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Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio as a Rapid Initial Diagnostic Test for SARS-CoV-2 Infection

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Abstract

Background: Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) SARS-CoV-2 assay remains the common test used to detect the coronavirus infection worldwide. Complete blood count (CBC) is a rapid and cost-effective test compared to RT-PCR, thus, it would be worthy to find a hematological indicator for SARS-CoV-2 infection. **Objectives:** This study aims to assess the efficacy of CBC indices as an initial diagnostic test for coronavirus 2019 (COVID-19) infection, which might be helpful during the outbreak of the disease. **Materials and Methods:** A retrospective, hospital based and case control study was carried out at Gezira isolation center for COVID-19, Gezira State, Sudan in the period from January to May 2021. A total of 178 COVID-19 patients with positive RT-PCR SARS-CoV-2 assay result and another 178 volunteers of apparently healthy people were included in this study. CBC as well as D-dimer and C-reactive protein (CRP) were recorded from patient's file and neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and lymphocyte-to-monocyte ratio (LMR) were calculated. Data were analyzed using Statistical Package for Social Science (SPSS) version 20. **Results:** Neutrophil percentage, total white blood cells (TWBCs) and platelet (PLT) were higher in the COVID-19 patients compared to their control, whereas, lymphocyte and monocyte showed lower percentages among the COVID-19 patients. Although the differences that observed in the means of PLT, neutrophils and monocytes between the case and control group were

significant, all these mean values of both groups were lying within the normal range. On the other hand, there was a highly significant elevation in NLR and PLR and quite good increasing in LMR level among COVID-19 patients compared to their control. The results of receiver operating characteristic curve (ROC) analysis showed that the area under the curve of NLR, PLR and LMR were 0.948 (P. value = 0.00, 95% CI: 0.925 - 0.972), 0.925 (P. value = 0.00, 95% CI: 0.896 - 0.954) and 0.643 (P. value = 0.00, 95% CI: 0.584 - 0.702), respectively, suggesting the efficacy of using these tests as diagnostic tests for COVID-19 infection. D-dimer and CRP level were highly elevated in COVID-19 patients with significant differences compared to control group. **Recommendation:** The study recommends using NLR, PLR and LMR as rapid initial diagnostic test for SARS-CoV-2 infection in the area/time of disease spread out.

Keywords

COVID-19, CBC, NLR, PLR, LMR

1. Introduction

In December 2019 a novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was occurred and causing coronavirus disease 2019 (COVID-19). The disease was initially introduced and reported to World Health Organization (WHO) on December 31, 2019 with outbreak of pneumonia of unknown origin in Wuhan, Hubei Province of China. On January 30, 2020, WHO declared the COVID-19 outbreak as public health emergency of international concern and later on as pandemic on March 11 [1] [2] [3].

Sudan confirmed the first imported case on 3rd March 2020. However, by the end of April 1, 2022, the total cases in Sudan had increased up to 61955 with 4907 deaths [4].

Coronaviruses are a large family of viruses that cause illness in human. There are several types of these viruses that are implicated in causing respiratory infections among human with different degrees of severity, the most common is Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) [5].

There are several symptoms for COVID-19, while the most common are general tiredness, fever, and dry cough. The disease may accompany further symptoms such as sore throat, nasal congestion, or diarrhea. Approximately, up to 80% of the patients can be recovered from the disease before referring to the hospital. On the other hand, fifth of COVID-19 patients develop severe illness and suffer difficulty breathing. People with different medical problems such as diabetes mellitus, hypertension, heart diseases, lung problems, and cancer are at higher risk of severe illness [6].

The clinical diagnosis of COVID-19 is mainly based on clinical manifesta-

tions, molecular diagnosis by RT-PCR, CT scan or chest x-ray, and several blood tests. Interestingly, several studies reported the alterations in various hematological parameters in patients with COVID-19, whereas the most common are lymphopenia, leukopenia, and thrombocytopenia. On the other hand, elevated CRP and D-dimer levels and other inflammatory markers, and abnormal renal and liver function were also reported previously [7]-[12]. Therefore, a retrospective analysis was done to assess the effect of COVID-19 on D-dimer, CRP and various hematological parameters among Sudanese COVID-19 patients hospitalized in Gezira State, central Sudan.

