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Original Article

Hematological Parameters in COVID-19 Patients: Association with Severity of the Disease

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Abstract

The novel coronavirus (COVID-19) produced severe acute respiratory coronavirus syndrome (SARS-CoV-2; formerly known as 2019-nCoV) and has mild to fatal symptoms. This study aimed to investigate the different blood markers in confirmed positive COVID-19 individuals and see how they associated with the severity of the condition. A cross-sectional study was conducted from September 2020 to March 2021 on seventy-six (20 female and 56 male) Iraqi patients unvaccinated against COVID-19. The mean age of the study subjects was (47.00±13.31; 43.86±14.27) for males and females, respectively. 68.42% of the cases with mild illness, 14.47% with moderate illness, and 17.10% were severely ill. The severity of COVID-19 was assessed by several hematological parameters, including white blood cell (WBC) count, derived indicators such as neutrophils to lymphocyte ratio (NLR) and IL6, C-reactive protein (CRP), D-dimer, and S-ferritin. The results showed that lymphocyte count was lower in severely ill patients compared to patients with mild and moderate symptoms, with a significant difference between the three groups (2.274.83). Additionally, the NLR results showed a significant rise (11.56±1.23) in severe COVID-19. The results of the present study indicated that serum levels of IL6, CRP, and S-ferritin revealed significant differences (41.20±6.23 pg/ml), (50.66±12.55 mg/l), and (454.60±95.69 ng/ml) at (P≤0.05) in sever ill compared with mild and moderately ill patients respectively. The results indicated a highly significant positive correlation between IL6 and severity of COVID-19 infection at P<0.01. Furthermore, a positive connection is seen in Neutrophil, CRP, and NLR (0.229, 0.264, and 0.277) at (P≤0.05) respectively.

Keywords: COVID-19, Disease Severity, Hematological Parameters, IL6, CRP

1. Introduction

The novel coronavirus (COVID-19) is responsible for severe acute respiratory coronavirus syndrome (SARS-CoV-2; previously known as 2019-nCoV) and has symptoms ranging from extremely mild to life-threatening (1). On January 30, 2020, the World Health Organization declared COVID-19 a global public health emergency due to the disease's rapid spread, which was already seen in December 2019 and January 2020 (2). Some complications include pneumonia, acute severe respiratory distress syndrome, renal insufficiency, and death (3).

Excessive inflammatory responses to SARS-CoV-2 are thought to impact disease severity and mortality in COVID-19-infected patients significantly. It has been linked to high levels of circulating cytokines, severe lymphopenia, and significant mononuclear cell infiltration in the lungs, spleen, heart, kidney, and lymph nodes (2). The World Health Organization (WHO) classified cases into three severity levels based on clinical symptoms: mild, severe, and critical. The C-reactive protein (CRP) is a systemic inflammatory response characterized by increased pro-inflammatory cytokines, such as interleukin-6. It can be triggered by

various factors, including infections, toxins, and others (4). To reduce case fatality, clinical monitoring and effective treatment measures were required. The CT scan was crucial in determining the severity of the disease (5).

Additionally, CRP levels can aid in the early detection of pneumonia (6). A combination of symptoms, risk factors, and a chest CT scan showing pneumonia characteristics can also be used to identify the infection (7). The CRP and interleukin 6 (IL-6) levels increased in the severe stage of the illness, according to a study by Liu, Li (8). A combination of laboratory testing was used to determine the prognosis and state of hyper inflammation, e.g., neutrophil-to-lymphocyte ratios (NLR). COVID-19 causes changes in lymphocytes, white blood cells, platelets, neutrophils, and other hematological markers (9). Lymphopenia was previously recorded and was the most prevalent blood count abnormality (10, 11).

