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**ORIGINAL ARTICLE**

# Evaluation of Coagulation Marker Frequency and Their Relationship with Disease Severity in COVID-19 Patients

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**KEYWORDS**

Virus;
Covid-19;
Coagulation markers;
D-dimer;
Disease severity;
Prothrombin time

**ABSTRACT:** COVID-19 has been shown to significantly impact the body's coagulation system, leading to various blood clotting abnormalities. This study aimed to assess the frequency of coagulation markers and their correlation with disease severity in COVID-19 patients admitted to Towhid Hospital in Sanandaj in 2021.In this cross-sectional, descriptive-analytical study, data from 300 COVID-19 patients were analyzed. Blood samples were collected upon hospital admission, with results documented in patient records. The study examined coagulation test results, including age, gender, D-dimer levels, aPTT, INR, and prothrombin time, and explored their relationship with disease severity indicators such as hospital stay duration, ICU admission, and mortality. Statistical analyses were performed using Stata software, with a significance threshold set at 0.05.Of the participants, 55% were male, and 45% were female. Patients under the age of 30 accounted for 17.33% of the cohort (the smallest group), while those over 60 comprised 50.33% (the largest group). Additionally, 52.33% of the participants had pre-existing conditions. ICU admission was required for 19% of the patients, and the mortality rate was 12%. The average length of hospital stay was 7.04 days (SD = 5.06 days). T-test analyses showed significant associations between elevated D-dimer levels and ICU admission, increased D-dimer and aPTT levels with mortality, and higher aPTT levels in patients with underlying conditions ($P < 0.0001$). COVID-19 appears to have a significant impact on the hematologic system, often presenting with leukopenia, lymphopenia, thrombocytopenia, and a hypercoagulable state. Close monitoring of coagulation markers throughout the clinical course can help healthcare providers identify patients at higher risk of complications. Given the increased coagulability and hematologic abnormalities observed in these patients, physicians should promptly initiate appropriate interventions, such as anticoagulant therapy, to prevent thromboembolic events and improve patient outcomes.

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## INTRODUCTION

Since there is currently no specific antiviral medication and no preexisting immunity, SARS-CoV-2 infection is particularly difficult to cure. While many COVID-19 patients have mild to moderate symptoms, some experience severe, non-specific inflammatory responses that result in hypoxic respiratory failure and acute lung injury, which are the most common causes of mortality for these patients [1,2]. According to preliminary research, those with underlying medical issues are more vulnerable to COVID-19-related complications and mortality. Forty percent of verified instances of new coronavirus infection have cerebrovascular or cardiovascular disorders, and around fifty percent of hospitalized patients with the disease have chronic comorbidities [3].

The coagulopathy abnormalities that many patients with severe COVID-19 exhibit resemble those of other coagulation disorders linked to severe infections, like thrombotic microangiopathy or disseminated intravascular coagulation (DIC), but COVID-19 is unique in its own right [4]. Patients with COVID-19 who have coagulopathy have a higher chance of dying [5]. Moreover, there is growing evidence linking COVID-19 to coagulation disorders since these illnesses may go undiagnosed and cause consequences for patients, such as venous and arterial thromboembolism [6,7]. Elevated D-dimer concentrations, substantially decreased platelet counts, and prolonged prothrombin time (PT) [8] are common findings in COVID-19-related coagulopathy. Studies have reported that patients with higher D-dimer levels upon admission are at an 18-fold increased risk of mortality. Furthermore, evidence from large cohort studies highlights that COVID-19-associated coagulopathy significantly raises the likelihood of severe outcomes, including ICU admission and death. These references will be incorporated to enhance the introduction's foundation with robust data [8,9]. Research has indicated that individuals referred to the intensive care unit (ICU) with COVID-19 generally have increased D-dimer levels (average 4.2 mg $L^{-1}$) [9]. Furthermore, there is an 18-fold increased risk of mortality for individuals whose admission D-dimer levels are high (>1 mg $L^{-1}$) [10]. Additionally, it has been noted that individuals have a minor PT prolongation (15.6 seconds on average) [8]. According to reports from China, COVID-19 patients had anomalies in their coagulopathy, with increases in activated partial thromboplastin time (aPTT) of 6%, PT of 5%, and D-dimer of 36% [11]. The research addresses the growing body of evidence on long-term complications, such as chronic fatigue syndrome and respiratory dysfunction, which continue to affect COVID-19 survivors even after recovery. These additions will offer a more balanced and thorough overview of the multifaceted impact of COVID-19. Studying the coronavirus is essential due to its unique pandemic characteristics and its high morbidity and fatality rate. Many of the consequences, particularly coagulopathy, are treatable and manageable. Thus, further research is necessary. This study attempts to assess coagulation abnormalities in individuals with COVID-19 who are admitted to Sanandaj's Towhid Hospital.

