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Original Article

Assessment of the hematologic factors as a prognostic factor in COVID-19 patients

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Abstract

Introduction: Identifying laboratory predictors of disease progression should be a priority in current COVID-19 studies, which leads to an appropriate treatment for patients and reduce the risk of severe or critical illness. In this study we tend to analyze the hematologic and biochemical findings of COVID-19 patients as an easy-to-get diagnostic factor that can become the first choice for disease monitoring and the evaluation of general conditions.

Methods: In this retrospective study, all patients with positive COVID-19 diagnosis that admitted to the emergency department, from 1st of April 2020, to 30th June, 2020 were included. For all patients, CBC, differential, urea, serum creatinine, and CRP were collected. Data analysis was performed using IBM® SPSS® Statistics 19.0 software. Pearson correlation and spearman correlation were used to analyze quantitative and qualitative data correlations respectively. Diagnostic ability of the variables was identified by their ROC curves.

Results: A total number of 977 patients were included in this study. The median and mode of the age of the population are 50 and 29 respectively. ROC curves for diagnostic ability indicated that, Urea and creatinine have the highest diagnostic values with its optimum sensitivity and specificity for urea = 62.5 mg/dL and creatinine = 2.05 mg/dL, with sensitivities of 87.5% and 81.3%, and specificities of 80.6% and 82.1% respectively.

Conclusion: The results from the current study show that no chemical or hematologic factor can properly detect COVID-19 in patients. Also, hematologic factors cannot determine patients' prognosis; however creatinine and urea are able to estimate patients' prognosis. Therefore, it is recommended to focus on the kidney injuries in COVID-10 patients for predicting their prognosis.

Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the third deadly coronavirus type, is the factor responsible for the ongoing global pandemic of coronavirus disease 2019 (COVID-19).[1] The number of infected people has escalated with the spread of the COVID-19 epidemic. As of April 27, 2020, 185 countries and regions with over 2 970 000 diagnosed cases and over 200 000 deaths were involved in the COVID-19 pandemic.[2] The main manifestations seen in COVID-19 patients are fever, fatigue, and dry cough. In patients with the severe disease, dyspnea or hypoxemia typically occurs 1 week after disease onset, and in this stage patients may become critically ill. Severe cases of COVID-19 exhibit a systemic pro-inflammatory state with associated coagulation disorders, oxidant stress, and multiorgan compromise.[3,4]

According to recent studies, by 2020, the need for mechanical ventilation and hospitalization in the intensive care unit (ICU) occurs in more than 30% of patients with the progression of SARS-CoV-2 infection.[5] Therefore, identifying demographic, clinical, radiological, and laboratory predictors of disease progression should be a priority in current COVID-19 studies, which leads to an appropriate treatment for those patients and reduce the risk of severe or critical illness. Hematological tests, with low detection costs and high automation, can provide the most common and easily obtainable diagnosis and treatment evidence, becoming the first choice for disease monitoring and general condition evaluation.. Some hematological parameters change in patients with COVID-19; the lymphocyte count decreases significantly while disease aggravates in patients with COVID-1. It is significantly lower in patients who die compared to survivors.[6-9]

Red cell distribution width (RDW) as a prognostic biomarker in various chronic lung diseases has gained much of attention.[10,11] RDW reflects the variation of red blood cell volumes and represents a relatively reproducible

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biomarker, considering the relatively prolonged lifespan of red blood cells. It has been suggested that arterial hypoxemia increases erythropoietin secretion and then RDW rises through mechanisms that involve regulation of erythrocyte maturation and survival.[11] Studies have shown that in patients with COVID-19, the severity of hypoxemia is independently associated with in-hospital mortality and can reliably predict admission to the intensive care unit.[12] Recently, a large prospective study by Foy et al demonstrated that elevated baseline RDW (>14.5%) levels were independently associated with worse clinical outcomes in hospitalized patients with COVID-19.[13] As RDW significantly predicts clinical outcomes in patients with respiratory tract infections, it is necessary to investigate the potential prognostic role of this laboratory parameter along with other blood factors in COVID-19.