According to various studies, NLR was higher in severe patients than in those with mild or moderate disease (12). Wang (2) claimed in previous research that increased CRP is associated with lung lesions and hence indicates the severity of the disease. The D-dimer is a fibrin degradation product, and its amount grows as the severity of community-acquired pneumonia increases (13). This study aimed to investigate the different blood markers in confirmed positive COVID-19 individuals and see how they associated with the severity of the condition.

2. Materials and Methods

2.1. Study Population

A cross-sectional study was conducted from September 2020 to March 2021. All patients aged (23-81) years with confirmed COVID-19 infection and who were unvaccinated against COVID-19 at Merjan Medical City Hospital, Babylon, Iraq, were included. Diagnosis of COVID-19 was made according to the clinical signs and diagnosis of the consultant physician. It mainly includes an epidemiological history, clinical symptoms, chest CT examination, and detection RT-PCR confirmed the results of COVID-19. According to National Health Commission (14), the clinical classification at admission consists of one of three types: mild, moderate, and severe cases.

2.2. Biological Markers

Blood samples from patients with positive RT-PCR results for SARS-CoV-2 were sent for Complete blood count (CBC), IL6, CRP, D-dimer, and S-ferritin as the biological markers examined in this study. The Beckman Coulter Analyzer system performs the CBC test automatically using Beckman Coulter Kit Solution (Beckman, Germany). Serum IL-6 assays, S-ferritin, and CRP, were determined by electro-chemiluminescence immunoassay (Roche Diagnostics GmbH, Mannheim, Germany).

2.3. Biostatistical Consideration

Data were analyzed using SPSS (version 20, SPSS Inc. Chicago, Illinois, USA). Descriptive statistics (mean, standard deviation) and differences were compared by one-way ANOVA at $P \leq 0.05$ using Duncan's Multiple Range Test to compare means and determine significance between variables ($P \leq 0.05$). It was conducted using a t-test student test for comparing two groups. Spearman correlation coefficient (r) determined the relationship between the studied parameters.

3. Results and Discussion

The global prevalence of COVID-19 patients has increased. When studying the COVID-19 outbreak, it is critical to evaluate clinical, demographic, and hematological variables. The current study enrolled 76 positive individuals with Covid-19 from Merjan Hospital in Babylon, Iraq. Based on the symptoms and confirmation by CT-scan and RT-PCR, as per the Government of Iraq Ministry of Health guidelines, cases were categorized as mild, moderate, and severely ill. The mild cases were (68.42%), (14.47%) with moderate symptoms, and (17.10%) cases were severely ill (Table 1).

Table 1. The study subjects' essential characteristics

Characteristics	All patients n=76	Mild 52(68.42%)	Moderate 11(14.42%)	Sever 13(17.10%)	*P*-value
			No %		
Female	20 (26.3%)	12(60%)	2 (10%)	6(30%)	0.041*
Male	56 (73.6%)	40(71.43%)	9(16.07%)	7 (12.50%)	
			Age (years)		
19-34	20	16 (80%)	3 (15%)	1(5%)	0.005*
35-50	33	26 (78.79%)	2 (6.06%)	5 (15.15%)	
51-66	17	9 (52.94%)	5 (29.41%)	3 (17.65%)	
67-82	6	1 (16.67%)	1 (16.67%)	4 (66.67%)	
Age mean (year)	Male	Female			
	Mean±S.D				
	47.00±13.31	43.86±14.27			0.860

3.1. Patients' Characteristics

Table 1 shows 76 patients with positive COVID-19, with a mean age of (47.00±13.31; 43.86±14.27) for males and females, respectively. Among the total individuals (76), 20 (26.31%) were females, while 56 (73.68%) were males. The age categories vary from (23-80) years; 26.3% were between the ages of 19 and 34, 43.4% were between the ages of 35 and 50, 22.3% were between the ages of 51 and 66, and 7.8% were between the ages of 67 and 82. It was found that significantly frequent patients in the age range from (35-50) years ($P \leq 0.05$). A previous study by Usul, Şan (15) reported a higher frequency of COVID-19 infection in males than females. Another recent meta-analysis of 3,111,714 reported global cases indicated no difference between males and females with confirmed COVID-19 infection (16). Previous studies by Klein and Morgan (17) and Mo, Xing (18) indicated that when COVID-19 progresses and becomes more severe, the hospitalization rate for males is 50 percent higher than for females.

