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Research Article

Clinical Outcome in Patients with COVID-19 and Comparison to Serum LDH and D-dimer Levels

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I N F O

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A B S T R A C T

Background: D-dimer and LDH are crucial biomarkers, particularly in view of the fact that they have been strongly linked to COVID-19 infection and have been linked to worse consequences in people who have severe viral infections.

Objectives: To determine how D-dimer and LDH correlated with clinical effects in COVID-19 patients who were hospitalised and how they forecasted the severity of COVID-19 patients.

Material and Methods: This was cross-sectional research conducted relatively early in the second wave of the pandemic. A total of 110 patients diagnosed with COVID-19 and admitted to the ICU from January 2021 to June 2021, were included in the study. The clinical outcome was evaluated in terms of discharge and death among patients requiring various forms of assisted ventilation.

Results: The average age of patients was 53.16 years (± 18.47 years). 35.5% of the patients were with comorbidities of which diabetes, hypertension, and COPD were around 80%. D-dimer was deranged in 2.7% of the subjects and LDH was deranged in 60% of the study subjects at the time of admission. Coming on to the outcome, all patients were put on assisted ventilation with 71.8% on NIV, 20% on HFNO, 1% on CPAP, and 7.2% on MV. During their hospital stays, 6 (5.45%) patients died and the remaining patients were discharged. A higher D-dimer value (> 1.5 µg/ml) during the hospital stay was found to be statistically significant with assisted ventilation and deaths of the admitted study subjects.

Conclusion: In our investigation, the biomarker D-dimer value was more associated than LDH with mortality in patients with COVID-19 infection.

Keywords: COPD, COVID-19, D-dimer, Diabetes Mellitus, HFNO, Hypertension, LDH

Introduction

A serious public health hazard has evolved in the form of the Coronavirus illness 2019 (COVID-19), which is brought on by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).[1] The overall prognosis for the illness varies. However, in some cases, organ malfunction, coagulation dysfunction, severe or critical disease, and acute respiratory distress syndrome are present.[2] A cytokine storm or viremia, as well as superinfection and organ failure, are likely to have activated the coagulation cascade in COVID-19, as evidenced by the frequent occurrence of diffuse intravascular coagulopathy and associated thrombotic sequelae.[3]

A biomarker that indicates the production and breakdown of fibrin is called D-dimer. It is found in both, plasma and whole blood.[4] It is found in the blood in small amounts in healthy people, but it is found in higher amounts in people with diseases that cause hyper-coagulation and more fibrinolytic activity. It is a fibrin breakdown product and a common biomarker for thrombotic diseases. D-dimer concentrations under 0.5 µg/ml are typically regarded as normal. Nevertheless, its levels increase with ageing and during pregnancy. Its level also increases when community-acquired pneumonia is more severe.[5] During the COVID-19 pandemic's outbreak, D-dimer has been recognised as a potential predictor of patient prognosis. It has shown promise in a number of studies for forecasting the severity of serious diseases.[6-9] The most commonly reported cause of D-dimer elevation in the literature is a rise in pro-inflammatory cytokines that is insufficiently controlled by anti-inflammatory components and overwhelms secondary homeostasis.[3] The signalling pathway that is dependent on hypoxia-inducible transcription factors is activated by hypoxia itself, predisposing to thrombosis. The most frequently impacted groups are older people and those with coexisting illnesses. In addition to having frequent comorbidities like hypertension, diabetes mellitus, and cardiovascular diseases, the patients may become more prone to thrombosis as they age.

One of these vital biomarkers is LDH, especially considering that higher LDH levels have previously been connected to worse outcomes in persons with other viral infections.[10-12] Patients with and without a severe condition may have significantly different amounts of LDH, according to preliminary data on COVID-19 patients.[13] It is a metabolic and immune surveillance prognostic biomarker that is produced by damaged cytoplasmic membranes in cells.[14,15] Inhibiting cytolytic cells and enhancing immune-suppressive cells are the results of LDH's increased lactate synthesis.[16] These modifications may hinder the immune system's ability to combat the virus, worsening the illness in those with high LDH.