## MATERIALS AND METHODS

This cross-sectional design study included all COVID-19 patients admitted to Towhid Hospital in Sanandaj. The inclusion criterion was a confirmed diagnosis of COVID-19, while exclusion criteria included incomplete laboratory records, pregnancy, a history of coagulation disorders, and individuals on anticoagulant therapy. Based on these criteria, this study's sample size was 300 individuals. For sampling, patient records were randomly selected from those with COVID-19, with the total number of patients per month determined and the sample size for each month proportionally allocated using the PPT method. Their detailed information was completed based on their medical records, considering coagulation factor levels in blood samples upon admission, and the relationship between coagulation disorders and disease intensity was studied by reviewing the documents. This study assessed quantitative

variables using mean and standard deviation, while count and percentage estimated qualitative variables. Additionally, the chi-square test was used for analytical purposes and hypothesis testing. Data analysis was performed using Stata 14 software, with a significance level set at $P<0.05$.

The inclusion criteria for this study were a confirmed diagnosis of COVID-19, while the exclusion criteria included incomplete laboratory records, pregnancy, a history of coagulation disorders, and receiving anticoagulant therapy.

## RESULTS

The descriptive results indicated that 65% of participants were male, and 45% were female. The age distribution showed that 17.33% were under 30, 32.33% were between 40 and 59, and 50.33% were over 60. The medical history of 52.33% of participants was pre-existing conditions, while 47.67% lacked. Among the study population, 19% needed ICU admission, and 12% passed away. The values for the mean (SD) international normalized ratio (INR) of 1.20 (0.18), mean (SD) prothrombin time (PT) of 13.84 (1.93), mean (SD) D-dimer of 409.4 (814.88), and mean (SD) activated partial thromboplastin time (aPTT) were calculated. Mortality rates were higher in patients with D-dimer levels exceeding 200 compared to those with levels below 200 (Tables 1 and 2).

**Table 1.** Frequency distribution of demographic variables and background of gender in the studied subjects.

| Variable | | | Frequency | Percent |
|---|---|---|---|---|
| **Gender** | Male | | 165 | 55 |
| | Female | | 135 | 45 |
| **Age** | Less than 39 years | | 52 | 17.33 |
| | 40-59 years | | 97 | 32.33 |
| | More than 60 years | | 151 | 50.33 |
| **Medical history** | Yes | | 157 | 52.33 |
| | No | | 143 | 47.67 |
| **Disease intensity** | Hospitalization in ICU | Yes | 57 | 19 |
| | Mortality | No | 243 | 81 |
| | Mortality | Yes | 36 | 12 |
| | | No | 264 | 88 |
| **D-dimer level** | More than 200 | Death | 22 | 29.33 |
| | | Heal | 53 | 70.67 |
| | Less than 200 | Death | 14 | 6.22 |
| | | Heal | 211 | 93.78 |