2. Materials and Methods

2.1. Study Design

A retrospective, hospital based and case control study was conducted on COVID-19 patients who were admitting at Gezira isolation center for COVID-19, Gezira State, Sudan in the period from January to May 2021.

2.2. Study Population and Sampling

The study recruited 178 subjects diagnosed to have COVID-19 and confirmed by positive (RT-PCR) SARS-CoV-2 assay result using nasopharyngeal swab samples [13]. The study also included 178 volunteers of apparently healthy people without any symptoms of COVID-19 or history of blood diseases taken as control group. Files of COVID-19 patients were selected randomly from the hospital medical records. D-dimer, CRP, WBCs, red blood cells (RBCs), hemoglobin (Hb), PLT, neutrophils, lymphocytes and monocytes of each subject were taken from patient's file, while NLR, PLR and LMR were calculated.

2.3. Inclusion and Exclusion Criteria

Hospitalized subjects with positive COVID-19 and negative subjects with all ages and both sexes were included in this study, while subjects with history of a disease which could influence the hematological profile or other medical condition such as liver disease or cardiovascular disease were excluded.

2.4. Ethical Consideration

The study was approved by the Ethics Committee of Faculty of Medicine, University of Gezira as well as the Ethics Committee of Ministry of Health, Gezira State, Sudan.

2.5. Data Analysis

The data were analyzed using Statistical Package for Social Science, Version.20.0. Independent samples t-test was used to compare the means of all study parameters between case and control groups. The results were presented as mean ± SE and $P \leq 0.05$ was considered as significant at 95% confidence interval. ROC curve analysis was used to obtain the diagnostic values of NLR, PLR and LMR.

3. Results

3.1. Study Population

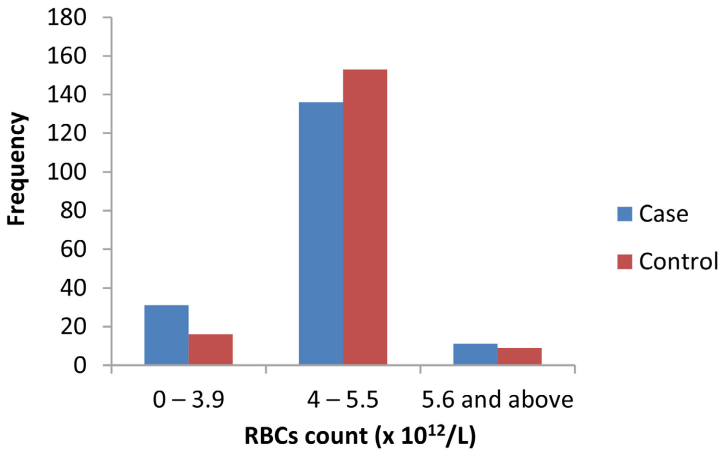
A total of 356 subjects were recruited in this study, which included 178 patients with positive (RT-PCR) SARS-CoV-2 assay result, were admitting at Gezira isolation center for COVID-19 and 178 subjects of apparently healthy people who taken as control. About two third (65.2%) of the COVID-19 patients in this study were males while females represented 34.8% of the total patients.

3.2. Complete Blood Count

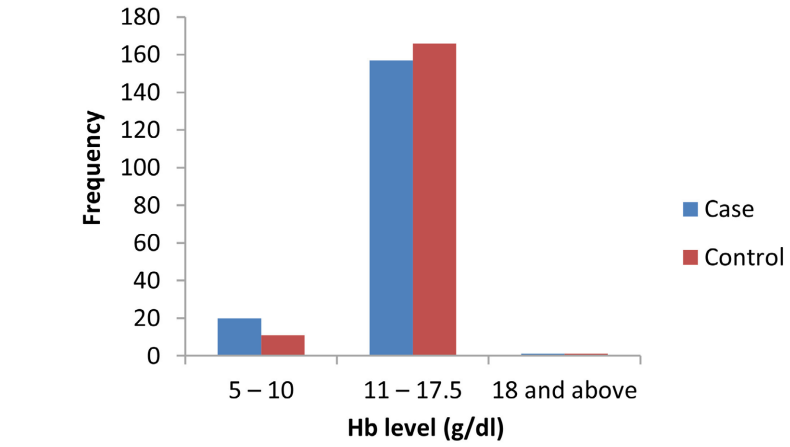
As can be seen in Table 1, there were significant differences between the case and control in the means of CBC component except RBCs (Figure 1(a)) and Hb (Figure 1(b)). However, the PLT count was higher in the COVID-19 patients compared to their control (Figure 1(c)). While the patient group presented higher TWBCs count and neutrophil percentage, their lymphocyte and monocyte showed lower percentages in comparison to control group (Figures 2(a)-(d), respectively). Although the differences that observed in the means of PLT, neutrophils and monocytes between the case and control group were significant, all these mean values of both groups were lying within the normal range.

