ISSN: 2588-4115; Infection Epidemiology and Microbiology. 2024;10(1):71-77 doi 10.52547/iem.10.1.71

Assessing the Relationship Between D-dimer and IL-6 Levels and Clinical Outcomes in Elderly COVID-19 Patients

ARTICLE INFO

Article Type
Original Article

Authors
Christopher Paul Clement Jenil Dhas, *MD*[1]
Yoganathan Chidambaram, *MD*[2]*
Srinivasan Kesavan, *MD*[1]
Kalaivanee Balasubramaniam, *DNB*[3]
Sujith Kumar Sivaraj, *MD*[4]
Saravanan Thangavelu, *MD*[4]

[1] Assistant Professor, Department of General Medicine, PSG Institute of Medical Sciences and Research, Coimbatore, India.
[2] Associate professor, Department of General Medicine, PSG Institute of Medical Sciences and Research, Coimbatore, India.
[3] Senior Resident, Department of General Medicine, PSG Institute of Medical Sciences and Research, Coimbatore, India.
[4] Professor, Department of General Medicine, PSG Institute of Medical Sciences and Research, Coimbatore, India.

**** Correspondence***
Associate Professor, Department of General Medicine PSG Institute of Medical Sciences and Research,Coimbatore,India.
Email: yoganathan8042@psgimsr.ac.in

How to cite this article
Clement Jenil Dhas C.P., Chidambaram Y., Kesavan S., Balasubramaniam K., Sivaraj S.K. Thangavelu S. Assessing the Relationship Between D-dimer and IL-6 Levels and Clinical Outcomes in Elderly COVID-19 Patients. Infection Epidemiology and Microbiology. 2024;10(1): 71-77.

Article History
Received: October 13, 2023
Accepted: February 06, 2024
Published: February 21, 2024

ABSTRACT

Background: This study aimed to evaluate serum levels of interleukin-6 (IL-6) and D-dimer and their association with morbidity and mortality in elderly coronavirus disease-19 (COVID-19) patients and to assess their clinical outcomes.

Materials & Methods: This retrospective observational study was conducted on elderly COVID-19 patients (≥60 years) diagnosed via reverse transcription-polymerase chain reaction (RT-PCR) or radiological tests in a South Indian tertiary care hospital. Data encompassed demographics, comorbidities, symptoms, IL-6 and D-dimer levels, oxygen (O_2) requirement, duration of hospital stay, and outcomes. Statistical analysis involved Chi-square test. A *p*-value of < .05 was considered statistically significant.

Findings: Among 1448 screened patients, 1380 patients with a mean age of 68.85±6.985 years were included in this study, of whom 61.67% were male. The mortality rate was 12.1% in males and 11% in females. Fever, cough, hypertension, and diabetes were common in most of the patients. The mean D-dimer and IL-6 levels were 2.687±5.189 mg/L fibrinogen equivalent units (FEU) and 95.72±335.62 pg/mL, respectively. Elevated D-dimer (71%) and IL-6 (87.7%) levels were significantly associated with oxygen requirement, morbidity, and mortality (*p*= .000). Sub-group analysis revealed a significant association between D-dimer and IL-6 levels and O_2 requirement and mortality in diabetic and hypertensive patients (*p*= .000).

Conclusion: Serum IL-6 and D-dimer levels are significantly associated with morbidity and mortality in elderly COVID-19 patients. Elevated levels of these biomarkers also influence O_2 requirement and mortality in patients with comorbidities, suggesting their potential use in risk stratification and management strategies for this vulnerable population.