Fever (64.47%), Nasal congestion (44.73%), Cough (73.68), and Diarrhea (51.31%) were the common symptoms table 2. A previous World Health Organization (19) study reported that COVID-19 typically causes a fever and cough between 2 and 14 days after exposure to the virus in some people, especially the elderly and those with underlying chronic health conditions. These symptoms can progress to pneumonia, characterized by chest tightness, discomfort, shortness of breath, and a dry cough that necessitates hospitalization.

Table 2. Frequency of different symptoms among COVID-19 patients

Characteristics	No % (76)
Symptoms	
Fever	49 (64.47%)
Diarrhea	39 (51.31%)
Cough	56 (73.68%)
Nasal congestion	34 (44.73%)

3.2. Hematological Parameters

Table 3 shows that lymphocytopenia was seen in severely ill patients compared to patients with mild and moderate symptoms, with a significant difference between the three groups (2.274.83). The results showed a rise (7.49±4.14) in neutrophil count in the severe patients but no significant differences among groups ill. For COVID-19 patients, the ratio of neutrophils to lymphocytes (NLR) predicts disease progression, critical cases, and death. The NLR results showed a significant rise (11.56±1.23) in severe COVID-19. A complete blood count is one of the most important and readily available investigations for COVID-19 infection detection and severity assessment. According to a previous study, the number of white blood cells (WBCs) increased with the severity of COVID-19 disease (20).

Increased neutrophils represent the severity of the

inflammatory response, whereas reduced lymphocytes suggest the severity of the immunological imbalance in COVID-19. The concept of NLR amplifies these correlations (21). The present results support Xu, Shi (22), who revealed that fatal SARS-CoV-2 infection cases had higher neutrophil numbers and lower lymphocyte counts. The measurement of lymphocyte functions has been proposed to determine the severity of COVID-19 disease (23). In various clinical conditions, the NLR has emerged as a powerful inflammatory marker with diagnostic and prognostic relevance. Lymphocytes and neutrophils have essential roles in the etiology of many diseases and immunological defense, according to a previous study (24). A previous study by (25) reported that Neutrophil counts are thought to reflect the inflammatory state as the disease progress. In contrast, lymphocyte counts are thought to represent the consequence of regulated immune responses. Al-Khafaji, Abdulla (26) noted the diagnosis that CT imaging is helpful along with CBC and CRP assays as a primary screening test.

Table 4 depicts comparisons of serum biochemistry parameters. A study of mild, moderate, and severe symptom patients revealed a significant difference in IL6, CRP, D-dimer, and S-ferritin levels.

The results of the present study indicate that serum levels of IL6, CRP, and S-ferritin revealed high significant differences (41.20±6.23 pg/ml), (50.66±12.55 mg/l), and (454.60±95.69 ng/ml) at ($P\leq0.05$) in sever ill compared with mild and moderately ills respectively. While the level of D-dimer suggests that significant deference (380.15±158.29 ng/ml) at ($P\leq0.05$) in moderate ill compared with mild and severe ills (235.41±78.52) and (315.19±140.25) ng/ml respectively. Regarding the level of zinc, there was no significant difference among the ill groups. Lymphopenia, CRP levels, ferritin, and D-dimer levels are used to determine the severity of the disease and thus the prognosis. Increased D-dimer and Fibrinogen degradation products suggest systemic hypercoagulability and may signify the onset of venous thromboembolism (27).