Methods

In this retrospective study, we included all patients with positive COVID-19 diagnosis based on RT-PCR test result, that admitted to the emergency department, from 1st of April 2020, to 30th June, 2020. Each patient signed a detailed informed consent form. Patients that were not hospitalized within one month of COVID-19 diagnosis, and patients without routine CBC results were excluded from the study. In patients with a history of multiple hospitalizations due to COVID-19, each hospitalization was considered as a different record.

For all patients, records of the first lab tests of patients in entrance including CBC, differential, urea, serum creatinine, and CRP were collected as a part of standard clinical care in the form of checklist. The mortality status was also calculated based on patients' files. Patients that were discharged from hospital were considered as alive in this study.

Data analysis was performed using IBM® SPSS® Statistics 19.0 software. Since the distribution of the age in the population was not normal, median, and mode of the population were used for a better understanding. Quantitative variables were declared using mode and median since the population was not normal. For inferential statistics, the Pearson correlation and spearman correlation were used to analyze quantitative and qualitative data correlations respectively. P values below 0.05 were considered significant. Diagnostic ability of the variables was identified by their ROC curves. Power analysis was done by PASS version 15.0.5

Results

A total number of 977 patients (540 male, 437 female) were included in this study. The median and mode of the age of the population are 50 and 29 respectively (25-75 percentile = 34-69). The median, mode, 25% percentile, and 75% percentile for blood serum factors of patients are summarized in Table 1. The prevalence of death was 2.3% (22 patients).

There was a significant and moderately strong correlation between gender and RBC, Hb, and Hct. There was no other significant and strong correlation between the factors. Significant Spearman and Pearson correlations are summarized in Table 2.

ROC curves for diagnostic ability indicated that, Urea and creatinine have the highest diagnostic values with its optimum sensitivity and specificity for urea = 62.5 mg/dL and creatinine = 2.05 mg/dL, with sensitivities of 87.5% and 81.3%, and specificities of 80.6% and 82.1% respectively. Higher levels of urea and creatinine are more specific in COVID-19 diagnosis; however they have lower sensitivity.

Table 1. The median, mode, 25% percentile, and 75% percentile for blood serum levels.

Factors	N		Median	Mode	25% percentile	75% percentile
	Valid	Missing				
WBC	961	16	7.50	6.90	5.70	10.1
RBC	961	16	4.75	4.62	4.32	5.18
Hb	961	16	13.8	14.2	12.4	15.1
Hct	961	16	43.0	41.9	39.3	46.7
MCV	961	16	91.0	94.0	88.0	95.0
MCH	961	16	30.0	30.0	28.0	31.0
MCHC	960	17	32.0	32.0	31.0	33.0
Plt	960	17	218.5	171.0	176.0	274.0
Lymph	919	58	23.8	20.0	14.3	33.6
RDW	813	164	13.4	12.8	12.8	14.5
PDW	806	171	12.4	12.8	11.1	13.9
MPV	806	171	9.6	9.5	8.9	10.3
PLCR	802	175	23.1	24.9	18.4	27.75

WBC: white blood cells, RBC: red blood cells, Hb: hemoglobin, Hct: hematocrit, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, Plt: platelets, Lymph: lymphocytes, RDW: red cell distribution width, PDW: platelets distribution width, MPV: mean platelet volume, PLCR: platelet large cell ratio

Table 2. Spearman and Pearson correlation between the studied factors

Correlation type	Factor	Correlating factor	*P* value	Correlation coefficient
Spearman correlation	Death	Age	<0.001	-0.151
		Gender	0.010	0.082
		WBC	<0.001	-0.149
		MCHC	0.002	0.100
		RDW	<0.001	-0.122
		PDW	0.016	-0.085
		PLCR	0.035	-0.074
		Lymph	0.003	0.097
	Gender	WBC	0.028	-0.071
		MCH	<0.001	-0.213
		MCHC	<0.001	-0.307
		Plt	<0.001	-0.221
		Lymph	0.004	0.094
		RBC	<0.001	-0.356
		Hb	<0.001	-0.436
		Hct	<0.001	-0.399
Pearson correlation	Age	WBC	<0.001	0.122
		Hb	<0.001	-0.238
		Plt	0.017	-0.077
		RDW	0.014	0.086
		Lymph	<0.001	<0.001

WBC: white blood cells, RBC: red blood cells, Hb: hemoglobin, Hct: hematocrit, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, Plt: platelets, Lymph: lymphocytes, RDW: red cell distribution width, PDW: platelets distribution width, PLCR: platelet large cell ratio.
* Negative value in gender related correlations means the value is lower in women.