Keywords: COVID-19, D-dimer, Geriatric, Interleukin-6, Mortality

CITATION LINKS

[1] World Health Organization. Statement on the fifteenth... [2] Becerra-Muñoz VM, et al. Clinical profile and predictors of in-hospital mortality... [3] Center for Disease Control and Prevention. Underlying medical conditions... [4] Azarudeen MJ, et al. Comparing COVID-19 mortality across ... [5] Gao Y, Ding M, Dong X, Zhang JJ, Kursat Azkur A, Azkur D, et al. Risk factors for severe and... [6] Eljilany I, Elzouki AN. D-Dimer, fibrinogen, and IL-6 in COVID-19 patients with... [7] Mittal K, Dhar M, Pathania M, Jha D, Saxena V. A comparative study of... [8] Sanyaolu A, Okorie C, Marinkovic A, Patidar R, Younis K, Desai P, et al. Comorbidity... [9] Mansell V, Hall Dykgraaf S, Kidd M, Goodyear-Smith F. Long COVID... [10] Rodriguez-Sanchez I, Rodriguez-Mañas L, Laosa O. Long COVID-19: The need for an... [11] Ulugerger Avci G, et al. Clinical outcomes of geriatric ... [12] Singhal S, Kumar P, Singh S, Saha S, Dey AB. Clinical features and outcomes... [13] Farid E, Sridharan K, Alsegai OA, Khawaja SA, Mansoor EJ, Teraifi NA, et al. Utility... [14] Ahirwar AK, Takhelmayum R, Sakarde A, Rathod BD, Jha PK, Kumawat R, et al. The study of serum... [15] Luporini RL, Rodolpho JM, Kubota LT, Martin AC, Cominetti MR, de Freitas Anibal F, et al. IL-6 and IL-10... [16] Kim BS, Shin JH. Association between D-dimer and long... [17] Miri C, Charii H, Bouazzaoui MA, Laouan Brem F, Boulouiz S, Abda N, et al. D-dimer... [18] Tanase DM, Gosav EM, Radu S, Ouatu A, Rezus C, Ciocoiu M, et al. Arterial hypertension and... [19] Bowker N, Shah RL, Sharp SJ, Stewart ID, Wheeler E, Ferreira MA, et al. Meta-analysis investigating... [20] Soni M, Gopalakrishnan R, Vaishya R, Prabu P. D-dimer level... [21] Milenkovic M, et al. D-dimer, CRP, PCT, and IL-6 levels... [22] Hwang J, Ryu HS, Kim HA, You SH, Kim MS, Baek MS, et al. Prognostic factors of... [23] Rehatta NM, Chandra S, Sari D, Lestari MI, Senapathi TG, Nurdin H, et al. Comorbidities and COVID-19... [24] Mishra Y, et al. Relation of D-dimer levels of COVID-19 ... [25] Phan F, et al. Cardiac adipose tissue volume and IL-6 ... [26] Huang S, Wang J, Liu F, Liu J, Cao G, Yang C, et al. COVID-19 patients...

Introduction

The World Health Organization (WHO) has confirmed that due to the decrease in the number of cases and deaths, COVID-19 (coronavirus disease-19) is no longer an emergency as it was during the pandemic [1]; however, recovery from the impact of the pandemic is far from over. Older patients aged 65 years and above are more vulnerable to COVID-19 infection, with a higher risk of poor outcomes and mortality [2]. Among several risk factors, age is considered to be the dominant risk factor for severe COVID-19, as the risk of death is 25-340 times higher in patients aged 50-85 years and above, who are usually along with other comorbidities like diabetes, hypertension, and chronic obstructive pulmonary disease. Furthermore, older patients with comorbidities are at higher risk of COVID-19 infection [3]. At the peak of the pandemic, the Union Health Ministry of India confirmed that approximately 75% of COVID-19 deaths occurred among the elderly [4].

Older patients typically have more comorbidities, weakened immune systems, and higher pro-inflammatory cytokines such as interleukin-6 (IL-6) which might otherwise be triggered by the virus itself as a result of activation and signalling of certain receptor families. In addition, elevated D-dimer levels could be due to sepsis-induced coagulopathy and are more common among severe COVID-19 patients. These parameters along with several others like C-reactive protein, procalcitonin, and other pro-inflammatory cytokines are indicators of the disease progression [5]. Elevated levels of these markers could also indicate an increased risk of venous thromboembolism and hence an increased risk of mortality due to thrombotic events [6].