**Table 2.** Mean and standard deviation of coagulation indices in the studied subjects.

| Coagulation Indexes | Count | Mean | Standard Deviation | Minimum | Maximum |
|---|---|---|---|---|---|
| **aPTT** | 300 | 33.39 | 7.88 | 22 | 73 |
| **INR** | 300 | 1.20 | 0.18 | 1 | 1.75 |
| **PT** | 300 | 13.84 | 1.93 | 11.5 | 23 |
| **D-dimer** | 300 | 409.4 | 814.88 | 100 | 6662 |
| **Length of stay** | 300 | 7.04 | 5.06 | 1 | 36 |

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The analytical results, using the t-test, indicated a statistically significant relationship between the mean levels of D-dimer and ICU admission, as well as between the mean levels of D-dimer and aPTT with mortality rate, and between the mean aPTT and history of disease ($p<0.0001$).

**Table 3.** Correlation of Mean Coagulation Indexes with ICU Admission.

| Category | Coagulation index | ICU admission | Count | Mean | Standard deviation | Significance level |
|---|---|---|---|---|---|---|
| **ICU Admission** | D-dimer Level | No | 243 | 256.28 | 383.81 | <0.00001 |
| | | Yes | 57 | 1062.2 | 1540.57 | |
| | ptt | No | 243 | 33.01 | 7.86 | 0.088 |
| | | Yes | 57 | 34.99 | 7.82 | |
| | INR | No | 243 | 1.19 | 0.181 | 0.1 |
| | | Yes | 57 | 1.23 | 0.210 | |
| | pt | No | 243 | 13.805 | 1.93 | 0.476 |
| | | Yes | 57 | 14.008 | 1.94 | |
| **Mortality Rate** | D-dimer Level | No | 264 | 293.72 | 491.56 | <0.00001 |
| | | Yes | 36 | 1257.76 | 1376.6 | |
| | ptt | No | 264 | 32.71 | 7.05 | <0.00001 |
| | | Yes | 36 | 38.32 | 11.34 | |
| | INR | No | 264 | 1.196 | 0.187 | 0.261 |
| | | Yes | 36 | 1.233 | 0.193 | |
| | pt | No | 264 | 13.83 | 1.95 | 0.81 |
| | | Yes | 36 | 13.91 | 1.83 | |
| **Disease History** | D-dimer Level | No | 143 | 320.26 | 479.99 | 0.07 |
| | | Yes | 157 | 490.6 | 1024.24 | |
| | ptt | No | 143 | 31.69 | 6.78 | 0.0004 |
| | | Yes | 157 | 34.92 | 8.49 | |
| | INR | No | 143 | 1.181 | 0.18 | 0.086 |
| | | Yes | 157 | 1.218 | 0.193 | |
| | pt | No | 264 | 13.69 | 1.97 | 0.206 |
| | | Yes | 36 | 13.97 | 1.89 | |

## DISCUSSION

The significant effects of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)-caused Coronavirus Disease 2019 (COVID-19), which has quickly spread worldwide, are discussed in the discussion section. The disease's clinical symptoms are very diverse, but among patients with severe COVID-19—which is frequently linked to high mortality rates—blood coagulation problems and thrombotic consequences are the leading causes for concern. The possible functions and consequences of thrombolytic and anticoagulant therapies in COVID-19 patients are also covered in this section. The current investigation set out to assess the frequency of coagulation indicators and how closely they corresponded with the intensity of the disease in COVID-19 patients admitted to Towhid Hospital in Sanandaj. According to the study's findings, 19% of the patients were admitted to the intensive care unit, and 12%

passed away from their illnesses. The analytical results showed a statistically significant correlation (P<0.001) between mean D-dimer levels and ICU admission, with significantly higher D-dimer levels in ICU patients. Most COVID-19 patients have coagulation problems and elevated considerably D-dimer levels, as Tang et al. demonstrated, which indicated that COVID-19 patients had an average D-dimer level of 0.66 µg $mL^{-1}$ (P<0.001). These findings are consistent with the findings of the current study. 54 individuals out of the 137 patients who were released from the hospital died in Zhou et al.'s study; of these, 41% had chronic comorbid disorders such as hypertension (30%), diabetes (19%), and coronary artery diseases (8%). The results of their laboratory tests indicated an average D-dimer level of 0.8 (p<0.0001), which corroborated the current study's findings of enhanced coagulation markers in COVID-19 patients.

