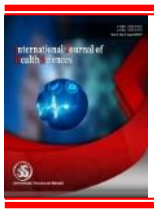

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Relationship between D-dimer Levels and Survival in a Sample of Iraqi Patients with COVID-19

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COVID-19;
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Abstract

Coronavirus disease 2019 was discovered in December 2019, in Wuhan, China. It was transmitted globally during the COVID-19 pandemic. Coagulopathy is one of the most common complications characterized by an increased D-dimer level. Objective: This study aimed to assess the relationship between the levels of D-dimer and other biomarkers with survival in a sample of Iraqi patients with COVID-19. Methods: A cross-section study included 103 patients affected by COVID-19, diagnosed by PCR and chest CT scan, (18 to 70 years old), and admitted at the isolation centers of the Khalis General Hospital and the Shifa Center in Baquba Teaching Hospital Diyala\ Iraq between November 2020 to end January 2021. The patients were divided into two groups: Group 1:(63) survivors patients, and Group 2: (40) non survivors patients. Results: The patients were divided into groups: 61.2% survivors patients, 38.8% non-survivors adult COVID-19 patients. The results include several biomarkers, each biomarker (mean± SE) was calculated in survivors and non-survivor patients. Serum ferritin, plasma D-dimer showed a statistically significant increase in non-survivors group (1777.8 ± 126.02, 3985.42 ± 1224.95) than survivors patients group (1182.7 ± 142.45, 1857.50 ± 291.21) with p-value ≥ 0.05. The ROC curve to determine the efficiency of D-dimer with non-survival in COVID-19 patients. The most sensitive biomarker for non-survival is D-dimer, (sensitivity 80% and specificity 65.5%). Conclusion: The high level of D-dimer in the non-survivors group, it may be due to the incidence of pulmonary embolism is highly observed in COVID-19 patients as D-dimer is the degradation of a blood clot.

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Contents

1 Introduction

The coronavirus disease 2019 (COVID-19) is one of the most prevalent diseases affecting society globally, is responsible for a sizable number of fatalities (Su et al., 2020; Di Gennaro et al., 2020). COVID-19 begins when COVID-19 is transmitted from one person to another through inhalation or oral ingestion of virus-containing droplets. COVID-19 spike protein binding to the angiotensin-converting enzyme 2 (ACE2) receptor may allow the virus to penetrate epithelial cells in the nasal or oral cavities (Roberts et al., 2020). The coronavirus, later identified as SARS-CoV-2, was linked to acute respiratory disease (Wijayanto et al., 2023). Most COVID-19 cases had only mild-moderate clinical manifestations, a significant number of patients may experience severe pneumonia, acute respiratory distress syndrome, multiple organ failure, and even death (Aditianingsih et al., 2022). Several studies and case reports had clarified the connection between acute coronary heart disease and COVID-19 (Shi et al., 2020). COVID-19 individuals had Greater D-dimer levels and more thrombotic events than non-COVID patients, according to an observational study of 115 STEMI patients (Choi et al., 2020; Becker, 2020). D-dimer, a high molecular weight fibrinogen was produced by fibrin degradation. It's widely accepted as a thromboembolism biomarker as well as a prognostic indicator for critically ill individuals. Because COVID-19 is a procoagulant condition, D-dimer has been investigated as a biomarker for disease severity prediction (Mcgonagle, 2020). Measurement of D-Dimer, products of fibrin degradation, has proven useful in evaluating patients severity with community-acquired pneumonia, 2009 novel influenza A (H1N1) and other members of the Coronaviridae family. COVID-19 infection is associated with an increased risk of venous thrombo-embolic events, and COVID-19 coagulation abnormalities are recognized as a major determinant of dismal prognosis. Patients with COVID-19 consistently and significantly have elevated D-dimer levels. The majority of data publications have linked this increase to coagulation activity, and D-dimers have been thought to be a sign of clot breakdown (Trimaille et al., 2020; Tang et al., 2020). Inflammation caused by SARS-CoV-2 can affect atherosclerotic plaques, induce prothrombotic changes in the blood and endothelium, and cause their instability, leading to myocardial infarction. Coagulation dysfunction in COVID-19 patients increased the development of severe disease and fatal outcomes and was characterized by increased D-dimer level and thrombus in arteries and veins (Poznyak et al., 2021).

The aims of this study were to assess the relationship between the levels of D-dimer and other biomarkers with survival in a sample of Iraqi patients with COVID-19.

2 Materials and Methods

A cross-sectional study included n=103 individuals with COVID-19 diagnosed by PCR and chest CT scan, composed of only males (18 to 70 years old). It was performed from the period from November 2020 to end of January 2021. The patients were divided into two groups:
Group 1: 63 (61.2%) survivors patients, Group 2: 40 (38.8%) non-survivors patients.
Samples (survivors and non-survivors) were obtained from isolation centers for COVID-19 patients from Khalis General Hospital and the Shifa Center Baquba Teaching Hospital Diyala Iraq.

Ethical considerations

The study has approval from the ethical committee at the Faculty of Medicine, Baghdad University, Iraq. Health Directorate of Diyala, Iraq. The patient's families endorsements in both written and oral forms were acquired for their patients to be enrolled in the study.

Study design

For COVID-19 patients, venous samples containing about 6 ml of blood were taken. Every blood sample was split into three parts: 1 ml of whole blood was used to measure CBC. 2ml was placed in an anticoagulant tube and centrifuged for 10 minutes at 3000 rpm to separate the plasma and measure the D-dimer. 3 ml in a plane tube separated by centrifugation at 3000 rpm for 10 min, the resulting serum was used for biochemistry measurement for ferritin and CRP.