Various risk factors, comorbidities, level of care, etc. affect vulnerable elderly patients both in terms of in-hospital mortality and long-term survival after discharge [7]. Therefore, identifying potential prognostic factors could help us be well-prepared to provide intensive care to the elderly in future pandemic-like scenarios.

To the best of our knowledge, no study in South India has assessed the association of D-dimer and IL-6 levels with mortality in geriatric COVID-19 patients.

Objectives: This retrospective study was conducted to gather the demographic and clinical information of elderly COVID-19 patients admitted to a tertiary care hospital. Additionally, the association of clinical outcomes with IL-6 and D-dimer levels and the association of comorbidities like hypertension and diabetes with morbidity and mortality in these patients were evaluated.

Materials and Methods

This retrospective observational study was conducted in a tertiary care hospital in Tamil Nadu, South India. The study was approved by the Institutional Human Ethics Committee (IHEC, Registration No. PSG/IHEC/2023/Appr/Exp/123).

The study included retrospective data of elderly in-patients aged 60 years and older, who were diagnosed with COVID-19 using RT-PCR (reverse transcription-polymerase chain reaction) or radiological COVID-19 tests. Patients with incomplete or no records and those voluntarily discharged against medical advice without completing their treatment regimen were excluded from the study. Incomplete records were those with no documentation of symptoms, comorbidities, or IL-6 and D-dimer levels.

The data of patients admitted between March and June 2021 were recorded. The patients' data recorded and analyzed were as follows: demographics, comorbidities, clinical presentations, diagnostic method used, serum IL-6 and D-dimer levels, oxygen

requirement, number of days in the hospital, and outcomes including discharge or death. Serum IL-6 (Elecsys IL-6, Roche diagnostics) and D-dimer (Innovance D-dimer, Siemens) levels were determined using commercially available kits, where the latter was reported in fibrinogen equivalent units (FEU, 30 kDa).

Statistical analysis: The extracted data were analyzed using R software. Continuous variables were presented as mean and standard deviation (SD), while categorical data were presented as frequency and percentage. Chi-square test was used to evaluate the association of D-dimer and IL-6 levels with oxygen requirement, morbidity, and mortality. Sub-group analysis was carried out to determine differences in D-dimer and IL-6 levels between patients with and without comorbidities. A *p*-value of < .05 was considered statistically significant.

Findings

A total of 4913 adult COVID-19 patients were admitted to the study centre from March to June 2021, of whom 1448 patients over 59 years of age were screened for the study. Furthermore, patients who were discharged against medical advice and patients with incomplete or unavailable data were excluded from the study. Finally, the records of the remaining 1380 patients were included in the study.

The mean age of the study population was 68.85±6.985 (SD) years. Most of the patients were male (61.67%, n=851), of whom 12.1% did not survive (n=103). Among females, 11% (n=58) died.

The clinical symptoms of the patients are listed in Table 1. The symptoms predominantly expressed were fever (63.7%, n=879) and cough (63.6%, n=878). Among the comorbidities evaluated, many patients had systemic hypertension (42.5%, n=586) and diabetes (52.4%, n=723) (Table 2).

The D-dimer values of the patients were between 0.08-21 mg/L fibrinogen equivalent units (FEU) with a mean value of 2.687±5.189 mg/L FEU. Similarly, IL-6 values also showed a high variation within the study population, as they were between 2-5000 pg/mL with a mean value of 95.72±335.62 pg/mL. Both D-dimer and IL-6 levels were abnormal among 71% (n=981) and 87.7% (n=1210) of patients, respectively. The average length of hospital stay was 8.05±5.136 days. Among female patients, 25.5% required oxygen (O_2) supplementation, while 28.9% (n=246) of males required O_2.