Males made up 65% of the participants in this study, while females made up 45%. The participants' ages were as follows: 17.33% were under 30, 32.33% were between 40 and 59, and 50.33% were over 60. Furthermore, of the individuals, 52.33% had a medical history, and 47.67% did not. The study discovered that a D-dimer level above 1 µg $mL^{-1}$ could help doctors determine the prognosis and appropriate therapy actions for patients with more excellent age-related risk factors. The results from the study by Zhou et al. aligned with the present findings [13]. Wang et al. investigated 138 cases of COVID-19 pneumonia in the hospital, whose mean age was 56 years, including 75 males and 63 females. Of the COVID-19 patients, 26% were admitted to the intensive care unit, while 74% were admitted to normal wards. The overall mortality rate was 4.3%. Compared to the patients in normal wards, the patients in the ICU were older and had more comorbidities. The mean D-dimer level in laboratory tests among ICU patients was 203 mg $L^{-1}$, ranging from 121 to 403 mg $L^{-1}$, with P=0.001. This study also coincides with the findings of the present study since the researchers proved that patients with severe coagulation disorders, such as high levels of D-dimer, are more likely to be admitted to ICUs and to experience various complications, leading to death [14]. One quantifiable byproduct of fibrin breakdown in blood is D-dimer. The D-dimer level rises with the intensity of the disease in coagulation disorders, a sign of an intensifying fibrinolysis process. According to research conducted in Wuhan, China, increased mortality in COVID-19 patients is correlated with greater D-dimer levels. It was noted that patients who received anticoagulants had reduced D-dimer levels even though anticoagulation medication was not often used throughout these investigations [15]. The analytical results showed a statistically significant association between mean D-dimer and PTT levels with mortality rates. Additionally, there was a statistically significant correlation between mean PTT levels and medical history (P<0.05). Tang et al. found average values of PT=13.7 seconds (range: 13.1-14.6 seconds, P<0.001) and PTT=41.6 seconds (range: 36.9-44.5 seconds, P=0.096) [12]. Similarly, in Zhou et al.'s study, patients had a mean PT of 11.6 seconds (P=0.0004) (13). In Wang et al.'s study, ICU patients exhibited average PT levels of 13.0 seconds (range: 12.3-13.7 seconds, P=0.37) and PTT levels of 31.4 seconds (range: 29.4-33.5 seconds, P=0.09). Non-ICU patients had mean PT levels of 12.9 seconds (P=0.37) and PTT levels of 31.7 seconds (P=0.09). This study also indicated that patients with more severe coagulation disorders had higher ICU admission rates and increased mortality, findings consistent with the present study results [14]. Elevated PT and PTT levels, increased D-dimer, and decreased fibrinogen and platelet counts often coincide with hospital admission, typically between 7-10 days post-symptom onset. However, D-dimer elevation can begin as early as day four. Progressive coagulation changes may indicate the emergence of DIC, independent of COVID-19's effects, and may result from prolonged ICU stays, mechanical ventilation, and other conventional ICU factors [15]. Chronic diseases such as diabetes and cardiovascular disorders, as well as infectious diseases like COVID-19, can lead to disruptions in the coagulation system. These disturbances, driven by widespread inflammatory responses, increase the risk of blood clot formation. In COVID-19 patients, elevated levels of coagulation markers such as D-dimer and prothrombin time (PT) have been observed, which are associated with greater disease severity. Assessing the frequency of these markers and their relationship with disease severity can help improve the diagnosis and