Table 1. Comparison of CBC means between case and control.

Parameter	COVID-19 patients		Control		P. Value
	N	(mean ± SE)	N	(mean ± SE)	
TWBCs ($\times 10^9$/L)		14.22 ± 0.56		6.26 ± 0.16	0.00
RBCs ($\times 10^{12}$/L)		4.49 ± 0.05		4.59 ± 0.04	0.10
Hb (g/dl)		13.06 ± 0.15		13.34 ± 0.13	0.16
PLT ($\times 10^9$/L)	178	324.38 ± 12.61	178	245.62 ± 6.64	0.00
Lymphocyte (%)		13.78 ± 0.80		38.45 ± 0.79	0.00
Monocyte (%)		3.32 ± 0.24		11.65 ± 0.40	0.00
Neutrophil (%)		83.04 ± 0.85		49.90 ± 0.93	0.00



(a)



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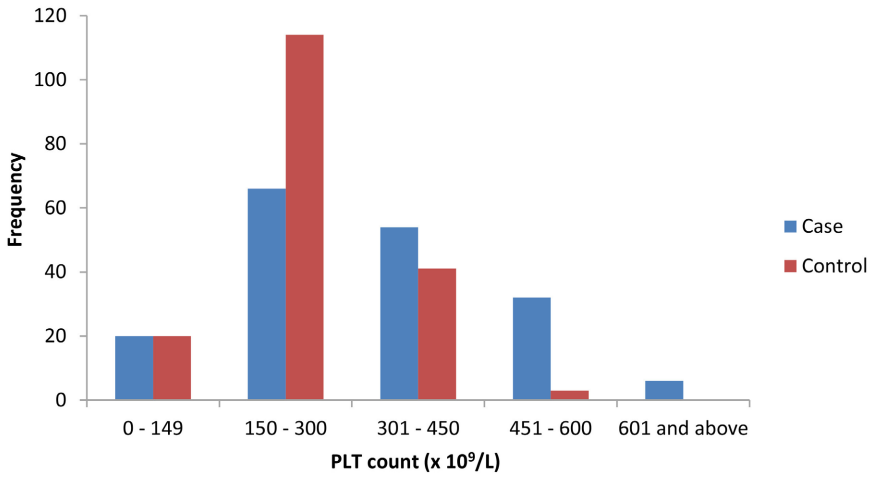


(c)

Figure 1. Distribution of the study subjects according to different (a) RBCs counts (b) Hb concentrations (c) PLT counts.

3.3. NLR, PLR and LMR Ratios

In order to gain better insight regarding diagnostic value of neutrophils, platelet and monocytes, receiver operating characteristic curve (ROC) analysis of NLR, PLR and LMR ratios were done. The results showed that the area under the curve of NLR, PLR and LMR were 0.948 (P. value = 0.00, 95% CI: 0.925 - 0.972), 0.925 (P. value = 0.00, 95% CI: 0.896 - 0.954) and 0.643 (P. value = 0.00, 95% CI: 0.584 - 0.702), respectively (**Figure 3**).