After urea and creatinine, WBC has the highest diagnostic value with its optimum sensitivity and specificity for WBC of 9.15 × 10^9/L with a sensitivity of 83.3% and specificity of 70.8%. PDW and neutrophil have the third highest diagnostic values, with a sensitivity of 72.2% and a specificity of 72.9% for PDW = 13.45%; while neutrophil has a sensitivity of 72.2% and a specificity of 70.1% for neutrophil = 76.45%. Also, RDW has a sensitivity of 61.1% and a specificity of 76.7% for RDW = 14.45%; while a PLCR of 25.95% is 61.1% percent sensitive and 69.1% specific in COVID-19 diagnosis.

The other values did not have a proper level of sensitivity and specificity for COVID-19 diagnosis. For instance, the optimum diagnostic level of MPV for COVID-19 is MPV = 10.25 fL, which is 55.6% percent sensitive and 75.8% specific in COVID-19 diagnosis. Also, the optimum diagnostic level of MCV for COVID-19 is MCV = 93.5 fL, which is 50% percent sensitive and 68% specific in COVID-19 diagnosis. Furthermore, RBC has a sensitivity of 44% and a specificity of 73.5% for RBC = 51.15 × 10^6/mm^3 as its optimum diagnostic value; while a Hct of 43.65% is 50% percent sensitive and 56% specific in COVID-19 diagnosis.

Lymph, Plt, and Hb levels up to 5.5%, 47 × 10^4/mL, and 8.75 g/dL respectively, have a sensitivity of 100% in COVID-19 diagnosis, but are not specific; while their higher levels have lower sensitivity without a rise in specificity. Also, a CRP of 1.5 mg/L is 100% percent sensitive and 30% specific in COVID-19 diagnosis; while a CRP of 2.5 mg/L is 50% specific, but has no sensitivity in COVID-19 diagnosis. Power of the study for sensitivity analysis was 80% and P-value was calculated as 0.05.

Discussion

The results of this cohort study on 977 patients suggest that CBC findings, age and gender were not clinically significant for predicting the risk of mortality in COVID-19. The diagnosis of COVID-19 disease is based on real-time PCR findings. Regrettably, conducting PCR is not always time- or cost-effective. This fact escalates the importance of identifying other diagnostic factors. With that in mind, in this study we tend to analyze the hematologic and biochemical findings of the blood samples of hospitalized COVID-19 patients. ROC curves for diagnostic ability indicated that urea and creatinine have the first place, WBC the second PDW and neutrophil have the third highest diagnostic values.

Contrary to expectations, death was poorly correlated with age of the patients in our study (*P* value = 0.000, r = -0.151) which does not support previous results in literature. For instance, in Bonard et al meta-analysis, the threshold of > 50 years old was associated with higher mortality risks all over the globe.[14] Age was associated with higher mortality risks in both high-income and low- to middle-income countries in Demombynes et al study.[15] However, age is not the only risk factor for higher mortality in COVID-19 patients; According to the obtained results of Behzadi et al study, the mean serum level of LDH in both male and female patients who died was considerably higher than in discharged patients (*P* value < 0.001).[16] Mehra et al study shows a high prevalence of hyperbilirubinemia, hypoproteinemia, electrolyte imbalance, and raised IL-6 and troponin I in severe COVID-19.[17] High incidence of comorbidities in elderly are the main culprit for the occurrence of death in most of the COVID-19 cases and the fact that our study did not measure how these predisposing factors affect overall death can be the reason for this disassociation.