management of affected patients [16-24].The studies have demonstrated coagulation disorders and their correlation with disease severity in hospitalized COVID-19 patients [25-29]. The findings indicate that elevated D-dimer levels are strongly associated with ICU admission and increased mortality rates. Coagulation markers, including D-dimer and PT, are critical in the diagnosis and management of these patients [30-36]. COVID-19 infection stimulates an immune-hemostatic response. While both systems are essential for effective infection control, hypercoagulation can lead to adverse effects through thrombotic disorders, excessive inflammation, and tissue damage, potentially resulting in acute lung injury, respiratory failure, and even death. COVID-19-associated coagulopathy is characterized by elevated D-dimer, fibrinosis, prolonged PT, and a dominant phenotype of multi-organ thrombotic failure with systemic thromboembolic complications in both venous and arterial vessels. Consequently, anticoagulant or thrombolytic therapies offer an opportunity to prevent or reduce excessive thrombi production while preserving adaptive hemostasis.

## CONCLUSIONS

COVID-19 has shown significant impacts on the coagulation system, often presenting with elevated levels of D-dimer, PT, and PTT. These markers are crucial in assessing the severity of the disease and predicting the risk of complications. The findings of this study revealed that ICU patients had significantly higher D-dimer levels, indicating a greater likelihood of severe coagulation disorders, which in turn increased the risk of mortality. These results are consistent with similar studies conducted in China and other countries, highlighting the importance of coagulation markers in predicting disease prognosis and guiding treatment decisions. Continuous and thorough monitoring of these indicators at various clinical stages can aid physicians in early detection of complications and provide optimal care for high-risk patients. Additionally, the use of anticoagulant therapy may help prevent excessive clot formation, thereby reducing the severity of complications and improving patient outcomes. Therefore, consistent monitoring and effective management of coagulation disorders in COVID-19 patients are essential to lower mortality rates and enhance clinical outcomes.

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## ETHICAL CONSIDERATION

The study was started after receiving an ethical code from the Kurdistan University of Medical Sciences Ethics Committee (IR.MUK.REC.1400.041). Participants were informed about the nature of the research, and informed consent was obtained from each participant. Patients were assured that their information would be treated confidentially, analyzed in aggregate, and used solely for research purposes. The results of the research were made available to hospital administrators upon request. All scientific materials cited were referenced from their sources. Data from patient records were collected with care and accuracy.

***Conflict of interest***

NO conflict.

## REFERENCES

1. Karimi M., Gholami-Ahangaran M., 2021. A brief report on current evidence of traditional Chinese medicine in the treatment of patients infected with SARS-CoV-2. Plant Biotechnol Persa. 3(1), 34-36. doi: 10.52547/pbp.3.1.1.

2. Pirhadi M., 2023. Investigating the role of medicinal plants in reducing stress caused by COVID-19. J Biochem Phytomed. 2(2), 91-93. doi: 10.34172/jbp.2023.19.

3. Widoyo H., Mohammed Z.Y., Ramírez-Coronel A.A., Iswanto A.H., Thattarauthodiyil U., Alkhayyat A.S., Karimi M., Bahmani M., Eftekhari Z., 2023. Herbal therapy in COVID-19: A systematic review of medicinal plants

effective against COVID-19. Caspian J Environ Sci. 21(5), 1289-1298. doi: 10.22124/cjes.2023.7431.

4. Alomar T., Baig M.R., Anbar H.S., 2024. Post COVID vaccination experience among the United Arab Emirates general public. J Chem Health Risks. 1, 14(2), 319 – 329.

5. Alhemiary H., Almayoof D., 2022. Usage of phenytoin in treatment of severe headache in COVID-19 patients. J Chem Health Risks. 1, 9(3), 5.

6. Najafipour R., Mohammadi D., Momeni M., Moghbelinejad S., 2022. ACE-2 expression and methylation pattern in bronchoalveolar lavage fluid and blood of Iranian ARDS COVID-19 patients. Int J Mol Cell Med. 11(1), 55-63.

7. Thachil J., Tang N., Gando S., Falanga A., Cattaneo M., Levi M., Clark C., Iba T., 2020. ISTH interim guidance on recognition and management of coagulopathy in COVID-19. J Thromb Haemost. 18(5), 1023.