According to numerous studies, LDH is a predictor of poorer effects in hospital-admitted patients.[10,17] SARS and other viral respiratory illnesses have served as the basis for many of the COVID-19 prognostic indicators and treatments, currently under investigation. Additionally, individuals with Middle East Respiratory Syndrome (MERS) had shown higher LDH concentrations.[18] In COVID-19 patients, high LDH levels seem to suggest that multiple organ failure and damage might have a greater impact on this condition and its clinical outcomes.

More and more focus is being paid to COVID-19's deviant coagulation parameters' prognostic value. Research opportunities were created by the abnormalities in the variables related to coagulation and their predictive significance in COVID-19 patients.[19] Monitoring coagulation factors has become a crucial part of illness treatment since it may call for extra therapies and may result in unfavourable effects.[20]

The aim of the current study was to determine how laboratory measures, specifically D-Dimer and LDH combined, predict the severity of COVID-19 patients and estimate how these parameters relate to clinical outcomes in COVID-19 patients who are hospitalised.

Material and Methods

The present cross-sectional observational study was conducted in a tertiary hospital from January 2021 to June 2021. In accordance with suggestions made by the World Health Organization, individuals who had a positive real-time fluorescence RT-PCR nucleic acid test result for COVID-19 were regarded as verified cases of COVID-19. After obtaining the participants' informed consent, we included 110 patients who arrived in the ICU from 1 January 2021 to 30 June 2021 since this was a time-frame research. Patients with moderate to severe illness who required admission to an intensive care unit (ICU) and had respiratory rates greater than 24/min or SpO_2 lower than 93% were included in the study. Adult patients with COVID-19 confirmation who were at least 18 years old and had a defined result (discharge or death) made up the study's subjects. During this research period, patients who were still hospitalised in the ICU and those who were discharged against medical recommendation were not included. The study comprised 110 patients who had been diagnosed with COVID-19 and hospitalised in the ICU. The information was collected and examined for the included study participants. Information on socio-demographic data, morbidity profile, oxygen requirement, NIV support, and laboratory parameters (serum LDH and D-dimer) during the hospital stay were retrieved. Clinical outcome in the present study was assessed in terms of discharge and death of the patients. In our hospital's setup, non-invasive ventilation (NIV), high-flow nasal oxygen (HFNO), continuous positive airway pressure (CPAP), and mechanical ventilation (MV) were all made available to patients who needed various forms of assisted ventilation.

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The highest D-dimer and LDH readings during 24 hours of admission, the highest values throughout the stay in the hospital, and the values at discharge were retrieved for each patient included in the study. D-dimer assay was done with the help of D dimer-nephelometry. The reference interval value in the lab was 0.5 µg/ml FEU. The DGKCH technique was employed as a diagnostic reagent for quantitative in vitro measurement of LDH in human serum and plasma. We chose the D-dimer values of 1.5 µg/ml and > 1.5 µg/ml from Poudel et al.'s study,[21] which offers a decent mix of specificity of 78.4% and sensitivity of 70.6%. The D-dimer value at this cutoff was three times greater than the generally agreed-upon upper limit of 0.5 µg/ml for normal.

Retrieved data were entered in an MS Excel sheet. Mean, standard deviation, and median, depending on the situation, were used to present continuous and categorical variables. Variables of a categorical nature were shown as n (%). A chi-squared test calculator was used to compare event frequencies between the groups of survivors and non-survivors, wherever it was necessary (p value). We considered something to be statistically significant if $p < 0.05$. R software, a statistical application, was utilised.

Ethical approval for the study was given by the Institutional Review Board, DY Patil Medical College and Hospital, Kolhapur, Maharashtra, India.

Results

110 suitable individuals were enrolled in the research study, 60 (54.5%) of whom were men, and 50 (45.5%) were women. The average age of those who enrolled was 53.16 years (± 18.47 years). 35.5% of the patients were with comorbidities, of which diabetes, hypertension, and COPD were around 80%. D-dimer was deranged in 2.7% of the subjects and LDH was deranged in 60% of the study subjects at the time of admission (Table 1).

Coming on to the outcome, all the patients were put on assisted ventilation with 71.8% on NIV, 20% on HFNO, 1% on CPAP, and 7.2% on MV. 6 (5.45%) patients died during their hospital stay and the rest were discharged (Tables 2 and 3).