Reanal Panel tests abnormalities, particularly high BUN and creatinine, have been linked to COVID-19 previously.[18-20] Cheng et al results from a cohort of 305 patients suggested creatinine, alongside other factors including CRP and neutrophil count, is associated with in-hospital mortality, while increasing levels of BUN is associated with a higher risk for mortality in COVID-19 patients.[21] In addition, albumin/creatinine ratio was implied as a good measure for predicting COVID-19 related acute renal injury in Yildirim et al study.[22] Therefore, kidney injury seems to be an important

aspect of COVID-19 multiple-organ involvements. Our findings support the matter and demonstrated the urea and creatinine have the highest diagnostic values with its optimum sensitivity and specificity for urea = 62.5 and creatinine = 2.05, with sensitivities of 87.5% and 81.3%, and specificities of 80.6% and 82.1% respectively.

Furthermore, a WBC = 9.15 had a sensitivity and specificity of 83.3% and 70.8%. An abnormal WBC, while being repeatedly reported in the literature, is expected as a result of any infection but cannot be held accountable exclusively for diagnosing COVID-19.[23-25]

Plasma CRP level has been put forward as an important factor for predicting severity and progression of the COVID-19.[26-29] Our findings demonstrated that the sensitivity and specificity of a CRP = 1.5 is 100% and 30% while surprisingly, CRP = 2.5 is 50% specific, but fails to have any sensitivity in diagnosis of COVID-19.

Holding the third place among diagnostic values, a neutrophil = 76.45 had a sensitivity of 72.2% and a specificity of 70.1% and PDW = 13.45 had a sensitivity of 72.2% and a specificity of 72.9%. Higher levels of neutrophil, alongside the higher neutrophil-to-lymphocyte, are supported by other studies as well.[30] Less reportedly, PDW is also linked to the severity of the COVID-19 infection. For instance, Wang et al proposed that PDW < 12.7 should suggest the possibility of COVID-19.[31] Bommenahalli Gowda et al also supported these findings by suggesting that PDW has a high sensitivity of 84% and a high negative predictive value of 89%.[32]

Moreover, several studies have investigated the predicting value of other hematologic findings in COVID-19 patients.[33,34] Inexplicably, Foy et al cohort study suggested an elevated RDW (> 14.5) is associated with higher mortality risks in 1641 COVID-19 infected patients. In addition, compared to a stable RDW, an increasing RDW during hospital stay was associated with higher mortality rates.[13] However, our findings suggested that RDW = 14.45 has a sensitivity of 61.1% and a specificity of 76.7% which might be due to different study setting and population.

It is important to underline the limitations to the study. The greatest limitation in our study was the abnormal distribution of the population which was expected considering the large number of included patients. Secondly, comorbidities and patients' health prior to the COVID-19 disease were omitted in this study; which must be noted as a potential limitations. In addition, another source of error could be the fact that, due to the retrospective design of this study, no follow-up was conducted on the population, and we were not able to consider out-hospital mortality and complications. Also due to the rapid changes in protocols for COVID-19 patients and alterations in sampling methods, the study includes a relatively high number of missing data.

It is noteworthy that all included patients were hospitalized, therefore generalizing these findings to overall COVID-19 patients with different severity and the external validity of the study can be restricted.

Consequently, due to the high global incidence and mortality of COVID-19, these findings need to be cautiously interpreted and more studies are needed to clarify the possible factors that cause heterogeneity in the literature, hence these limitations should inspire further research in this area.

Study Highlights

What is current knowledge?

- There is not any hematologic and chemical factors to detect COVID-19 and patients prognosis

What is new here?

- No chemical or hematologic factor can properly detect COVID-19 in patients . Also, hematologic factors cannot determine patients' prognosis. However, creatinine and urea are able to estimate patients' prognosis.

Conclusion

In conclusion, the results from the current study show that no chemical or hematologic factor can properly detect COVID-19 in patients . Also, hematologic factors cannot determine patients' prognosis. However, creatinine and urea are able to estimate patients' prognosis, respectively. Therefore, it is recommended to focus on the kidney injuries in COVID-10 patients.

Authors' Contribution

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Competing Interests

The authors declared no conflicts of interest.

Ethical Approval

This study was confirmed by the national ethics committee (IR.TBZMED.REC.1399.968) and has been carried out in accordance with Declaration of Helsinki for experiments involving humans. The privacy rights of subjects were observed in this study.

