COVID-19 management: applications to resource scarcity scenarios. PeerJ. 2020;8:e9482.
3. Segalo S, Kiseljakovic E, Papic E, Joguncic A, Pasic A, Sahinagic M, et al. The Role of Hemogram-derived Ratios in COVID-19 Severity Stratification in a Primary Healthcare Facility. Acta Inform medica AIM J Soc Med Informatics Bosnia Herzegovina Cas Drus za Med Inform BiH. 2023 Mar;31(1):41–7.
4. Zhao Q, Meng M, Kumar R, Wu Y, Huang J, Deng Y, et al. Lymphopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A systemic review and meta-analysis. Int J Infect Dis IJID Off Publ Int Soc Infect Dis. 2020 Jul;96:131–5.
5. Xu P, Zhou Q, Xu J. Mechanism of thrombocytopenia in COVID-19 patients. Ann Hematol. 2020 Jun;99(6):1205–8.
6. Abd El-Lateef AE, Ismail MM, Thabet G, Cabrido N-A. Complete blood cells count abnormalities in COVID-19 patients and their prognostic significance: Single center study in Makkah, Saudi Arabia. Saudi Med J. 2022 Jun;43(6):572–8.
7. Feng X, Li S, Sun Q, Zhu J, Chen B, Xiong M, et al. Immune-inflammatory parameters in COVID-19 cases: a systematic review and meta-analysis. Front Med. 2020;7:301.
8. Słomka A, Kowalewski M, Żekanowska E. Coronavirus disease 2019 (COVID–19): A short review on hematological manifestations. Pathogens. 2020;9(6):493.
9. Bellou V, Tzoulaki I, van Smeden M, Moons KGM, Evangelou E, Belbasis L. Prognostic factors for adverse outcomes in patients with COVID-19: a field-wide systematic review and meta-analysis. Eur Respir J. 2022;59(2).
10. Sudre CH, Lee KA, Ni Lochlainn M, Varsavsky T, Murray B, Graham MS, et al. Symptom clusters in COVID-19: A potential clinical prediction tool from the COVID Symptom Study app. Sci Adv. 2021;7(12):eabd4177.
11. Kermali M, Khalsa RK, Pillai K, Ismail Z, Harky A. The role of biomarkers in diagnosis of COVID-19–A systematic review. Life Sci. 2020;254:117788.
12. Rasband WS. US National Institutes of Health. http//imagej nih gov/ij/. 2011;
13. Suárez-Del-Villar-Carrero R, Martinez-Urbistondo D, Cuevas-Sierra A, Ibañez-Sustacha I, Candela-Fernandez A, Dominguez-Calvo A, et al. Hematological- and Immunological-Related Biomarkers to Characterize Patients with COVID-19 from Other Viral Respiratory Diseases. J Clin Med. 2022 Jun;11(13).
14. Aghbash PS, Rasizadeh R, Shirvaliloo M, Nahand JS, Baghi HB. Dynamic alterations in white blood cell counts and SARS-CoV-2 shedding in saliva: an infection predictor parameter. Front Med. 2023;10:1208928.
15. Huang I, Pranata R. Lymphopenia in severe coronavirus disease-2019 (COVID-19): systematic review and meta-analysis. J intensive care. 2020;8:36.
16. Russo A, Tellone E, Barreca D, Ficarra S, Laganà G. Implication of COVID-19 on Erythrocytes Functionality: Red Blood Cell Biochemical Implications and Morpho-Functional Aspects. Int J Mol Sci. 2022 Feb;23(4).
17. Peeling RW, Heymann DL, Teo Y-Y, Garcia PJ. Diagnostics for COVID-19: moving from pandemic response to control. Lancet (London, England). 2022 Feb;399(10326):757–68.
18. Toori KU, Qureshi MA, Chaudhry A, Safdar MF. Neutrophil to lymphocyte ratio (NLR) in COVID-19: A cheap prognostic marker in a resource constraint setting. Pakistan J Med Sci. 2021;37(5):1435–9.

19. Liu G, Zhang S, Hu H, Liu T, Huang J. The role of neutrophil-lymphocyte ratio and lymphocyte–monocyte ratio in the prognosis of type 2 diabetics with COVID-19. Scott Med J [Internet]. 2020 Aug 30;65(4):154–60. Available from: https://doi.org/10.1177/0036933020953516
20. Ravindra R, Ramamurthy P, Aslam S SM, Kulkarni A, K S, Ramamurthy PS. Platelet Indices and Platelet to Lymphocyte Ratio (PLR) as Markers for Predicting COVID-19 Infection Severity. Cureus. 2022 Aug;14(8):e28206.
21. Velazquez S, Madurga R, Castellano JM, Rodriguez-Pascual J, de Aguiar Diaz Obregon SR, Jimeno S, et al. Hemogram-derived ratios as prognostic markers of ICU admission in COVID-19. BMC Emerg Med. 2021 Jul;21(1):89.
22. Wong HYF, Lam HYS, Fong AH-T, Leung ST, Chin TW-Y, Lo CSY, et al. Frequency and Distribution of Chest Radiographic Findings in Patients Positive for COVID-19. Radiology. 2020 Aug;296(2):E72–8.
23. Kaya T, Nalbant A, Kılıççıoğlu GK, Çayır KT, Yaylacı S, Varım C. The prognostic significance of erythrocyte sedimentation rate in COVID-19. Rev Assoc Med Bras. 2021;67:1305–10.
24. Ahnach M, Zbiri S, Nejjari S, Ousti F, Elkettani C. C-reactive protein as an early predictor of COVID-19 severity. J Med Biochem. 2020;39(4):500.
25. Tonduangu N, Le Borgne P, Lefebvre F, Alame K, Bérard L, Gottwalles Y, et al. Prognostic value of C-reactive protein to lymphocyte ratio (CLR) in emergency department patients with SARS-CoV-2 infection. J Pers Med. 2021;11(12):1274.
26. Castanheira FVS, Kubes P. Neutrophils during SARS-CoV-2 infection: Friend or foe? Immunol Rev. 2023 Mar;314(1):399–412.
27. McKenna E, Wubben R, Isaza-Correa JM, Melo AM, Mhaonaigh AU, Conlon N, et al. Neutrophils in COVID-19: Not Innocent Bystanders. Front Immunol. 2022;13:864387.