D-dimer levels showed a significant association with morbidity in terms of hospital stay less than five days (p= .000). D-dimer levels were also significantly associated with mortality (p= .000). Similarly, significant associations were observed between IL-6 levels and morbidity and mortality (p= .000). Chi-square tests also revealed a significant association between serum IL-6 and D-dimer levels and O_2 requirement (p= .000) (Tables 3 and 4).

Sub-group analysis: The t-test done to determine the difference in IL-6 and D-dimer levels between patients with and without diabetes revealed no significant difference between the two groups (D-dimer, p=.166; IL-6, p= .426) (Tables S1 and S2). The ANOVA test results revealed significant differences in both serum biomarker levels among diabetic patients with respect to their O_2 requirement (D-dimer, p= .000) and mortality (IL-6, p= .000); however, duration of hospitalization did not differ in this set of patients (Tables S3 and S4).

Similarly, in patients with and without hypertension, IL-6 levels were not significantly different (p= .655); however, D-dimer levels were significantly different (p= .014) (Tables S5 and S6). Both D-dimer and IL-6 levels were also found to be significantly different in hypertensive patients with respect to their O_2 requirement (p= .000)

Table 1) Distribution of symptoms among the studied patients

Variables	Sub-Category	Frequency (%)
Fever	Yes	879 (63.7)
	No	501 (36.3)
Cough	Yes	878 (63.6)
	No	502 (36.4)
Dyspnea	Yes	332 (24.1)
	No	1048 (75.9)
Loose stool	Yes	124 (9.0)
	No	1256 (91.0)
Myalgia	Yes	45 (3.3)
	No	1335 (96.7)
Fatigue	Yes	17 (1.2)
	No	1363 (98.8)
Asymptomatic	Yes	49 (3.6)
	No	1331 (96.4)

Table 2) Distribution of comorbidities among the patients

Variables	Sub-Category	Frequency (%)
Systemic hypertension	Yes	586 (42.5)
	No	794 (57.5)
CAD	Yes	155 (11.2)
	No	1225 (88.2)
Dyslipidaemia	Yes	29 (2.1)
	No	1351 (97.9)
Hypothyroidism	Yes	73 (5.3)
	No	1307 (94.7)
CVA	Yes	27 (2.0)
	No	1353 (98.0)
Chronic kidney disease	Yes	29 (2.1)
	No	1351 (97.9)
Chronic liver disease	Yes	13 (0.9)
	No	1367 (99.1)
COPD/Asthma	Yes	56 (4.1)
	No	1324 (95.9)
Diabetes	Yes	723 (52.4)
	No	657 (47.6)

Abbreviations: CAD: coronary artery disease, CVA: cerebrovascular accident, COPD: Chronic obstructive pulmonary disease

and mortality (p= .000). While morbidity did not show a significant association with IL-6 levels in hypertensive patients (p=0.312), it had a significant association with D-dimer levels (p= .018) (Tables S7 and S8).

Discussion

To the best of our knowledge, this is the first study conducted in South India to investigate the clinical profile and association of serum biomarkers such as D-dimer and IL-6 levels with morbidity and mortality in geriatric COVID-19 patients.

Age and comorbidities such as hypertension and diabetes are considered as strong risk factors for the COVID-19 disease severity and progression [3, 8]. The risk of long-term COVID infection and post-COVID syndrome has also been reported to be higher among older patients and those with pre-COVID comorbidities [9, 10]. Identifying risk factors pre-emptively among the geriatric population could improve the COVID-19 prognosis and in turn reduce the risk of post-COVID complications in these patients. In the current study, most of the patients presented with fever and cough, and among comorbidities, most of them had hypertension and diabetes. Similar trends in geriatric populations have been reported in a Turkish study [11] and a meta-analysis conducted in the early stages of the pandemic[12].