Table 3. Hematological parameters in different illness groups of COVID-19 patients

Severity Parameters	Mild	Moderate	Sever
		Mean±S.E	
RBC ($\times10^6$/µl)	4.82±0.07[a]	4.77±0.18[a]	4.68±0.16[a]
WBC (cell$\times10^3$/µl)	7.86±1.13[a]	8.01±0.38[a]	9.70±0.22[a]
Lym (cell$\times10^3$/µl)	3.28±2.77[a]	4.85±8.80[b]	2.27±4.83[a]
Neu (cell$\times10^3$/µl)	6.78±1.71[a]	7.33±3.08[a]	7.49±4.14[a]
Bas (cell$\times10^3$/µl)	0.82±0.19[b]	0.54±0.27[a]	1.02±0.40[b]
Eos (cell$\times10^3$/µl)	1.23±0.25[b]	0.41±0.11[a]	0.47±0.14[a]
HCT (%)	38.66±0.78[a]	34.05±3.77[a]	36.82±1.90[a]
HGB	12.84±0.22[a]	12.80±0.55[a]	12.23±0.64[a]
Neu /Lym ratio (NLR)	2.99±0.29[a]	2.42±0.69[a]	11.56±1.23[b]

Different letters in the same row mean a significant difference

Table 4. Values of different serum biochemical parameters in different illness groups of COVID-19 patients

Severity Parameters	Mild	Moderate	Sever
		Mean±S.E	
IL-6 (pg/ml)	6.07±0.94[a]	5.26±1.02[a]	41.20±6.23[b]
CRP (mg/L)	20.72±4.35[a]	17.58±13.19[a]	50.66±12.55[b]
D-dimer(ng/ml)	235.41±78.52[a]	380.15±158.29[c]	315.19±140.25[b]
S-ferritin(ng/ml)	326.41±46.33[a]	330.05±86.35[a]	454.60±95.69[b]
Zinc	61.63±1.34[a]	64.73±3.23[a]	64.31±2.23[a]

Different letters in the same row mean a significant difference

Furthermore, CRP can be used as a predictor of pneumonia and the severity of COVID (28, 29). IL-6 is a crucial measure in determining the severity of the cytokine storm and inflammation in COVID-19 disease. IL-6, a pleiotropic cytokine, can influence various immune and physiological processes, including the production of acute-phase protein and inflammation and the activation of antigen-specific immune responses, apoptosis, hematopoiesis, differentiation, and cellular metabolism (30).

3.3. The Person Correlation Analysis of COVID-19 Patients

As shown in table 5, the correlation between all study markers WBC types (Neutrophil, Lymphocyte, Basophil, and Eosinophil), RBC, HCT, HGB, IL6, D-dimer, S-ferritin, CRP, NLR, and Zinc of the patient group was explained. A critical, highly significant positive correlation was found between IL6 and severity (0.455) at ($P \leq 0.05$) levels. Furthermore, a positive connection is seen in Neutrophil, CRP, and NLR (0.229, 0.264, and 0.277) at ($P<0.05$), respectively.

Several studies have found that increased sera IL-6 levels in patients with COVID-19 infection were positively connected with severity and death (31). As previously stated by Fox, Akmatbekov (32), they found that the severity of pulmonary immune damage is associated with the presence of large numbers of neutrophils and macrophages in the lung tissues. A study by Wang (2) noted that the CRP levels are positively associated with inflammatory severity and represent the severity of lung lesions.

According to the findings of this study, the levels of IL-6 in the severe group (41.2) were significantly higher than in the mild (6.07) and moderate groups (5.26) (Figure 1).

Some researchers found IL-6 expression in COVID-19 patients, implying that increased IL-6 and other cytokine levels were associated with disease severity (33). High IL-6 levels in COVID-19 patients are thought to be the most objective proof of the ongoing "cytokine storm," as seen in patients with septic shock and heart surgery (34, 35). The present study revealed the levels of CRP in the severe group (50.66) were significantly higher than in the mild (20.72) and moderate groups (17.58) (Figure 2).