3.4. D-Dimer and CRP Levels

Table 2 presents the plasma level of D-dimer and CRP in both COVID-19 patients and their control group. The estimation of D-dimer was done for only 200 subjects (100 case and 100 control). However, the mean of plasma level of D-dimer was clinically elevated (almost 7 times above the reference value) in the patients group (**Figure 4(a)**) and the comparison of this mean with that obtained by the control group showed high significant difference between the two

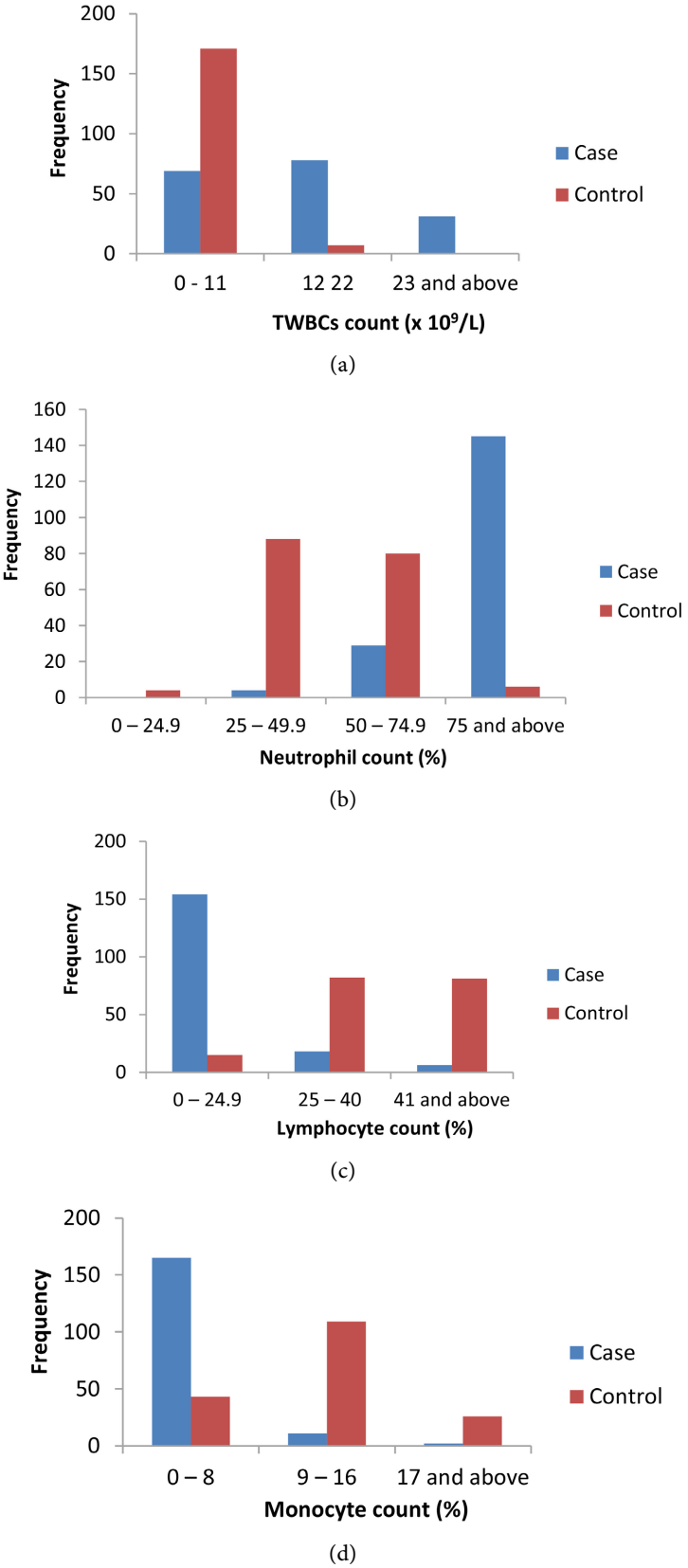


Figure 2. Distribution of the study subjects according to different (a) TWBCs counts (b) neutrophil counts (c) lymphocyte counts (d) monocyte counts.

Table 2. Comparison of D-dimer and CRP means between case and control.

