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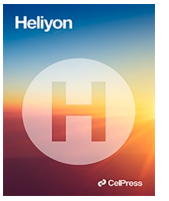

Can mean platelet volume be a prognosis predictor in viral infections: An example of Covid-19

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ABSTRACT

Purpose: This study revealed the utility of mean platelet volume (MPV) as a mortality marker in SARS-CoV-2 infection, as well as its connection with other inflammatory indicators such as procalcitonin (PCT) and neutrophil-lymphocyte ratio (NLR).

Methods: A total of 1528 patients (853 males and 653 females; mean age: 64.33 ± 16.36 years; range, 18–100 years) were hospitalized with COVID-19 between March 2020 and December 2022. The patients' demographic and clinical information, including ward and critical care data, were gathered from their medical records. On the first and last days, the PCT, NLR, and MPV values of the patients, who were divided into groups based on their hospitalization and outcomes, were analyzed.

Results: When the relevant laboratory data from the first and last days were compared, each group was statistically significant ($p < 0.05$). There was a moderate association between the final MPV values and the PCT and NLR values of the patients admitted to the ward ($r = 0.448$ and $r = 0.397$, respectively, where $p < 0.01$). There was also a substantial and moderate correlation between the final MPV levels and the PCT and NLR values of patients admitted to the intensive care unit ($r = 0.613$ and $r = 0.361$, respectively, $p < 0.01$). When compared to the patients' outcomes, the MPV had greater specificity and AUC values than the PCT and NLR (94.4 %, 0.968, 80.6 %, 0.923, 81 %, 0.845, respectively).

Conclusion: In patients hospitalized with COVID-19, the specificity of MPV values at the point of sickness severity and outcome was shown to be greater than PCT and NLR values, and MPV values may be a more accurate predictor of mortality than PCR and NLR.

1. Introduction

In December 2019, a new bat-origin coronavirus (2019-nCoV), also known as "Severe Acute Respiratory Syndrome-Coronavirus 2" (SARS-CoV-2), which emerged in Wuhan city of Hubei Province, of the People's Republic of China can infect humans, was detected [1]. The disease caused by this virus has been officially named "Coronavirus Disease 2019 (COVID-19)" by the World Health Organization (WHO). WHO declared COVID-19 an "international public health emergency" on January 30. It was announced as a pandemic on March 11, with a high incidence of COVID-19 cases in 113 countries.

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It is more contagious than the SARS-CoV virus but less likely to cause death. The incubation period of the disease varies between 2 and 14 days. Its clinical forms include a broad spectrum from asymptomatic infection to death. While coronaviruses affect the respiratory system more, SARS-CoV-2 can also affect the cardiovascular, gastrointestinal, hepatobiliary, renal, and central systems and cause multiorgan failure [2,3]. Although it is diagnosed serologically, additional parameters are needed in addition to radiological imaging in treatment follow-up and prognosis. While rapid tests and PCR measurements hold diagnostic value, it is essential to acknowledge that they, in isolation, do not suffice for triage and prognostic follow-up [4,5]. Simultaneously, as the number of patients rapidly increases, the burden on laboratories can impede their functioning.

Although laboratory findings are nonspecific, the most common laboratory findings at the time of diagnosis are low albumin (75.8 %), high C-reactive protein (CRP) (58.3 %), increased lactate dehydrogenase (57 %), and lymphopenia (43.1 %) [6]. In addition, elevated liver enzymes, D-dimer, and ferritin levels are frequently detected. Elevated CRP, D-dimer, serum ferritin, prolonged prothrombin time, elevated troponin, elevated creatinine phosphokinase, and hypoxemia are poor prognostic factors [7]. At the same time, hematological changes are expected in COVID-19 patients, and a decrease in lymphocyte and platelet counts is observed. Elevated platelet activity is frequently observed in viral infections, with platelet indices serving as valuable indicators of this phenomenon. While D-dimer holds significance in the context of thrombosis, CRP and ferritin levels are crucial in assessing the infection burden. Additionally, indices such as mean platelet volume (MPV), platelet crit (PCT), and platelet distribution width (PDW) play a pivotal role in determining disease severity, contingent upon the synthesis of proinflammatory cytokines. Furthermore, elevated troponin levels are indicative of cardiac myocyte damage [8]. Studies have shown that platelet count is associated with the disease's severity and mortality risk. Mortality was found to be higher, specifically in severe thrombocytopenia (platelet count $<$50,000) [9].