In patients with COVID-19, a higher D-dimer value (> 1.5 µg/ml) at hospital stay and in-hospital mortality were significantly associated over the course of the hospitalisation (Table 2), whereas, higher LDH was not associated with any of the outcomes such as assisted ventilation or death of the study subjects (Table 3).

Table 1.Sociodemographic Characteristics and Values of Subjects at the Time of Admission

Variables		Frequency	Percentage
Age group (years)	< 20	1	0.9
	21-30	21	19.1
	31-40	10	9.1
	41-50	11	10.0
	51-60	26	23.6
	> 60	41	37.3
Gender	Male	60	54.5
	Female	50	45.5
Comorbidities	Yes	39	35.5
	No	71	64.5
Type of comorbidities (n = 39)	DM	10	9.0
	HTN	12	10.9
	COPD	9	8.1
	Others	8	7.2
D-dimer	Normal	107	97.3
	Deranged	3	2.7
LDH	Normal	44	40.0
	Deranged	66	60.0

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Table 2.Levels of D-dimer of Subjects during the Hospital Stay

Progress		D-Dimer < 1.5 µg/ml n (%)	D-Dimer > 1.5 µg/ml n (%)	Total	p Value
Assisted ventilation	Non-Invasive Ventilation (NIV)	67 (95.7)	12 (30.0)	79 (71.8)	< 0.05*
	High Flow Nasal Oxygen (HFNO)	3 (4.3)	19 (47.5)	22 (20.0)	
	Continuous Positive Airway Pressure (CPAP)	0 (0.0)	1 (2.5)	1 (1)	
	Mechanical Ventilation (MV)	0 (0.0)	8 (20.0)	8 (7.2)	
Outcome	Discharge	70 (100.0)	34 (85.0)	104 (94.5)	< 0.05*
	Death	0 (0.0)	6 (15.0)	6 (5.45)	
Total		70	40	110	

(p < 0.05* significant).

Table 3.Levels of LDH of Subjects during the Hospital Stay

Progress		LDH < 125-343 U/L (Normal) n (%)	LDH > 343 U/L (High) n (%)	Total	p Value
Assisted Ventilation	Non-Invasive Ventilation (NIV)	9 (100.0)	70 (69.3)	79 (71.8)	0.697
	High Flow Nasal Oxygen (HFNO)	0 (0.0)	22 (21.8)	22 (20.0)	
	Continuous Positive Airway Pressure (CPAP)	0 (0.0)	1 (0.9)	1 (1)	
	Mechanical Ventilation (MV)	0 (0.0)	8 (7.9)	8 (7.2)	
Outcome	Discharge	9 (100.0)	95 (94.0)	104 (94.5)	0.45
	Death	0 (0.0)	6 (6.0)	6 (5.45)	
Total		9	101	110	

Discussion

The current study was conducted during the very early stages of the 2nd wave of the pandemic in India (from January to June 2021). 110 patients admitted to the hospital with a diagnosis of COVID-19 were included in the study. In the hospital, cases were handled depending on the resources and regulations that were available; the latter were not set up right once and changed over time. Typically, D-dimer levels were checked at check-in, during the hospital stay, and again after release. During the research period, the majority of the care was symptomatic and included antipyretics, analgesics, and extra oxygen, as necessary.

In this study, it was discovered that in patients with COVID-19, assisted breathing, and in-hospital death were significantly associated with a higher D-dimer value over the course of the hospitalisation. Prior to the 2019 COVID-19 pandemic, in spite of some evidence showing D-dimer to be a useful biomarker for viral or bacterial pneumonia, it was not treated as one.[5] However, numerous COVID-19 sufferers have since mentioned having high D-dimer levels and thrombotic issues. D-dimer levels of more than 0.5 µg/ml were found in 260 out of 560 people (46%) according to Guan et al.[22]

Several types of research have looked into the connection between the initial D-dimer values and the severity and course of the illness. D-dimer may be a useful early predictor for foreseeing patient in-hospital death. According to Zhang et al.'s study in China, which included 343 patients, the optimal cutoff for D-dimer was found to be 2 µg/ml.[8] A D-dimer concentration of greater than 2 µg/ml at the time of admission was associated with an increased risk of mortality, according to another study done in China (Odds Ratio 10.17 (95%) CI 1.10-94.38).[7] In a comparable