The neutrophils lymphocyte ratio (NLR) was significantly higher in severe (11.56) than in mild and moderate ill (2.99 and 2.42), respectively (Figure 3).

Table 5. Pearson correlation coefficient between severity of disease and all parameters

		HCT	HGB	LYM	Neu	Bas	Eos	RBC	D-dimer	S ferritin	IL6	CRP	Zinc	WBC	NLR
Severity of disease	r	-.147	-.119	-.086	.229*	.030	-.216	-.101	.075	.133	.455**	.264*	.126	.094	.277*
	Sig.	.204	.307	.462	.046	.796	.060	.384	.519	.252	.000	.021	.277	.422	.015

*. Correlation is significant at the 0.05 level (2-tailed)

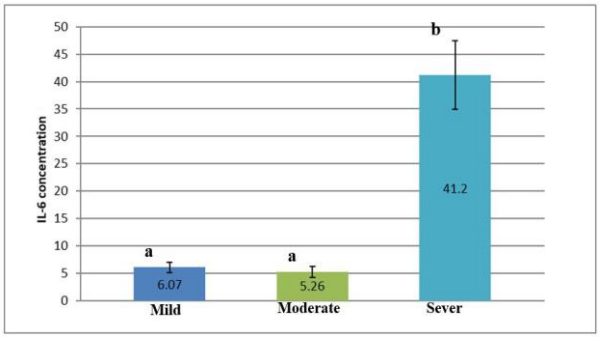

Figure 1. IL6 (pg/ml) in various levels of COVID-19-infected patients

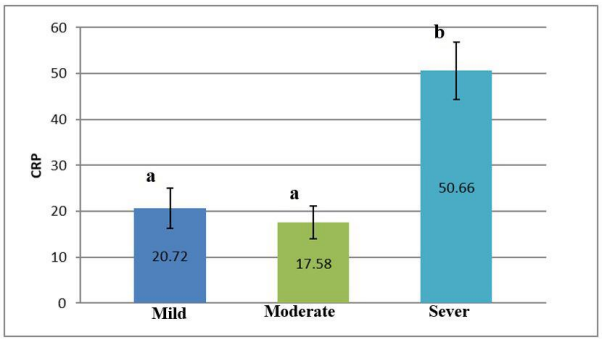

Figure 2. CRP (mg/L) in different levels of COVID-19-infected patients

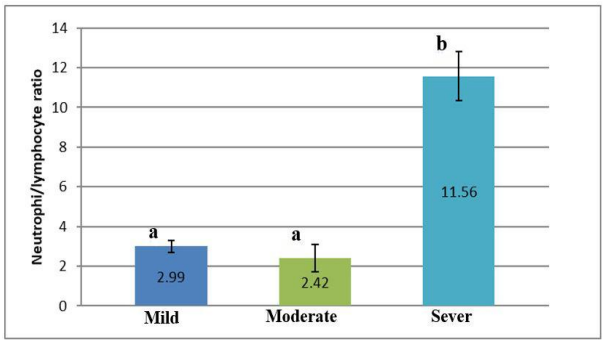

Figure 3. Neutrophil's lymphocyte ratio (NLR) in different levels of COVID-19-infected patients

Several studies reported that patients with severe COVID-19 infection had a higher NLR than those with less severe COVID-19 infection (36, 37).

In this study, we assessed the hematological and serum parameters in a peripheral blood sample from Iraqi COVID-19 patients. These indicators can be used to detect and assess illness progression, and cautions can be taken for the patient before the patient's clinical condition worsens, potentially lowering morbidity and mortality.

Authors' Contribution

Study concept and design: A. A. A.
Acquisition of data: A. A. A.
Analysis and interpretation of data: T. A. A.
Drafting of the manuscript: E. F. A. A.
Critical revision of the manuscript for important intellectual content: A. A. A.
Statistical analysis: T. A. A.
Administrative, technical, and material support: E. F. A. A.