One of the parameters routinely reported in a complete blood count is MPV. This value provides information about the platelet size. Thrombosis-related disorders, as well as infectious and inflammatory processes, can all have an impact on MPV [10]. Platelets activated by classical agonists like ADP, TXA2, and PAF, in addition to inflammatory cytokines like IL-1, IL-6, and TNF-alpha, rapidly accumulate at the site of damage. Platelets undergo a shape change, the formation of pseudopodia, the local release of cytoplasmic granules, and subsequent aggregation when activated. As a result, these processes are crucial in initiating fibrosis and inflammatory responses [11]. Several studies have found that MPV increases inflammatory processes in the respiratory system [12,13].

This article revealed the significance of MPV as a valuable indicator of mortality in individuals infected with COVID-19. It further explored the association between MPV and other markers of inflammatory parameters.

2. Methods

2.1. Study population

Patients who applied to the Covid Emergency Service of the Süleyman Demirel University Medical Faculty Hospital and were hospitalized with the diagnosis of COVID-19 between March 2020 and December 2022 had their procalcitonin (PCT), neutrophil/lymphocyte ratio (NLR), and mean platelet volume (MPV) measured at the time of admission to the emergency room and in the final days of the hospital. The data collection was created by reaching the MPV levels backward. Real-Time PCR equipment was used to investigate oro-nasopharyngeal swab samples taken from patients with Covid-19 symptoms, and 1528 patients diagnosed with COVID-19 and whose laboratory parameters were assessed during their first and last days in the hospital were included in the study.

Our study is a retrospective, and inclusion criteria were as follows: patients with positive PCR test, over 18 years of age, hospitalized, and whose laboratory results were obtained at the time of admission and during the hospitalization process were included.

Exclusion criteria for the trial included patients under the age of 18, concurrent pregnancy, chronic disease, cancer, and inability to get laboratory results.

PCT (ng/ml), NLR, and MPV (fl) results were scanned retrospectively in the groups separated according to their hospitalization and discharge status, and the data were recorded.

2.2. Ethics

The study was performed in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the local ethics committee (protocol code: 2023/35, committee number: 12867572-0s0.01.04–466896), and written informed consent was obtained from all the participants.

2.3. Measurement of samples

A complete blood count (including neutrophils, leukocytes, and MPV) was performed using flow cytometry on a blood sample collected in a purple tube containing the EDTA anticoagulant. The analysis was carried out in the Medical Biochemistry Laboratory using a Beckman Coulter DXH 800 complete blood count analyzer. NLR was calculated by dividing neutrophil and lymphocyte counts by each other. As the laboratory's limit, a range of 6.9–10.3 fl for MPV was considered normal.

The PCT test was performed on serum samples from patients in the Medical Microbiology Laboratory using the electrochemiluminescence immunoassay method on the Roche Cobas 6000 modular system according to the manufacturer's instructions. PCT values were considered negative if they were less than 0.5 ng/ml, borderline if they were between 0.5 and 2 ng/ml, and high if they were greater than 2 ng/ml.

PCR assay was performed with Rotor-Gene Q MDx 5plex HRM (CA).

2.4. Statistical analyses

Shapiro-Wilk test was used for normality test of PCT, NLR and MPV levels. The groups did not show a normal distribution. Differences in the mean of continuous variables (PCT, N/L, MPV) between groups (service-intensive care hospitalization, discharge-exitus), Kruskall-Wallis test, MannWhitney-U for analysis of differences between groups, laboratory for the first and last day examined between groups and between groups Wilcoxon Signed Rank Test was used for the analysis of the values, Spearman's Rank Order Correlation test was used for the correlation between the laboratory values of the first and last day between the groups. The ROC Curve analysis was used to determine the sensitivity and specificity of the laboratory values. $P < 0.05$ was considered statistically significant. Statistical analysis was performed using IBM SPSS 25.0 (SPSS for Windows, SPSS Inc., Chicago, IL, USA), MedCalc® Statistical Software version 20.218 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2023).