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study conducted in India, the optimal value for the highest D-dimer measurement during the hospital stay to predict hospital death was 2.01 µg/ml, but the appropriate cut-off value for admission D-dimer to predict hospital mortality was found to be 1.44 µg/ml.[23] Those with COVID-19 who presented with high D-dimer levels were at an increased risk of suffering a serious disease and passing away, according to a thorough analysis published in August 2020. Furthermore mentioned was the lack of a solid cut-off value for predicting undesirable events.[24] For every 1 µg/ml increase in admission D-dimer, retrospective research in the United States with 1065 hospitalised patients found a hazard ratio of 1.06 (95% CI 1.04-1.08, p = 0.001) for all-cause mortality.[25]

According to a comprehensive study by Rostami et al., the average D-dimer level was 0.58 µg/ml in 1551 patients with moderate sickness and 3.55 µg/ml in 708 patients with severe disease.[26] Patients with higher D-dimer levels at the time of admission were at a higher risk of mortality (relative risk, RR 1.82) and illness severity (RR 1.58) compared to those with normal levels of D-dimer, according to Gungor et al.[27] A similar meta-analysis found that the relative risk of mortality was 4.60 (95% CI 2.72-7.79), using 0.5 µg/ml as the threshold value.[15] A second meta-analysis of six trials revealed that COVID-19 patients with higher D-dimers had worse clinical results in terms of mortality, ICU admission, and acute respiratory distress syndrome (ARDS).[16]

According to a recent study, the laboratory data of hospitalised patients revealed that D-dimer had an excellent track record of accurately predicting their death and COVID-19 severity.[28] Although further research is needed in this area, a better predictive value may be provided by taking into account the whole trajectory of D-dimer during hospital admission compared to the admission D-dimer only.

In the current investigation, it was discovered that higher LDH levels were not linked to any of the outcomes, including assisted ventilation or death of the study subject, whereas Henry et al.'s[13] pooled analysis showed a link between raised LDH concentration and poorer outcomes in COVID-19 patients, particularly those with increased LDH had odds of severe illness that were 6 times higher and odds of death that were 16 times higher. However, in all three research that listed death as an outcome, greater LDH levels were found in > 95% of non-survivors as opposed to 60% of survivors. Fewer research participants, other morbidities that determine how severe COVID-19 patients are, and regional variance might all be factors contributing to this disparity. Data from meta-analyses can be heterogeneous, and the bulk of the studies was conducted in China, which may have led to conclusions that differ from those of the current study.

LDH release and tissue damage mediated by cytokines are potential effects of severe infections.[17] Patients having severe COVID-19 infections may produce increased levels of LDH in the circulation because LDH is present in lung tissue. This condition is evident by a severe form of interstitial pneumonia that frequently evolves into acute respiratory distress syndrome. However, it is not clear how the various LDH isoenzymes are associated with the LDH rise seen in COVID-19. Thrombotic microangiopathy is found to be associated with higher LDH levels. It may lead to heart injury and renal failure.[18-20] The presence of thrombocytopenia and high D-dimer values in patients with severe COVID-19 suggests that a hypercoagulable condition may be responsible for the severity of the illness and death.[21,22]

In a study by Mohsin et al. conducted in Iraq,[29] they discovered that patients with severe coronavirus symptoms had much higher levels of LDH and D-dimer than those with no coronavirus infection or an infection with very moderate symptoms (p = 0.001). Results differed from those of our study, which may be a result of the study population's diverse sociodemographic makeup.

The fact that our hospital serves a diverse population in this region and that the study was carried out at its most severe time (during the COVID-19 second wave) is a major asset of ours.

There are certain restrictions with our study, namely the limited sample size. Due to the nature of our study, selection bias is a significant drawback. The study excluded asymptomatic individuals with high oxygen saturation not admitted to a hospital. Several otherwise eligible cases had to be excluded since there were insufficient diagnostic procedures and health records, notably D-dimer at arrival. D-dimer readings may also be impacted by the amount of time between the onset of the disease and hospital admission.

Our study discovered that D-dimer, a widely accessible, reasonably priced, and simple-to-administer laboratory test, exhibited very good predictive power for in-hospital death in COVID-19 patients. It can assist with management choices and act as a statistic for identifying high-risk situations. Including D-dimer in the routine patient evaluation and COVID-19 patient risk analysis may be useful in resolving this world health issue.