Parameter	COVID-19 patients		Control		P. Value
	N	(mean ± SE)	N	(mean ± SE)	
D-dimer (ng/ml)	100	3373.29 ± 334.85	100	357.38 ± 61.33	0.00
CRP (mg/L)	178	123.29 ± 8.12	178	5.22 ± 0.56	0.00

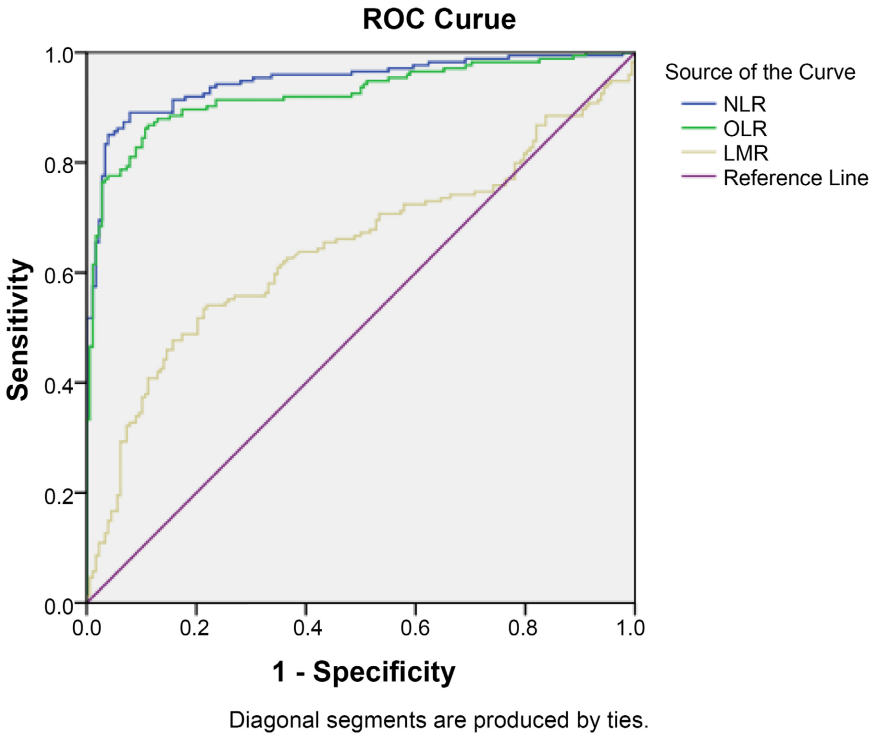
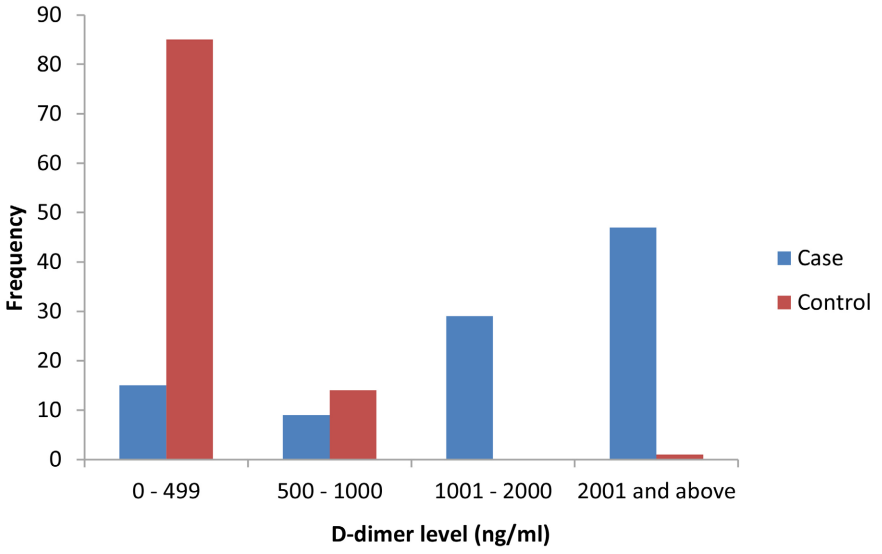
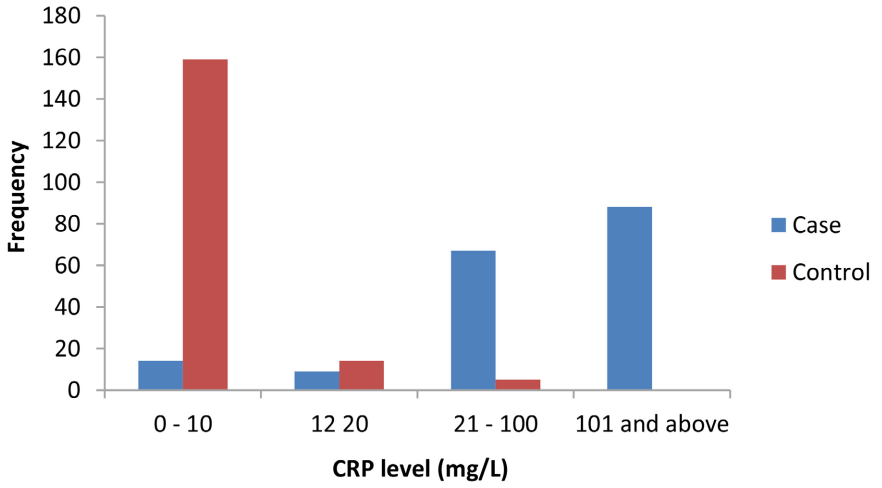