3. Results

The study encompassed a total of 1528 individuals who tested positive for COVID-19 through PCR tests. Among them, there were 653 females and 853 males. The participants' ages ranged from 18 to 100 years, with a mean age of 64.33 ± 16.36. When the PCT, NLR and MPV values of all patients were benchmarked on the first and last days, the results were statistically significant for all parameters (Table 1).

The PCT, NLR, and MPV values of the patients, who were divided into groups according to their hospitalization and outcomes, were examined on the first and last days, and all comparisons between the groups were found to be statistically significant ($p < 0.05$) (Table 2).

According to the hospitalization status, there was a moderate correlation between the last MPV values and the PCT and NLR values of the patients admitted to the ward ($r = 0.448$ and $r = 0.397$, where $p < 0.01$, respectively). Also, there was a strong and moderate correlation between the final MPV values and the PCT and NLR values of patients who were admitted to the intensive care unit ($r = 0.613$ and $r = 0.361$, where $p < 0.01$, respectively) (Table 3).

As shown in Fig. 1 and Table 4, the MPV had higher specificity and AUC values than PCT and NLR when evaluated according to the patients' outcomes (94.4 %, 0.968, 80.6 %, 0.923, 81 %, 0.845, respectively).

4. Discussion

Even though SARS-CoV-2 infection is diagnosed by serology, it is also clinically important to keep an eye on biochemical, radiological and hematologic parameters [14]. Platelet volume is a laboratory index automatically generated from a routine complete blood count to predict platelet function and activation [15–17]. This study analyzed MPV, PCT, and NLR values on admission and the last day of hospitalization for patients with positive PCR tests. As a result of this study, it was observed that the last-day values of the patients who were discharged after their treatment was completed were lower than the first day, while the last-day values of those who died were significantly higher.

Many investigations have shown that PCT and NLR levels correlate with clinical severity [4,18–22] These indicators were higher in our study, particularly in patients hospitalized to the intensive care unit who died; MPV values also linked with PCT and NLR levels.

Takahashi et al. investigated gender differences in immune responses to COVID-19 in a 2020 study. Men had higher levels of proinflammatory chemokines and cytokines, while women had a stronger T-cell response. However, when gender was considered, there were no significant differences in laboratory parameters, hospital stays, or patient outcomes found between the two groups in our study. Women and men are disproportionately affected, according to global studies conducted in the United States, Europe, and China. Although preliminary data suggested that men were more severely affected that women, another similar research concluded that the disease killed more women than men [12,13,23,24]. We believe that factors such as occupational exposure, viral load, comorbidities, and advanced age, in addition to the immune system response, play an important role in disease response.

In their study from 2020, Ergenc et al. said that the rise in CRP and NLR levels played a role in SARS-CoV-2 infection deaths [25]. In another study, the NLR, CRP, and platelet levels of 443 PCR-positive COVID-19 patients were retrospectively examined, and it was argued that NLR was the best marker among them [26]. At the same time, a 2021 study conducted in India investigating the role of hematologic biomarkers other than MPV in COVID-19 infection determined that NLR was the most effective complete blood count parameter in discriminating between mild and severe cases [27]. The studies conducted by Xu JB et al. and Heesom et al. revealed a

Table 1
Comparison of blood values taken on the first day of and last day of admission of all patients included in the study.

	Patients (n = 1528)	p
First PCT	3.32 ± 13.62	<0.05
Last PCT	4.86 ± 16.19	
First NLR	12.09 ± 13.94	<0.05
Last NLR	11.07 ± 16.91	
First MPV	8.95 ± 1.00	<0.05
Last MPV	8.96 ± 1.53	

PCT: ProcalcitoninNLR: Neutrophil-to-lymphocyte ratio MPV: Mean Platelet Volume.