Conclusion

The ideal threshold level of admission D-dimer for the prediction of mortality in COVID-19 patients, with great specificity as well as sensitivity, is 1.5 µg/ml. For patients with COVID-19, the D-dimer value is a reliable biomarker for predicting death. D-dimer may therefore be a rapid and

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affordable laboratory indication for COVID-19 prediction.

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References

1. Fauci AS, Lane HC, Redfield RR. Covid-19—navigating the uncharted. N Engl J Med. 2020;382(13):1268-9. [PubMed] [Google Scholar]
2. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020;18(4):844-7. [PubMed] [Google Scholar]
3. Wool GD, Miller JL. The impact of COVID-19 disease on platelets and coagulation. Pathobiology. 2021;88(1):15-27. [PubMed] [Google Scholar]
4. Weitz JI, Fredenburgh JC, Eikelboom JW. A test in context: D-dimer. J Am Coll Cardiol. 2017 Nov 7;70(19):2411-20. [PubMed] [Google Scholar]
5. Querol-Ribelles JM, Tenias JM, Grau E, Querol-Borras JM, Climent JL, Gomez E, Martinez I. Plasma d-dimer levels correlate with outcomes in patients with community-acquired pneumonia. Chest. 2004 Oct;126(4):1087-92. [PubMed] [Google Scholar]
6. 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. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020 Mar 28;395(10229):1054-62. [PubMed] [Google Scholar]
7. Yao Y, Cao J, Wang Q, Shi Q, Liu K, Luo Z, Chen X, Chen S, Yu K, Huang Z, Hu B. D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study. J Intensive Care. 2020;8:49. [PubMed] [Google Scholar]
8. Zhang L, Yan X, Fan Q, Liu H, Liu X, Liu Z, Zhang Z. D-dimer levels on admission to predict in-hospital mortality in patients with Covid-19. J Thromb Haemost. 2020 Jun;18(6):1324-9. [PubMed] [Google Scholar]
9. Soni P, Solu MG, Garg V, Pathria A, Shah S, Mundra A. Organophosphate poisoning predicting the need for mechanical ventilator support. Int J Sci Stud. 2016;4(6):5. [Google Scholar]
10. Chen Y, Tong X, Wang J, Huang W, Yin S, Huang R, Yang H, Chen Y, Huang A, Liu Y, Chen Y, Yuan L, Yan X, Shen H, Wu C. High SARS-CoV-2 antibody prevalence among healthcare workers exposed to COVID-19 patients. J Infect. 2020 Sep;81(3):420-6. [PubMed] [Google Scholar]
11. Tao RJ, Luo XL, Xu W, Mao B, Dai RX, Li CW, Yu L, Gu F, Liang S, Lu HW, Chen KB, Bai JW, Ji XB, Gu SY, Sun XL, Dai FH, Jiang P, Cao WJ, Xu JF. Viral infection in community-acquired pneumonia patients with fever: a prospective observational study. J Thorac Dis. 2018 Jul;10(7):4387-95. [PubMed] [Google Scholar]
12. Chiang CH, Shih JF, Su WJ, Perng RP. Eight-month prospective study of 14 patients with hospital-acquired severe acute respiratory syndrome. Mayo Clin Proc. 2004 Nov;79(11):1372-9. [PubMed] [Google Scholar]
13. Henry BM, de Oliveira MH, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. Clin Chem Lab Med. 2020 Jun 25;58(7):1021-8. [PubMed] [Google Scholar]
14. Kuang ZS, Yang YL, Wei W, Wang JL, Long XY, Li KY, Tong CY, Sun Z, Song ZJ. Clinical characteristics and prognosis of community-acquired pneumonia in autoimmune disease-induced immunocompromised host: a retrospective observational study. World J Emerg Med. 2020;11(3):145-51. [PubMed] [Google Scholar]
15. Ding J, Karp JE, Emadi A. Elevated lactate dehydrogenase (LDH) can be a marker of immune suppression in cancer: interplay between hematologic and solid neoplastic clones and their microenvironments. Cancer Biomark. 2017 Jul 4;19(4):353-63. [PubMed] [Google Scholar]
16. Mangalmurti N, Hunter CA. Cytokine storms: understanding COVID-19. Immunity. 2020 Jul 14;53(1):19-25. [PubMed] [Google Scholar]
17. Erez A, Shental O, Tchebiner JZ, Laufer-Perl M, Wasserman A, Sella T, Guzner-Gur H. Diagnostic and prognostic value of very high serum lactate dehydrogenase in admitted medical patients. Isr Med Assoc J. 2014 Jul;16(7):439-43. [PubMed] [Google Scholar]
18. Assiri A, Al-Tawfiq JA, Al-Rabeeah AA, Al-Rabiah FA, Al-Hajjar S, Al-Barrak A, Flemban H, Al-Nassir WN, Balkhy HH, Al-Hakeem RF, Makhdoom HQ, Zumla AI, Memish ZA. Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study. Lancet Infect Dis. 2013 Sep;13(9):752-61. [PubMed] [Google Scholar]
19. Terpos E, Ntanasis-Stathopoulos I, Elalamy I, Kastritis E, Sergentanis TN, Politou M, Psaltopoulou T, Gerotziafas G, Dimopoulos MA. Hematological findings and complications of COVID-19. Am J Hematol. 2020;95(7):834-47. [PubMed] [Google Scholar]
20. Arifputra J, Haroen H, Rotty LW, Lasut PF, Hendratta C. Coagulopathy of Coronavirus Disease 2019: a case series. Open Access Macedon J Med Sci [Internet]. 2021 Jun 7 [cited 2022 Oct 7]. Available from: https://doi.org/10.3889/oamjms.2021.6026 [Google Scholar]
21. Poudel A, Poudel Y, Adhikari A, Aryal BB, Dangol D, Bajracharya T, Maharjan A, Gautam R. 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. 2021 Aug 26;16(8):e0256744. [PubMed] [Google Scholar]

22. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DS, Du B, Li LJ, Zeng G, Yuen KY, Chen RC, Tang CL, Wang T, Chen PY, Xiang J, Li SY, Wang JL, Liang ZJ, Peng YX, Wei L, Liu Y, Hu YH, Peng P, Wang JM, Liu JY, Chen Z, Li G, Zheng ZJ, Qiu SQ, Luo J, Ye CJ, Zhu SY, Zhong NS; China Medical Treatment Expert Group for Covid-19. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020 Apr 30;382(18):1708-20. [PubMed] [Google Scholar]
23. 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. [PubMed] [Google Scholar]
24. Shah S, Shah K, Patel SB, Patel FS, Osman M, Velagapudi P, Turugam MK, Lakkireddy D, Garg J. Elevated D-dimer levels are associated with increased risk of mortality in Coronavirus Disease 2019: a systematic review and meta-analysis. Cardiol Rev. 2020;28(6):295-302. [PubMed] [Google Scholar]
25. Naymagon L, Zubizarreta N, Feld J, van Gerwen M, Alsen M, Thibaud S, Kessler A, Venugopal S, Makki I, Qin Q, Dharmapuri S, Jun T, Bhalla S, Berwick S, Christian K, Mascarenhas J, Dembitzer F, Moshier E, Tremblay D. Admission D-dimer levels, D-dimer trends, and outcomes in COVID-19. Thromb Res. 2020 Dec;196:99-105. [PubMed] [Google Scholar]
26. Rostami M, Mansouritorghabeh H. D-dimer level in COVID-19 infection: a systematic review. Expert Rev Hematol. 2020;13: 1265–1275. doi: 10.1080/17474086.2020.1831383 [PubMed] [Google Scholar]
27. Gungor B, Atici A, Baycan OF, Alici G, Ozturk F, Tugrul S, et al. Elevated D-dimer levels on admission are associated with severity and increased risk of mortality in COVID-19: A systematic review and meta-analysis. Am J Emerg Med. 2021;39: 173–179. doi: 10.1016/j.ajem.2020.09.018 [PMC free article] [PubMed] [Google Scholar]
28. Qeadan F, Tingey B, Gu LY, Packard AH, Erdei E, Saeed AI. Prognostic values of serum ferritin and D-dimer trajectory in patients with COVID-19. Viruses. 2021 Mar 5;13(3):419. [PubMed] [Google Scholar]
29. Mohsin RH, Hussein DS, Abed AS. Evaluation of a few biomarkers among COVID-19 patients. J Commun Dis. 2022 Mar 16;82-90. [Google Scholar]

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