Ethics

The study protocol was reviewed by the University Committee on health studies which uses the guidelines of MOH and MOHSER, and approved under number 389 in / 2020.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Gao Z, Xu Y, Sun C, Wang X, Guo Y, Qiu S, et al. A systematic review of asymptomatic infections with COVID-19. J Microbiol Immunol Infect. 2021;54(1):12-6.
2. Wang L. C-reactive protein levels in the early stage of COVID-19. Med Mal Infect. 2020;50(4):332-4.
3. Lai C-C, Shih T-P, Ko W-C, Tang H-J, Hsueh P-R. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. Int J Antimicrob Agents. 2020;55(3):105924.
4. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 2020;46(5):846-8.
5. Lin C, Ding Y, Xie B, Sun Z, Li X, Chen Z, et al. Asymptomatic novel coronavirus pneumonia patient outside Wuhan: the value of CT images in the course of the disease. Clin Imaging. 2020;63:7-9.
6. Warusevitane A, Karunatilake D, Sim J, Smith C, Roffe C. Early diagnosis of pneumonia in severe stroke: clinical features and the diagnostic role of C-reactive protein. PloS one. 2016;11(3):e0150269.
7. Velavan TP, Meyer CG. The COVID-19 epidemic. Tropical medicine & international health. 2020;25(3):278.
8. Liu F, Li L, Xu M, Wu J, Luo D, Zhu Y, et al. Prognostic value of interleukin-6, C-reactive protein, and procalcitonin in patients with COVID-19. J Clin Virol. 2020;127:104370.
9. Soni M. Evaluation of eosinopenia as a diagnostic and prognostic indicator in COVID-19 infection. Int J Lab Hematol. 2021;43:137-41.
10. Mousavi SA, Rad S, Rostami T, Rostami M, Mousavi SA, Mirhoseini SA, et al. Hematologic predictors of mortality in hospitalized patients with COVID-19: a comparative study. Hematology. 2020;25(1):383-8.
11. Sanchez-Pina JM, Rodríguez Rodriguez M, Castro Quismondo N, Gil Manso R, Colmenares R, Gil Alos D, et al. Clinical course and risk factors for mortality from COVID-19 in patients with haematological malignancies. Eur J Haematol. 2020;105(5):597-607.
12. Liu Y, Du X, Chen J, Jin Y, Peng L, Wang HH, et al. Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19. J Infect. 2020;81(1):e6-e12.
13. Querol-Ribelles JM, Tenias JM, Grau E, Querol-Borras JM, Climent JL, Gomez E, et al. Plasma d-dimer