Table 2
Comparison of first and last day parameters of PCT, NLR, and MPV values of between groups.

Groups		First PCT	Last PCT	First NLR	Last NLR	First MPV	Last MPV
Hospitalization	Ward (n = 1396)	3.31 ± 13.86	4.46 ± 15.34	11.27 ± 13.12	10.65 ± 16.62	8.93 ± 1.01	8.89 ± 1.49
	ICU (n = 132)	3.36 ± 10.81	9.11 ± 22.97	20.78 ± 18.68	15.51 ± 19.19	9.12 ± 0.87	9.68 ± 1.70
p		<0.05		<0.05		<0.05	
Outcome	Discharge (n = 1091)	2.51 ± 11.63	0.61 ± 4.16	10.34 ± 11.79	5.79 ± 6.80	9.01 ± 1.01	8.20 ± 0.88
	Exitus (n = 437)	5.33 ± 17.50	15.49 ± 26.76	16.47 ± 17.50	24.37 ± 25.25	8.80 ± 0.96	10.85 ± 1.10
p		<0.05		<0.05		<0.05	

PCT: ProcalcitoninNLR: Neutrophil-to-lymphocyte ratio MPV: Mean Platelet Volume ICU: Intensive Care Unit Laboratory for the first and last day examined between groups and between groups Wilcoxon Signed Rank Test was used for the analysis of the values.

Table 3
Correlation between last day MPV values and PCT and NLR values according to hospitalization status.

Ward	Last PCT		Last NLR		Last MPV	
	r	p	r	p	r	p
Last PCT	–	–	0.483	<0.01	0.448	<0.01
Last NLR	0.483	<0.01	–	–	0.397	<0.01
Last MPV	0.448	<0.01	0.397	<0.01	–	–
ICU	Last PCT		Last NLR		Last MPV	
	r	p	r	p	r	p
Last PCT	–	–	0.392	<0.01	0.613	<0.01
Last NLR	0.392	<0.01	–	–	0.361	<0.01
Last MPV	0.613	<0.01	0.361	<0.01	–	–

PCT: ProcalcitoninNLR: Neutrophil-to-lymphocyte ratio MPV: Mean Platelet Volume ICU: Intensive Care Unit If the r value is between 0.4 and 0.6, it indicates a moderate correlation; 0.6–0.8 indicates a strong correlation.

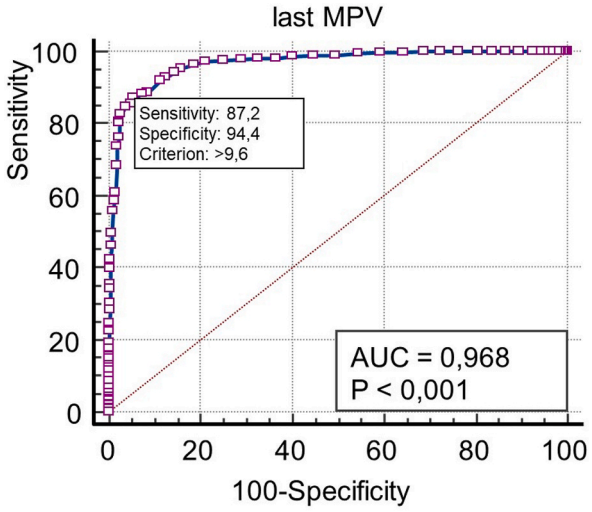

Fig. 1. ROC analysis of MPV Value by Outcome Status.

correlation between the requirement for ventilation and levels of PCT. They concluded that PCT levels are directly proportional to the severity of the disease, indicating that patients with severe infection, specifically those in the critical group, exhibit higher PCT levels compared to patients with moderate infection [28,29]. A comprehensive review of 52 articles and 6230 patients underscored that PCT levels were elevated in individuals with severe disease, while lower in those with mild disease, and further demonstrated an association between PCT levels and morbidity and mortality [30].