Systemic and inflammatory biomarkers like D-dimer and IL-6 are exploited to identify high-risk patients and predict mortality. Elevated D-dimer levels indicate coagulopathy which could lead to thromboembolic events, and elevated IL-6 levels indicate systemic inflammation contributing to the development of acute respiratory distress syndrome (ARDS) [13, 14]. In the present study, both D-dimer and IL-6 levels were abnormal among the majority of patients, and normal levels were significantly associated with better prognosis in terms of hospital stay less than 5 days and oxygen requirement. Both were also significantly

Table 3) Association of D-dimer levels with O_2 requirement, morbidity, and mortality in COVID-19 patients

Clinical Characteristics	Subcategory	Normal D-Dimer Levels		Total	X^2 statistic, d.f., *P-Value*
		No	Yes		
Hospital stay less than 5 days	No	695	192	887	X^2=64.977, d.f=1, *p*=.000*
	Yes	285	208	493	
Death	No	826	393	1219	X^2=53.749, d.f=1, *p*=.000*
	Yes	154	7	161	
Oxygen requirement	No	638	342	980	X^2=89.884, d.f=1, *p*=.000*
	Yes	361	39	400	

d.f: degrees of freedom, * indicates significance at *p*< .05.

Table 4) Association of IL-6 levels with O_2 requirement, morbidity, and mortality in COVID-19 patients

Clinical Characteristics	Subcategory	Normal IL-6 Levels		Total	X^2 statistic, d.f., *P-Value*
		No	Yes		
Hospital stay less than 5 days	No	820	67	887	X^2=52.199, d.f=1, *p*=.000*
	Yes	390	103	493	
Death	No	1051	168	1219	X^2=20.703, d.f=1, *p*=.000*
	Yes	159	2	161	
Oxygen requirement	No	851	359	1210	X^2=20.870, d.f=1, *p*=.000*
	Yes	148	22	170	

d.f: degrees of freedom. * indicates significance at *p*< .05.

associated with mortality. This finding is similar to the findings of a few other studies, indicating that IL-6 and D-dimer levels are significantly associated with mortality [14, 15]. However, serum levels of both D-dimer and IL-6 have been reported to be high among hypertensive and diabetic patients, thereby increasing the risk of mortality [16–19]. In the present study, both D-dimer and IL-6 levels were slightly high in patients with comorbid diabetes but not in those with hypertension, which resulted in insignificant association of serum biomarker levels with comorbidities, except for D-dimer levels which were significantly different in patients with comorbid hypertension.

D-dimer levels >2.01 mg/mL and IL-6 levels >74.98 pg/mL have been reported to be a predictor of in-hospital mortality among the elderly [20, 21]. In the present study, however, the mean D-dimer and IL-6 values were higher than the cut-off value, which could be due to a few outlier patients with D-dimer levels as high as 20 mg/mL FEU and IL-6 values >5000 pg/mL. Although there was a significant association between D-dimer and IL-6 levels and mortality, the mortality rate among the present study population was only 11.6%. This low mortality rate could also be attributed to the absence of severe comorbidities like coronary artery disease (CAD), chronic kidney or liver disease, cerebrovascular accident, etc. [22, 23] among most of the patients in the current study. However, we found a significant association between mortality and comorbid hypertension and diabetes. Other studies have reported similar findings, indicating that increased mortality in patients with comorbidities like diabetes and hypertension is associated with elevated D-dimer and IL-6 levels [24–26]. Oxygen requirement was also influenced by both D-dimer and IL-6 levels in patients with comorbidities in the present study, but morbidity was not affected by these factors. While this study highlights the potential utility of IL-6 and D-dimer as indicators of

severe disease or adverse outcomes, and given the mortality rate among the current study population, it is evident that various factors including comorbidities should be considered for prognosis in geriatric COVID-19 patients along with serum biomarkers. Differences in disease severity and mortality among patients of different ages could provide insights to clinicians to implement a better treatment approach for patients [14]. Furthermore, the study findings emphasize the need for close monitoring of comorbidities during risk stratification.

Strengths and limitations: The strengths of this study include the large sample size and the focus on geriatric patients, which is overlooked in most other studies. However, retrospective design, single-centre data, and medical record data could introduce bias.