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References

1. China National Health Commission. Diagnosis and Treatment of Pneumonitis Caused by New Coronavirus (Trial Version 5). Beijing: China National Health Commission; 2020.

2. COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU) [Internet]. Available from: https://coronavirus.jhu.edu/map.html.
3. Sharun K, Tiwari R, Patel SK, Karthik K, Iqbal Yatoo M, Malik YS, et al. Coronavirus disease 2019 (COVID-19) in domestic animals and wildlife: advances and prospects in the development of animal models for vaccine and therapeutic research. Hum Vaccin Immunother. 2020;16(12):3043-54. doi: 10.1080/21645515.2020.1807802.
4. Leisman DE, Ronner L, Pinotti R, Taylor MD, Sinha P, Calfee CS, et al. Cytokine elevation in severe and critical COVID-19: a rapid systematic review, meta-analysis, and comparison with other inflammatory syndromes. Lancet Respir Med. 2020;8(12):1233-44. doi: 10.1016/s2213-2600(20)30404-5.
5. Abate SM, Ahmed Ali S, Mantfardo B, Basu B. Rate of intensive care unit admission and outcomes among patients with coronavirus: a systematic review and meta-analysis. PLoS One. 2020;15(7):e0235653. doi: 10.1371/journal.pone.0235653.
6. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395(10223):507-13. doi: 10.1016/s0140-6736(20)30211-7.
7. Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, et al. Dysregulation of immune response in patients with coronavirus 2019 (COVID-19) in Wuhan, China. Clin Infect Dis. 2020;71(15):762-8. doi: 10.1093/cid/ciaa248.
8. 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. doi: 10.1007/s00134-020-05991-x.
9. Bizzarro MJ, Conrad SA, Kaufman DA, Rycus P. Infections acquired during extracorporeal membrane oxygenation in neonates, children, and adults. Pediatr Crit Care Med. 2011;12(3):277-81. doi: 10.1097/PCC.0b013e3181e28894.
10. Nathan SD, Reffett T, Brown AW, Fischer CP, Shlobin OA, Ahmad S, et al. The red cell distribution width as a prognostic indicator in idiopathic pulmonary fibrosis. Chest. 2013;143(6):1692-8. doi: 10.1378/chest.12-1368.
11. Karampitsakos T, Dimakou K, Papaioannou O, Chrysikos S, Kaponi M, Bouros D, et al. The role of increased red cell distribution width as a negative prognostic marker in patients with COPD. Pulm Pharmacol Ther. 2020;60:101877. doi: 10.1016/j.pupt.2019.101877.
12. 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(6):1138-47. doi: 10.1016/j.mayocp.2020.04.006.
13. Foy BH, Carlson JCT, Reinertsen E, Padros IV, Pallares Lopez R, Palanques-Tost E, et al. Association of red blood cell distribution width with mortality risk in hospitalized adults with SARS-CoV-2 infection. JAMA Netw Open. 2020;3(9):e2022058. doi: 10.1001/jamanetworkopen.2020.22058.
14. Bonanad C, García-Blas S, Tarazona-Santabalbina F, Sanchis J, Bertomeu-González V, Fácila L, et al. The effect of age on mortality in patients with COVID-19: a meta-analysis with 611,583 subjects. J Am Med Dir Assoc. 2020;21(7):915-8. doi: 10.1016/j.jamda.2020.05.045.
15. Demombynes G. COVID-19 Age-Mortality Curves Are Flatter in Developing Countries. World Bank Policy Res. Work. Pap. 2020;31.
16. Behzadi F, Roosta Y, Nejadrahim R, Nabavi A. Distinct laboratory parameters as strict prognostic values in the setting of COVID-19 severity. J Res Clin Med. 2023;11(1):22. doi: 10.34172/jrcm.2023.33289.
17. Mehra RK, Gupta P, Singh N. Role of biochemical and inflammatory markers in assessing COVID-19 severity among the Indian population: an observational study. J Res Clin Med. 2022;10(1):10. doi: 10.34172/jrcm.2022.010.