In a study published in 2020, it was discovered that the MPV levels were significantly higher in asymptomatic COVID-19-infected children [14]. D-dimer and MPV were examined as prognostic markers in a 2022 study conducted by Durmuş Kocak et al. A moderate correlation was found between MPV values 8.1, with an emphasis on the high negative predictive value, and the need for intensive care hospitalization [31]. Similarly, in our investigation, the MPV levels decreased in the discharged group while they were found to be

Table 4
Sensitivity and specificity, criterion value, and AUC value of last day MPV, PCT, and NLR values measured according by outcome status.

	Groups		
	Last MPV	Last PCT	Last NLR
Specificity (%)	94.4	80.6	81
Sensitivity (%)	87.2	90.2	75.7
Criter (Cutoff Value)	>9.6	>.0.27	>7.75
AUC	0.968	0.923	0.845
p	<0.001	<0.001	<0.001

PCT: ProcalcitoninNLR: Neutrophil-to-lymphocyte ratio MPV: Mean Platelet Volume AUC: Area Under the Curve.

significantly higher in the death group, and our findings were correlated with those of this study and the literature.

Numerous studies in the literature show that MPV levels are elevated or inversely related to inflammatory processes [12,32–36]. Compared to previous studies, MPV measurement in our study demonstrated greater sensitivity and specificity. This observation is explained by the fact that COVID-19 infection not only causes inflammation but also thrombotic complications, particularly in ICU patients [37]. Similar to COVID-19, we propose that MPV can be used as a potent marker for the prognosis of inflammatory diseases with thrombotic processes. The widespread use of MPV testing is also facilitated by its accessibility and low cost. In addition to well-established parameters like NLR and PCT, we also discovered that MPV plays a more significant role in inflammatory diseases. In diseases like COVID-19, where both inflammation and thrombotic events take place, we think that MPV may have a higher prognostic value. To support these findings, however, additional research is required.

Among the indicators examined in terms of outcome status, the MPV level demonstrated a better specificity than PCT and NLR levels. We also obtained a higher AUC value in the prediction of separating patients with demised from those who were released. According to the ROC analysis we performed in our study, the specificity of MPV values at the point of illness severity and outcome was shown to be greater than PCT and NLR values. Furthermore, the AUC of the test, which reflects the test's ability to discriminate dying patients from people discharged with healing based on patient outcomes, was shown to be greater than the others. In conclusion, MPV may be a better predictor of death than PCR and NLR.

It is paramount to comprehend how the correlation between hematologic parameters such as MPV, PCT, and NLR may be applied in future clinical contexts. For instance, a study incorporating these biomarkers into various artificial intelligence algorithms revealed that the algorithm excelled in terms of diagnostic accuracy and triage speed [38]. Another study found that an automated testing device capable of sampling and evaluating results autonomously could offer rapid and effective results, particularly for screening large groups (e.g., healthcare workers) [39]. Additionally, it holds significant value to consider how these findings might be integrated into routine clinical practice. For instance, further investigations into these biomarkers are warranted to assess their faster and safer utilization across diverse patient populations and healthcare settings. Subsequent research endeavors should prioritize translating these correlations into practical tools and strategies that enhance patient care and outcomes.

5. Limitations

Although our study emphasizes the importance of MPV in a disease characterized by inflammatory and thrombotic processes, it is important to note that we had some limitations. Access to variant information was not possible because COVID-19 mutation and variant analyses were conducted at the ministry level during the period of our investigation. When the data from the last period in which dominant mutations were observed were analyzed, no significant difference was found compared to the first period, which could affect the results of our study. Our research was carried out in a single center in a province with a population of 300k people. As a result, it is critical to emphasize that by improving facilities, a larger audience could be reached. Since our research was carried out in a pandemic hospital, it was confined to the evaluation of COVID-19 patients, making it difficult to compare and evaluate patients with other infectious diseases.

Data availability statement

The data related to my study is stored in a repository, but it is not publicly available, but it is subject to permission to be shared after application to the hospital information system.