Figure 3. The ROC curves of NLR, PLR and LMR for differentiating between the COVID-19 patients and their control.



(a)



(b)

Figure 4. Distribution of the study subjects according to different (a) D-dimer levels (b) CRP levels.

groups (P. value = 0.00). A similar pattern was also observed with the CRP level (**Figure 4(b)**), showing elevation in the patient group up to 11 times above the reference value, with a significant difference in the means between the patient and control groups (P. value = 0.00).

4. Discussion

In this study, the majority (two third) of the COVID-19 patients were males, this finding is consistent with other studies, showing that COVID-19 was more common among males compared to their counterpart [14] [15] [16] [17].

The comparison of CBC results between the COVID-19 patients and their control revealed various alterations had occurred in the hematological indicators. There were no differences noticed in the RBC count and Hb concentration between the two groups. These results were similar to earlier studies conducted on COVID-19 patients in different populations [9] [10] [14] [18]. However, in comparison to control group, the COVID-19 patients showed higher neutrophil percentage, WBCs and PLT counts, and lower lymphocyte and monocyte percentage. The substantial decreasing that observed in the lymphocyte percentage among patients group and the significant difference of its mean when compared with that of control group, suggest lymphopenia is an important hematological characteristic of these patients. Indeed, majority of the studies that related to COVID-19 indicated lymphopenia among patients with COVID-19 was common and proposed the reliability of using lymphocyte count as a diagnostic test for the disease [7] [9] [12] [19]. The means of neutrophils, PLT and monocytes in both case and control groups were lying within the normal range, despite the significant differences that observed between the two groups. Therefore, and for getting more insight, NLR, PLR and LMR ratios were calculated and the results showed highly significant elevation in NLR and PLR and quite good increasing

in LMR level among COVID-19 patients compared to their control, whereas ROC analysis diagnostic values suggest the efficacy of using these tests as diagnostic tests for COVID-19 infection. However, several studies reported the diagnostic and prognostic roles of NLR, PLR and LMR tests in coronavirus disease [19] [20] [21] [22]. On the other hand, although the ratio of NLR, PLR and LMR were found to have predictive value for prognosis of various diseases such as esophageal cancer [23], osteosarcoma [24], Crohn's Disease [25] and Erythema Nodosum Leprosum [26], but using of these tests along with the other symptoms and clinical examinations during COVID-19 outbreak would be valuable in the diagnosis of this disease.

On the other hand, both D-dimer and CRP levels showed significant differences between COVID-19 patients and their control group. In other words, approximately 7 times elevation in D-dimer level was observed with COVID-19 patients and more than 9 times when compared to control group, whereas CRP level increased up to 24 times in these patients compared to control group and 11 times above the reference value. The high elevation in plasma level of D-dimer and CRP among COVID-19 patients was previously reported by different studies [10] [14] [16] [17] [19].

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Conflicts of Interest

The authors have no conflict of interests to declare.