Conclusion

This retrospective observational study demonstrated a significant association between serum IL-6 and D-dimer levels and morbidity and mortality in elderly COVID-19 patients. Additionally, higher levels of these serum biomarkers in COVID-19 patients along with comorbidities such as hypertension and diabetes significantly influenced oxygen requirement and mortality but not morbidity. These findings highlight the potential utility of these biomarkers in risk stratification and management strategies for this vulnerable and high-risk population. Further prospective research with a larger sample size is necessary to validate these findings, explore their clinical implications, as well as identify the risk of long-term COVID and post-COVID syndrome in elderly COVID-19 patients.

Acknowledgments

None.

Ethical permissions: The study was approved by the Institutional Human Ethics Committee (IHEC, Registration no. PSG/IHEC/2023/Appr/Exp/123), and since this research was a retrospective study, it was exempted from informed consent.

Conflicts of interests: The authors declare no conflict of interest.

Source of Funding: This study did not receive any specific grants or funds from public, government, or not-for-profit sector.

Data availability statement: The data will be shared upon reasonable request from the corresponding author.

Authors' contributions: CJD was involved in concept, design, and final drafting. YC was involved in patient recruitment, data analysis, manuscript writing, and final drafting. SMD was involved in data collection and manuscript writing. KB was involved in data collection and data interpretation. SKS was involved in data monitoring and data interpretation. ST was involved in data monitoring, data interpretation, and final drafting. All authors reviewed the final manuscript.

References

1. World Health Organization. Statement on the fifteenth meeting of the IHR (2005) Emergency Committee on the COVID-19 pandemic. Geneva: World Health Organization;2005.
2. Becerra-Muñoz VM, Núñez-Gil IJ, Eid CM, Garcia Aguado M, Romero R, Huang J, et al. Clinical profile and predictors of in-hospital mortality among older patients hospitalised for COVID-19. Age Ageing.2021;50(2):326–34.
3. Center for Disease Control and Prevention. Underlying medical conditions associated with higher risk for severe COVID-19: Information for healthcare professionals. Atlanta: Center for Disease Control and Prevention;2022.
4. Azarudeen MJ, Aroskar K, Kurup KK, Dikid T, Chauhan H, Jain SK, et al. Comparing COVID-19 mortality across selected states in India: The role of age structure. Clin Epidemiol Glob Health. 2021;12:100877.
5. Gao Y, Ding M, Dong X, Zhang JJ, Kursat Azkur A, Azkur D, et al. Risk factors for severe and critically ill COVID-19 patients: A review. Allergy. 2021;76(2):428–55.
6. Eljilany I, Elzouki AN. D-Dimer, fibrinogen, and