CRediT authorship contribution statement

Nesrin Gökben Beceren: Writing – review & editing, Writing – original draft, Resources, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization. **Hamit Hakan Armağan:** Visualization, Supervision, Methodology, Conceptualization. **Furkan Çağrı Oğuzlar:** Writing – review & editing, Writing – original draft, Supervision. **Ezgi Cesur:** Resources, Investigation, Data curation. **Osman Gürdal:** Methodology, Formal analysis, Data curation. **Önder Tomruk:** Visualization, Supervision, Investigation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] W.H. Organization, World Health Organization Coronavirus Disease (COVID-19) Dashboard, World Health Organization, 2020.
[2] Y. Atici, et al., COVID-19 enfeksiyonunda hematolojik ve enflamatuvar parametrelerin incelenmesi, Avrasya Saglık Bilimleri Dergisi 5 (3) (2022) 37–44.
[3] T.C. Ministry of Health, Ayaktan Basvuran Hastalar Icin Olasi Covid-19 Vaka Sorgulama Kilavuzu, 2020, 8 March 2023]; Available from: https://covid19.saglik.gov.tr/Eklenti/37810/0/covid19-vaka-sorgulama-kilavuzu-a41pdf.pdf.
[4] Dejan Dobrijević, et al., Could platelet indices have diagnostic properties in children with COVID-19? J. Clin. Lab. Anal. 36 (2022), e24749 https://doi.org/10.1002/jcla.24749, 12.
[5] Dejan Dobrijević, et al., Clinical hematochemical parameters in differential diagnosis between pediatric SARS-CoV-2 and influenza virus infection: an automated machine learning approach, Children 10 (22 Apr. 2023) 5, https://doi.org/10.3390/children10050761, 761.
[6] N. Chen, et al., Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study, Lancet 395 (10223) (2020) 507–513.
[7] S.Y. Cho, et al., Mean platelet volume and mean platelet volume/platelet count ratio in infective endocarditis, Platelets 25 (8) (2014) 559–561.
[8] A. Kant, E. Aydın, H. Kılıç Yılmaz, G. Yılmaz, COVID-19 Hastalarinda kardïyak troponïn-I'NIN cïnsïyet ïlïşkilï prognostïk değerï, Kırıkkale Uni Tıp Derg. 23 (1) (2021) 125–131.
[9] S.Y. Cho, H.J. Lee, T.S. Park, Mean platelet volume in patients with increased γ-glutamyl transferase, Platelets 26 (3) (2015) 283–284.
[10] B. Shah, et al., Mean platelet volume and long-term mortality in patients undergoing percutaneous coronary intervention, Am. J. Cardiol. 111 (2) (2013) 185–189.
[11] B. Linke, et al., Activated Platelets Induce an Anti-inflammatory Response of Monocytes/macrophages through Cross-Regulation of PGE 2 and Cytokines, vol. 2017, Mediators of Inflammation, 2017.
[12] Y. Feng, et al., Elevated serum levels of CCL17 correlate with increased peripheral blood platelet count in patients with active tuberculosis in China, Clin. Vaccine Immunol. 18 (4) (2011) 629–632.
[13] J.T. Flynn, Evaluation and management of hypertension in childhood, Prog. Pediatr. Cardiol. 12 (2) (2001) 177–188.
[14] H. Gumus, A. Demir, A. Yükkaldıran, Is mean platelet volume a predictive marker for the diagnosis of COVID-19 in children? Int. J. Clin. Pract. 75 (4) (2021), e13892.
[15] R.M. Elshazli, et al., Diagnostic and prognostic value of hematological and immunological markers in COVID-19 infection: a meta-analysis of 6320 patients, PLoS One 15 (8) (2020), e0238160.
[16] H. Ergenç, et al., C-reactive protein and neutrophil–lymphocyte ratio as predictors of mortality in coronavirus disease 2019, Rev. Assoc. Méd. Bras. 67 (2021) 1498–1502.
[17] W.-j. Guan, et al., Clinical characteristics of coronavirus disease 2019 in China, N. Engl. J. Med. 382 (18) (2020) 1708–1720.
[18] F. Liu, et al., Prognostic value of interleukin-6, C-reactive protein, and procalcitonin in patients with COVID-19, J. Clin. Virol. 127 (2020), 104370.