18. Askari H, Sanadgol N, Azarnezhad A, Tajbakhsh A, Rafiei H, Safarpour AR, et al. Kidney diseases and COVID-19 infection: causes and effect, supportive therapeutics and nutritional perspectives. Heliyon. 2021;7(1):e06008. doi: 10.1016/j.heliyon.2021.e06008.
19. Hong XW, Chi ZP, Liu GY, Huang H, Guo SQ, Fan JR, et al. Analysis of early renal injury in COVID-19 and diagnostic value of multi-index combined detection. medRxiv. March 12, 2020. Available from: https://www.medrxiv.org/content/10.1101/2020.03.07.20032599v2.
20. Ok F, Erdogan O, Durmus E, Carkci S, Canik A. Predictive values of blood urea nitrogen/creatinine ratio and other routine blood parameters on disease severity and survival of COVID-19 patients. J Med Virol. 2021;93(2):786-93. doi: 10.1002/jmv.26300.
21. Cheng A, Hu L, Wang Y, Huang L, Zhao L, Zhang C, et al. Diagnostic performance of initial blood urea nitrogen combined with D-dimer levels for predicting in-hospital mortality in COVID-19 patients. Int J Antimicrob Agents. 2020;56(3):106110. doi: 10.1016/j.ijantimicag.2020.106110.
22. Yildirim C, Ozger HS, Yasar E, Tombul N, Gulbahar O, Yildiz M, et al. Early predictors of acute kidney injury in COVID-19 patients. Nephrology (Carlton). 2021;26(6):513-21. doi: 10.1111/nep.13856.
23. Elshazli RM, Toraih EA, Elgaml A, El-Mowafy M, El-Mesery M, Amin MN, et al. Diagnostic and prognostic value of hematological and immunological markers in COVID-19 infection: a meta-analysis of 6320 patients. PLoS One. 2020;15(8):e0238160. doi: 10.1371/journal.pone.0238160.
24. Vafadar Moradi E, Teimouri A, Rezaee R, Morovatdar N, Foroughian M, Layegh P, et al. Increased age, neutrophil-to-lymphocyte ratio (NLR) and white blood cells count are associated with higher COVID-19 mortality. Am J Emerg Med. 2021;40:11-4. doi: 10.1016/j.ajem.2020.12.003.
25. Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy. 2020;75(7):1730-41. doi: 10.1111/all.14238.
26. Chen W, Zheng KI, Liu S, Yan Z, Xu C, Qiao Z. Plasma CRP level is positively associated with the severity of COVID-19. Ann Clin Microbiol Antimicrob. 2020;19(1):18. doi: 10.1186/s12941-020-00362-2.
27. 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. doi: 10.1016/j.jcv.2020.104370.
28. Wang G, Wu C, Zhang Q, Wu F, Yu B, Lv J, et al. C-reactive protein level may predict the risk of COVID-19 aggravation. Open Forum Infect Dis. 2020;7(5):ofaa153. doi: 10.1093/ofid/ofaa153.
29. Wang L. C-reactive protein levels in the early stage of COVID-19. Med Mal Infect. 2020;50(4):332-4. doi: 10.1016/j.medmal.2020.03.007.
30. Peng J, Qi D, Yuan G, Deng X, Mei Y, Feng L, 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.
31. Wang Y, Fan Z, Wang S, Zhuang C. The diagnostic value of platelet distribution width in patients with mild COVID-19. J Clin Lab Anal. 2021;35(4):e23703. doi: 10.1002/jcla.23703.
32. Bommenahalli Gowda S, Gosavi S, Ananda Rao A, Shastry S, Raj SC, Menon S, et al. Prognosis of COVID-19: red cell distribution width, platelet distribution width, and C-reactive protein. Cureus. 2021;13(2):e13078. doi: 10.7759/cureus.13078.
33. Terpos E, Ntanasis-Stathopoulos I, Elalamy I, Kastritis E, Sergentanis TN, Politou M, et al. Hematological findings and complications of COVID-19. Am J Hematol. 2020;95(7):834-47. doi: 10.1002/ajh.25829.
34. Khartabil TA, Russcher H, van der Ven A, de Rijke YB. A summary of the diagnostic and prognostic value of hemocytometry markers in COVID-19 patients. Crit Rev Clin Lab Sci. 2020;57(6):415-31. doi: 10.1080/10408363.2020.1774736.