levels correlate with outcomes in patients with community-acquired pneumonia. Chest. 2004;126(4):1087-92.
14. Commission NH. Translation: Diagnosis and treatment protocol for novel coronavirus pneumonia (trial version 7). Infect Microbes Dis. 2020;2(2):48-54.
15. Usul E, Şan İ, Bekgöz B, Şahin A. Role of hematological parameters in COVID-19 patients in the emergency room. Biomark Med. 2020;14(13):1207-15.
16. Peckham H, de Gruijter NM, Raine C, Radziszewska A, Ciurtin C, Wedderburn LR, et al. Male sex identified by global COVID-19 meta-analysis as a risk factor for death and ITU admission. Nat Commun. 2020;11(1):1-10.
17. Klein SL, Morgan R. The impact of sex and gender on immunotherapy outcomes. Biol Sex Differ. 2020;11(1):1-10.
18. Mo P, Xing Y, Xiao Y, Deng L, Zhao Q, Wang H, et al. Clinical characteristics of refractory COVID-19 pneumonia in Wuhan, China. Clin Infect Dis. 2020.
19. Organization WH. Coronavirus disease 2019 (COVID-19): situation report, 73. 2020.
20. Di Gennaro F, Pizzol D, Marotta C, Antunes M, Racalbuto V, Veronese N, et al. Coronavirus diseases (COVID-19) current status and future perspectives: a narrative review. Int J Environ Res Public Health. 2020;17(8):2690.
21. Zahorec R, Hulin I, Zahorec P. Rationale Use of Neutrophil-to-lymphocyte ratio for early diagnosis and stratification of COVID-19. Bratisl Lek Listy. 2020;121(7):466-70.
22. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med. 2020;8(4):420-2.
23. Bajgain KT, Badal S, Bajgain BB, Santana MJ. Prevalence of comorbidities among individuals with COVID-19: A rapid review of current literature. Am J Infect Control. 2021;49(2):238-46.
24. Wang W, Wang Y, Qu C, Wang S, Zhou J, Cao W, et al. The RNA genome of hepatitis E virus robustly triggers an antiviral interferon response. Hepatology. 2018;67(6):2096-112.
25. Kwon JH, Jang JW, Kim YW, Lee SW, Nam SW, Jaegal D, et al. The usefulness of C-reactive protein and neutrophil-to-lymphocyte ratio for predicting the outcome in hospitalized patients with liver cirrhosis. BMC Gastroenterol. 2015;15(1):1-7.
26. Al-Khafaji NS, Abdulla AA, Kunwar PS, Mohammed SS, Mohammed RK, Al-Marzoki AH, et al. Coronaviruses seven outbreaks associated with OC43, 229E, severe acute respiratory syndrome-CoV1, NL63, HKU1, Middle East respiratory syndrome coronavirus, and severe acute respiratory syndrome-CoV2. Drug Invent Today. 2020;13(6).
27. Wool GD, Miller JL. The impact of COVID-19 disease on platelets and coagulation. Pathobiology. 2021;88(1):15-27.
28. Cekerevac I, Turnic TN, Draginic N, Andjic M, Zivkovic V, Simovic S, et al. Predicting severity and intrahospital mortality in COVID-19: the place and role of oxidative stress. Oxid Med Cell Longev. 2021;2021.
29. Pimentel MA, Redfern OC, Hatch R, Young JD, Tarassenko L, Watkinson PJ. Trajectories of vital signs in patients with COVID-19. Resuscitation. 2020;156:99-106.
30. Moore JB, June CH. Cytokine release syndrome in severe COVID-19. Science. 2020;368(6490):473-4.
31. Coperchini F, Chiovato L, Croce L, Magri F, Rotondi M. The cytokine storm in COVID-19: An overview of the involvement of the chemokine/chemokine-receptor system. Cytokine Growth Factor Rev. 2020;53:25-32.
32. Fox SE, Akmatbekov A, Harbert JL, Li G, Brown JQ, Vander Heide RS. Pulmonary and cardiac pathology in African American patients with COVID-19: an autopsy series from New Orleans. Lancet Respir Med. 2020;8(7):681-6.
33. Gong J, Dong H, Xia Q, Huang Z, Wang D, Zhao Y, et al. Correlation analysis between disease severity and inflammation-related parameters in patients with COVID-19 pneumonia. MedRxiv. 2020.
34. Honore PM, Hoste E, Molnár Z, Jacobs R, Joannes-Boyau O, Malbrain ML, et al. Cytokine removal in human septic shock: where are we and where are we going? Ann Intensive Care. 2019;9(1):1-13.
35. Le RQ, Li L, Yuan W, Shord SS, Nie L, Habtemariam BA, et al. FDA approval summary: tocilizumab for treatment of chimeric antigen receptor T cell-induced severe or life-threatening cytokine release syndrome. Oncologist. 2018;23(8):943-7.
36. Chan AS, Rout A. Use of neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios in COVID-19. J Clin Med Res. 2020;12(7):448.
37. Lagunas-Rangel FA. Neutrophil-to-lymphocyte ratio and lymphocyte-to-C-reactive protein ratio in patients with severe coronavirus disease 2019 (COVID-19): a meta-analysis. J Med Virol. 2020.