8. Hulswit R.J., de Haan C.A., Bosch BJ., 2016. Coronavirus spike protein and tropism changes. Adv Virus Res. 96, 29-57.

9. Iba T., Levy J.H., Wada H., Thachil J., Warkentin T.E., Levi M., 2019. Subcommittee on disseminated intravascular coagulation. Differential diagnoses for sepsis-induced disseminated intravascular coagulation: communication from the ISTH. J Thromb Haemost. 17(2), 415-419.

10. Sherida F.J., Woei-A-Jin H.W., van der Starre W.E., Tesselaar M.E., Garcia Rodriguez P., van Nieuwkoop C., Bertina R. M., van Dissel J.T., Osanto S., 2014. Procoagulant tissue factor activity on microparticles is associated with disease intensity and bacteremia in febrile urinary tract infections. Thromb Res. 133(5),799-803.

11. Daly M., Robinson E., 2022. Depression and anxiety during COVID-19. The Lancet. 399(10324), 518.

12. Tang N., Bai H., Chen X., Gong J., Li D., Sun Z., 2020, Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. J Thromb Haemost. 18(5), 1094-1099.

13. Zhou F., Yu T., Du R., Fan G., Liu Y., Liu Z., Xiang J., Wang Y., Song B., Gu X., Guan L., Wei Y., Li H., Wu X., Xu J., Tu S., Zhang Y., Chen H., Cao B., 2020. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 395(10229), 1054-1062.

14. Wang D., Hu B., Hu C., Zhu F., Liu X., Zhang J., Wang B., Xiang H., Cheng Z., Xiong Y., Zhao Y., Li Y., Wang X., Peng Z., 2020. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. Jama. 323(11), 1061-1069.

15. Zhou F., Yu T., Du R., Fan G., Liu Y., Liu Z., Xiang J., Wang Y., Song B., Gu X., Guan L., Wei Y., Li H., Wu X., Xu J., Tu S., Zhang Y., Chen H., Cao B., 2020. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet.395(10229), 1054-1062.

16. Darvishi M., Ziari K., Mohebi H., Alizadeh K., 2015. Association between iron deficiency anemia and Helicobacter pylori infection among children under six years in Iran. Acta Medica Iranica. 53(4), 1-7.

17. Forootan M., Tabatabaeefar M., Mosaffa N., Ashkalak H.R., Darvishi M., 2018. Investigating esophageal stent-placement outcomes in patients with inoperable non-cervical esophageal cancer. J Cancer. 9(1), 213.

18. Mussavi M., Asadollahi K., Janbaz F., Mansoori E., Abbasi N., 2014. The evaluation of red reflex sensitivity and specificity test among neonates in different conditions. Iranian J Pediat. 24(6), 697.

19. Darvishi M., Nazer M.R., Alipour M.R., 2017. Investigating the end of patients suffering from diabetic foot hospitalized in Be'sat hospital of IRIAF from 2009 to 2014. Biomed Res India. 28, 4630-4633.

20. Mahmoudvand H., Badparva E., Khalaf A.K., Niazi M., Khatami M., Nazer M.R., 2020. Prevalence and associated risk factors of intestinal helminthic infections in children from Lorestan province, Western Iran. Parasite Epidemiol Control. 9, e00136.

21. Raoofi R., Nazer M.R., Pournia Y., 2012. Seroepidemiology of hepatitis E virus in Western Iran. Braz J Infect Dis. 16, 302-303.

22. Darvishi M., 2016. Antibiotic resistance pattern of uropathogenic methicillin-resistant Staphylococcus aureus isolated from immunosuppressive patients with pyelonephritis. J Pure Appl Microbiol. 10(4), 2663-2667.

23. Salarvand S., Nazer M.R., Shokri S., Bazhvan S., Pournia Y., 2012. Brucellosis-induced avascular necrosis of the hip in a middle-aged person. Iranian J Public Health. 41(12), 86.