References

[1] Jee, Y. (2020) WHO International Health Regulations Emergency Committee for the COVID-19 Outbreak. *Epidemiol Health*, **42**, e2020013. https://doi.org/10.4178/epih.e2020013

[2] Eurosurveillance Editorial Team (2020) Note from the Editors: World Health Organization Declares novel Coronavirus (2019-nCoV) Sixth Public Health Emergency of International Concern. *Eurosurveillance*, **25**, e200131. https://doi.org/10.2807/1560-7917.ES.2020.25.5.200131e

[3] Gallegos A. (2020) WHO Declares Public Health Emergency for Novel Coronavirus. Medscape Medical News. https://www.medscape.com/viewarticle/924596

[4] World Health Organization (2020) WHO Coronavirus (COVID-19) Dashboard. https://covid19.who.int/region/emro/country/sd

[5] Lombardi, A.F., Afsahi, A.M., Gupta, A. and Gholamrezanezhad, A. (2021) Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), Influenza, and COVID-19, Beyond the Lungs: A Review Article. *La radiologia medica*, **126**, 561-569. https://doi.org/10.1007/s11547-020-01311-x

[6] World Health Organization (2020) WHO Director-General's Opening Remarks at

the Media Briefing on COVID-19—11 March 2020. https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020

[7] Tong, X., Cheng, A., Yuan, X., Zhong, X., Wang, H., Zhou, W., Xu, X. and Li, Y. (2021) Characteristics of Peripheral White Blood Cells in COVID-19 Patients Revealed by a Retrospective Cohort Study. *BMC Infectious Diseases*, **21**, Article No. 1236. https://doi.org/10.1186/s12879-021-06899-7

[8] Sharif, F., Khan, S., Junaid, A., Jahangir, S., Saeed, M., Ijaz, M., *et al.* (2021) Early Hematological Indicators of Severe COVID-19 Disease in Hospitalized Patients: Data from a South Asian Population. *International Journal of Laboratory Hematology*, **43**, 1237-1242. https://doi.org/10.1111/ijlh.13533

[9] Lanini, S., Montaldo, C., Nicastri, E., Vairo, F., Agrati, C., Petrosillo, N., *et al.* (2020) COVID-19 Disease-Temporal Analyses of Complete Blood Count Parameters Over Course of Illness, and Relationship to Patient Demographics and Management Outcomes in Survivors and Non-Survivors: A Longitudinal Descriptive Cohort Study. *PLoS One*, **15**, e0244129. https://doi.org/10.1371/journal.pone.0244129

[10] Fu, J., Kong, J., Wang, W., Wu, M., Yao, L., Wang, Z., *et al.* (2020) The Clinical Implication of Dynamic Neutrophil to Lymphocyte Ratio and D-dimer in COVID-19: A Retrospective Study in Suzhou China. *Thrombosis Research*, **192**, 3-8. https://doi.org/10.1016/j.thromres.2020.05.006

[11] Napoli, C., Benincasa, G., Criscuolo, C., Faenza, M., Liberato, C. and Rusciano, M. (2021) Immune Reactivity during COVID-19: Implications for Treatment. *Immunology Letters*, **231**, 28-34. https://doi.org/10.1016/j.imlet.2021.01.001

[12] Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., *et al.* (2020) Clinical Features of Patients Infected with 2019 Novel Coronavirus in Wuhan, China. *The Lancet*, **395**, 497-506. https://doi.org/10.1016/S0140-6736(20)30183-5

[13] Paradiso, A.V., De Summa, S., Loconsole, D., Procacci, V., Sallustio, A., Centrone, F., *et al.* (2020) Rapid Serological Assays and SARS-CoV-2 Real-Time Polymerase Chain Reaction Assays for the Detection of SARS-CoV-2: Comparative Study. *Journal of Medical Internet Research*, **22**, e19152. https://doi.org/10.2196/19152

[14] Pan, F., Yang, L., Li, Y., Liang, B., Li, L., Ye, T., *et al.* (2020) Factors Associated with Death Outcome in Patients with Severe Coronavirus Disease-19 (COVID-19): A Case-control Study. *International Journal of Medical Sciences*, **17**, 1281-1292. https://doi.org/10.7150/ijms.46614

[15] Zhou, F., Yu, T., Du, R., Fan, G., Liu, Y., Liu, Z., *et al.* (2020) Clinical Course and Risk Factors for Mortality of Adult in Patients with COVID-19 in Wuhan, China: A Retrospective Cohort Study. *The Lancet*, **395**, 1054-1062. https://doi.org/10.1016/S0140-6736(20)30566-3

[16] Naymagon, L., Zubizarreta, N., Feld, J., van Gerwen, M., Alsen, M., Thibaud, S., *et al.* (2020) Admission D-dimer Levels, D-dimer Trends, and Outcomes in COVID-19. *Thrombosis Research*, **196**, 99-105. https://doi.org/10.1016/j.thromres.2020.08.032