[19] G. Lippi, M. Plebani, B.M. Henry, Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: a meta-analysis, Clin. Chim. Acta 506 (2020) 145–148.
[20] G. Lippi, M. Plebani, Procalcitonin in patients with severe coronavirus disease 2019 (COVID-19): a meta-analysis, Clinica chimica acta; international journal of clinical chemistry 505 (2020) 190.
[21] B. Karaca, Erişkin yaş grubunda Covid-19 klinik bulguları, Journal of Biotechnology and Strategic Health Research 4 (2020) 85–90.
[22] L. Heesom, et al., Procalcitonin as an antibiotic stewardship tool in COVID-19 patients in the intensive care unit, Journal of Global Antimicrobial Resistance 22 (2020) 782–784.
[23] H. Cai, Sex difference and smoking predisposition in patients with COVID-19, Lancet Respir. Med. 8 (4) (2020) e20.
[24] S.A. Kharroubi, M. Diab-El-Harake, Sex-differences in COVID-19 diagnosis, risk factors and disease comorbidities: a large US-based cohort study, Front. Public Health 10 (2022), 1029190.
[25] A.J. Rodriguez-Morales, et al., Clinical, laboratory and imaging features of COVID-19: a systematic review and meta-analysis, Trav. Med. Infect. Dis. 34 (2020), 101623.
[26] W. Shang, et al., The value of clinical parameters in predicting the severity of COVID-19, J. Med. Virol. 92 (10) (2020) 2188–2192.
[27] M. Pujani, et al., Association of Hematologic biomarkers and their combinations with disease severity and mortality in COVID-19-an Indian perspective, American journal of blood research 11 (2) (2021) 180.
[28] J.-b. Xu, et al., Associations of procalcitonin, C-reaction protein and neutrophil-to-lymphocyte ratio with mortality in hospitalized COVID-19 patients in China, Sci. Rep. 10 (1) (2020) 1–10.
[29] A.-P. Yang, et al., The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients, Int. Immunopharm. 84 (2020), 106504.
[30] A. Yuri Gasparyan, et al., Mean platelet volume: a link between thrombosis and inflammation? Curr. Pharmaceut. Des. 17 (1) (2011) 47–58.
[31] N. Durmus Kocak, et al., Use of radiology, D-Dimer, and mean platelet volume combination as a prognostic marker in hospitalized coronavirus disease-19 patients, Front. Med. 8 (2022), 788551.
[32] G. Delgado-García, et al., Mean platelet volume is decreased in adults with active lupus disease, Rev. Bras. Reumatol. 56 (2016) 504–508.
[33] G. Gunluoglu, et al., Mean platelet volume as an inflammation marker in active pulmonary tuberculosis, Multidisciplinary Respiratory Medicine 9 (1) (2014) 1–5.
[34] A. Korniluk, et al., Mean Platelet Volume (MPV): New Perspectives for an Old Marker in the Course and Prognosis of Inflammatory Conditions, Mediators of inflammation, 2019, p. 2019.
[35] E. Ünsal, et al., Potential role of interleukin 6 in reactive thrombocytosis and acute phase response in pulmonary tuberculosis, Postgrad. Med. 81 (959) (2005) 604–607.
[36] O. Yüksel, et al., An overlooked indicator of disease activity in ulcerative colitis: mean platelet volume, Platelets 20 (4) (2009) 277–281.
[37] F. Klok, et al., Incidence of thrombotic complications in critically ill ICU patients with COVID-19, Thromb. Res. 191 (2020) 145–147.
[38] Dejan Dobrijević, et al., Clinical hematochemical parameters in differential diagnosis between pediatric SARS-CoV-2 and influenza virus infection: an automated machine learning approach, Children 10 (22 Apr. 2023) 5, https://doi.org/10.3390/children10050761, 761.
[39] Dejan Dobrijević, et al., Clinical hematochemical parameters in differential diagnosis between pediatric SARS-CoV-2 and influenza virus infection: an automated machine learning approach, Children 10 (22 Apr. 2023) 5, https://doi.org/10.3390/children10050761, 761.