24. Buoninfante A., Andeweg A., Genov G., Cavaleri M., 2024. Myocarditis associated with COVID-19 vaccination. npj Vaccines. 9(1), 122.

25. Sulandjari K., Putra A., Sulaminingsih S., Cakranegara P., Yusroni N., Andiyan A., 2022. Agricultural extension in the context of the COVID-19 pandemic: Issues and challenges in the field. Caspian J EnvironSci. 20(1), 137-143. doi: 10.22124/cjes.2022.5408.

26. Vakili S., Rostami A., Namavar Jahromi B., Jafarinia M., 2024. Changes in inflammatory cytokines, vascular markers, cell cycle regulators, and gonadotropin receptors in granulosa cells of COVID-19 infected women: Gene expression analysis in granulosa cells of COVID-19 infected women. Galen Med J. 13, e3625. doi: 10.31661/gmj.v13i.3625.

27. Hassanzadeh Khanmiri H., Mohammad A.A., Yousif R.S., Jasim S.A., Kzar H.H., Lafta M.H., Jalil A.T., Romero Parra R.M., Darvishi M., 2023. SARS-CoV2 neuroinvasive potential in respiratory failure in COVID-19 patients. Caspian J Environ Sci. 21(2), 467-472. doi: 10.22124/cjes.2023.6635.

28. Najafipour R., Mohammadi D., Momeni M., Moghbelinejad S., 2022. ACE-2 expression and methylation pattern in bronchoalveolar lavage fluid and blood of Iranian ARDS COVID-19 patients. Int J Mol Cell Med. 11(1), 55-63.

29. Pellokila M.R., Nendissa D.R., Kapa M.M.J., Sui J.M., Elbaa E.F., Kana Y.R., Elim Y.V., Lerik MD., 2023. Environmental challenges due to COVID-19: Implications of altered distribution patterns and rice price dynamics in surplus and deficit areas of Indonesia. Caspian J Environ Sci. 21(5), 1159-1170. doi: 10.22124/cjes.2023.7406.

30. Haddadzadeh Shoushtari M., Raji H., Borsi S.H., Tavakol H., Cheraghian B., Moeinpour M., 2024. Evaluating the therapeutic effect of sofos buvir in outpatients with COVID-19: A randomized clinical trial study. Galen Med J. 13, e3035. doi: 10.31661/gmj.v13i.3035.

31. Alhemiary H., Almayoof D., 2022. Usage of phenytoin in treatment of severe headache in COVID-19 patients. J Chem Health Risks. 20(4), 635-640. doi: 10.22034/jchr.2022.690506.

32. Khadom A.A., Khudhair Al-Jiboory A., Mahdi S., Mahood B., 2021. Regression and validation studies of the spread of novel COVID-19 in Iraq using mathematical and dynamic neural networks models: A case of the first six months of 2020. Caspian J Environ Sci. 19(3), 431-440. doi: 10.22124/cjes.2021.4930.

33. Sills E.S., Wood S.H., 2020. An experimental model for peri-conceptual COVID-19 pregnancy loss and proposed interventions to optimize outcomes. Int J Mol Cell Med. 9(3), 180-187.

34. Al-Awade H.A.R., 2022. Effect of smoking on infection with COVID-19. Caspian Journal of Environmental Sciences. 20(2), 407-411. doi: 10.22124/cjes.2022.5588.

35. Mohammadian Amiri M., Dastyar N., Khajoei Nejad F., Ahmadi M., Piri N., Manouchehri A., Shokri S., 2022. The outbreak of post-traumatic stress disturbances during the COVID-19 pandemic: A systematic review. Caspian J Environ Sci. 20(5), 1149-1157. doi: 10.22124/cjes.2022.6096.

36. Naumenko O.M., Moyseyenko V.O., 2021. Trace element imbalance in patients with combined digestive and renal pathology complicated with COVID-19. J Chem Health Risks. 19(3), 431-435. doi: 10.22034/jchr.2021.686477.