[17] Poudel, A., Poudel, Y., Adhikari, A., Aryal, B.B., Dangol, D., Bajracharya, T., *et al.* (2021) D-dimer as A Biomarker for Assessment of COVID-19 Prognosis: D-dimer Levels on Admission and its Role in Predicting Disease Outcome in Hospitalized Patients with COVID-19. *PLoS One*, **16**, e0256744. https://doi.org/10.1371/journal.pone.0256744

[18] Piagnerelli, M., Vanderelst, J., Rousseau, A., Monteyne, D., Perez-Morga, D., Biston, P., *et al.* (2022) Red Blood Cell Shape and Deformability in Patients with COVID-19

Acute Respiratory Distress Syndrome. *Frontiers in Physiology*, **13**, 849910. https://doi.org/10.3389/fphys.2022.849910

[19] Sukrisman, L., Sinto, R. and Priantono, D. (2021) Hematologic Profiles and Correlation Between Absolute Lymphocyte Count and Neutrophil/Lymphocyte Ratio with Markers of Inflammation of COVID-19 in an Indonesian National Referral Hospital. *International Journal of General Medicine*, **14**, 6919-6924. https://doi.org/10.2147/IJGM.S337440

[20] Seyit, M., Avci, E., Nar, R., Senol, H., Yilmaz, A., Ozen, M., *et al.* (2021) Neutrophil to Lymphocyte Ratio, Lymphocyte to Monocyte Ratio and Platelet to Lymphocyte Ratio to Predict the Severity of COVID-19. *The American Journal of Emergency Medicine*, **40**, 110-114. https://doi.org/10.1016/j.ajem.2020.11.058

[21] Eslamijouybari, M., Heydari, K., Maleki, I., Moosazadeh, M., Hedayatizadeh-Omran, A., Vahedi, L., *et al.* (2020) Neutrophil-to-Lymphocyte and Platelet-to-Lymphocyte Ratios in COVID-19 Patients and Control Group and Relationship with Disease Prognosis. *Caspian J Intern Med*, **11**, 531-535.

[22] Jain, R., Gopal, A., Pathak, B.K., Mohakuda, S.S., Tilak, T. and Singh, A.R. (2021) Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio and Their Role as Predictors of Disease Severity of Coronavirus Disease 2019 (COVID-19). *Journal of Laboratory Physicians*, **13**, 58-63. https://doi.org/10.1055/s-0041-1723057

[23] Sun, Y. and Zhang, L. (2018) The Clinical Use of Pretreatment NLR, PLR, and LMR in Patients with Esophageal Squamous Cell Carcinoma: Evidence from a Meta-analysis. *Cancer Management and Research*, **10**, 6167-6179. https://doi.org/10.2147/CMAR.S171035

[24] Yapar, A., Tokgöz, M.A., Yapar, D., Atalay, İ.B., Ulucaköy, C. and Güngör, B.Ş. (2021) Diagnostic and Prognostic Role of Neutrophil/Lymphocyte Ratio, Platelet/Lymphocyte Ratio, and Lymphocyte/Monocyte Ratio in Patients with Osteosarcoma. *Joint Diseases and Related Surgery*, **32**, 489-496. https://doi.org/10.52312/jdrs.2021.79775

[25] Feng, J.R., Qiu, X., Wang, F., Chen, P.F., Gao, Q., Peng, Y.N., *et al.* (2017) Diagnostic Value of Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio in Crohn's Disease. *Gastroenterology Research and Practice*, **2017**, Article ID: 3526460. https://doi.org/10.1155/2017/3526460

[26] Tanojo, N., Damayanti, Utomo, B., Ervianti, E., Murtiastutik, D., Prakoeswa, C.R.S., *et al.* (2022) Diagnostic Value of Neutrophil-to-Lymphocyte Ratio, Lymphocyte-to-Monocyte Ratio, and Platelet-to-Lymphocyte Ratio in the Diagnosis of Erythema Nodosum Leprosum: A Retrospective Study. *Tropical Medicine and Infectious Disease*, **7**, 39. https://doi.org/10.3390/tropicalmed7030039