IL-6 in COVID-19 patients with suspected venous thromboembolism: A narrative review. Vasc Health Risk Manag. 2020;16:455-62.
7. Mittal K, Dhar M, Pathania M, Jha D, Saxena V. A comparative study of mortality differences and associated characteristics among elderly and young adult patients hospitalised with COVID-19 in India. BMC Geriatr. 2023;23:1–9.
8. Sanyaolu A, Okorie C, Marinkovic A, Patidar R, Younis K, Desai P, et al. Comorbidity and its impact on patients with COVID-19. SN Compr Clin Med. 2020;2:1069-76.
9. Mansell V, Hall Dykgraaf S, Kidd M, Goodyear-Smith F. Long COVID and older people. Lancet Healthy Longev. 2022;3(12):e849–54.
10. Rodriguez-Sanchez I, Rodriguez-Mañas L, Laosa O. Long COVID-19: The need for an interdisciplinary approach. Clin Geriatr Med. 2022;38(3):533-44.
11. Ulugerger Avci G, Bektan Kanat B, Suzan V, Can G, Korkmazer B, Karaali R, et al. Clinical outcomes of geriatric patients with COVID-19: review of one-year data. Aging Clin Exp Res. 2022;34(2):465–74.
12. Singhal S, Kumar P, Singh S, Saha S, Dey AB. Clinical features and outcomes of COVID-19 in older adults: A systematic review and meta-analysis. BMC Geriatr.2021;21(1):1-9.
13. Farid E, Sridharan K, Alsegai OA, Khawaja SA, Mansoor EJ, Teraifi NA, et al. Utility of inflammatory biomarkers in patients with COVID-19 infections: Bahrain experience. Biomark Med. 2021;15(8):541-9.
14. Ahirwar AK, Takhelmayum R, Sakarde A, Rathod BD, Jha PK, Kumawat R, et al. The study of serum hsCRP, ferritin, IL-6, and plasma D-dimer in COVID-19: A retrospective study. Horm Mol Biol Clin Investig. 2022;43(3):337–44.
15. Luporini RL, Rodolpho JM, Kubota LT, Martin AC, Cominetti MR, de Freitas Anibal F, et al. IL-6 and IL-10 are associated with disease severity and higher comorbidity in adults with COVID-19. Cytokine.2021;143:155507.
16. Kim BS, Shin JH. Association between D-dimer and long-term mortality in patients with acute severe hypertension visiting the emergency department. Clin Hypertens. 2023;29(1):16.
17. Miri C, Charii H, Bouazzaoui MA, Laouan Brem F, Boulouiz S, Abda N, et al. D-dimer level and diabetes in the COVID-19 infection. Clin Appl Thromb Hemost. 2021;27:10760296211045902.
18. Tanase DM, Gosav EM, Radu S, Ouatu A, Rezus C, Ciocoiu M, et al. Arterial hypertension and interleukins: Potential therapeutic target or future diagnostic marker? Int J Hypertens. 2019;2019.
19. Bowker N, Shah RL, Sharp SJ, Stewart ID, Wheeler E, Ferreira MA, et al. Meta-analysis investigating the role of interleukin-6 mediated inflammation in type 2 diabetes. EbioMedicine. 2020;61:103062.
20. Soni M, Gopalakrishnan R, Vaishya R, Prabu P. D-dimer level is a useful predictor for mortality in patients with COVID-19: Analysis of 483 cases. Diabetes Metab Syndr. 2020;14(6):2245-9.
21. Milenkovic M, Hadzibegovic A, Kovac M, Jovanovic B, Stanisavljevic J, Djikic M, et al. D-dimer, CRP, PCT, and IL-6 levels at admission to ICU can predict in-hospital mortality in patients with COVID-19 pneumonia. Oxid Med Cell Longev. 2022;2022.
22. Hwang J, Ryu HS, Kim HA, You SH, Kim MS, Baek MS, et al. Prognostic factors of COVID-19 infection in elderly patients: A multicenter study. J Clin Med. 2020;9(11):1–13.
23. Rehatta NM, Chandra S, Sari D, Lestari MI, Senapathi TG, Nurdin H, et al. Comorbidities and COVID-19 status influence the survival rate of geriatric patients in intensive care units: a prospective cohort study from the Indonesian Society of Anaesthesiology and Intensive Therapy. BMC Geriatr.2022;22(1):1–9.
24. Mishra Y, Pathak BK, Mohakuda SS, Tilak TV, Sen S, Harikrishnan P, et al. Relation of D-dimer levels of COVID-19 patients with diabetes mellitus. Diabetes Metab Syndr. 2020;14(6):1927–30.
25. Phan F, Boussouar S, Lucidarme O, Zarai M, Salem JE, Kachenoura N, et al. Cardiac adipose tissue volume and IL-6 level at admission are complementary predictors of severity and short-term mortality in COVID-19 diabetic patients. Cardiovasc Diabetol.2021;20:1–10.
26. Huang S, Wang J, Liu F, Liu J, Cao G, Yang C, et al. COVID-19 patients with hypertension have more severe disease: A multicenter retrospective observational study. Hypertens Res.2020;43(8):824–31.