Statistical analysis

All statistical analysis was done using the Statistical Package for the Social Sciences (SPSS) version 24.0 software. The mean and the S.E. were calculated for all numeric parameters. T test of independent samples was used to determine the statistically significant difference between groups. P value equal or less than 0.05 is considered as a cut-off point for statistical significance. ROC test (Receiver Operating Characteristic test) was used to study the sensitivity and specificity of the critical value of the studied parameters with the outcome.

3 Results and Discussions

The current study is a cross-sectional study that involves 103 COVID-19 male patients, with mean± SE of age 45.7 ± 1.7 years. The patients were divided to two groups: 63 (61.2%) alive patients and 40 (38.8%) dead patients. Approximately all patients (except two of them) have higher CRP,39 of them were non-survivors and 59 were survivor patients which is known to be an indicator of the inflammatory condition. More than half of the participants 72 (69.9%) had lymphopenia, 30 of them were non-survivors and 42 were survivors and 31 (30%) had normal lymphocytes. Also 82 (79.6%) had Leukocytosis 36 were non-survivors and 46 were survivors and 21(20.4%) had normal WBC which goes with the common laboratory finding in COVID-19 patients. The cytokines markers that included serum ferritin and plasma D-dimer, 96 (9.23%) of the enrolled patients had a high level of serum ferritin,39 of them were non-survivors and 57 were survivors and only 7(6.8%) of all enrolled patients For had normal ferritin level, 101 out of 103 (98.1%) of patients had high plasma D-dimer level, 40 of them were non-survivors and 61 were survivors patients.

Table 1
Study laboratory characteristics of participants, frequency, and percentage

	Reference range		NO.	No. survivors	No. Non-survivors	Percent
CRP level (mg/l)	≥ 5	Normal CRP level	2	1	1	1.9%
		high CRP level	101	62	39	98.1%
lymphocyte level (103/uL)	1 – 3.70	Low lymphocyte count	72	42	30	69.9%
		Normal lymphocyte count	31	21	10	30%
WBC level (103/uL)	3 – 15	normal WBC count	21	17	4	20.4%
		Leukocytosis	82	46	36	79.6%
Ferritin level (ng\ml)	30 – 300	normal ferritin level	7	6	1	6.8%
		high ferritin level	96	57	39	93.2%
D-dimer level(ng/ml)	198	normal D-dimer level	2	2	0	1.9 %
		high D-dimer level	101	61	40	98.1 %

In table 2, the patients were divided into two groups according to their survival, the mean ±SE of a biomarker for each group was measured, results showed that mean ±SE of age were non statistical (p≥ 0.05) different between the alive and dead patient group. The mean ±SE of age was 52.77 ± 2.04 and 57.80 ± 2.93 yrs. The mean ±SE of CRP, WBC and lymphocyte count were nonstatistical (p≥ 0.05) different between the alive and dead patient group (Demelo-Rodríguez et al., 2020; Suryasa et al., 2021).

The mean ±SE of CRP was 182.91 ± 27.83 and 194.29 ± 23.005 mg/l, WBC was 14.27 ± 0.70 *103and 16.18 ± 0.93 *103µl and lymphocyte was 0.98 ± 0.09*103and 0.82 ± 0.07*103 µl in alive and dead group respectively. D-dimer and ferritin mean ±SE showed statistically significant differences (p≤ 0.05) between non-survivors group which was higher (3985.42 ± 1224.95) (1777.8 ± 126.02) ng/ml than the survivors group of the patient (1857.50 ± 291.21) (1182.7 ± 142.45) ng/ml, p-value< 0.04, p< 0.005 respectively.

Table 2
Comparison of mean ± SE values among two groups

	Survivors (n= 63) Mean ± SE	Non-survivors (n= 40) Mean ± SE	p-value
age yrs.	52.77 ± 2.04	57.80 ± 2.93	0.15
CRP (mg/l)	182.91 ± 27.83	194.29 ± 23.005	0.77
WBC (10^3/uL)	14.27 ± 0.70	16.18 ± 0.93	0.10
LYMPH(10^3/ul)	0.98 ± 0.09	0.82 ± 0.07	0.24
Ferritin(ng\ml)	1182.7 ± 142.45	1777.8 ± 126.02	0.005*
D-dimer(ng/ml)	1857.50 ± 291.21	3985.42 ± 1224.95	0.04*

*Significant p-value ≤ 0.05 ** Significant p-value ≤ 0.01

ROC test (Receiver Operating Characteristic test) was used to study the sensitivity and specificity of the critical value of the studied parameters with the outcome (alive and dead). If the AUC is less than 50%, the ROC result should be neglected as the cut-off point will point to being (alive) instead of being (dead) and the result should not be accounted for in explaining the model result. If the AUC is around 50%, the ROC result means the variable tested is associated with the absence of outcome (the result is random and not accurate). If the AUC is more than 60-70%, then it implies that the model is accurate in predicting the outcome (Ozen et al., 2021; Gungor et al., 2021; Schafer et al., 2022; Yu et al., 2020).

Table3
The results of ROC for all biomarkers in non- survivors patients with COVID-19

Test Result Variable(s)	Area	Area%	Cut-off Value	SE	P-value	Sensitivity %	Specificity %	Asymptotic 95% Confidence Interval	
								Lower Bound	Upper Bound
CRP(mg\L)	0.611	61.1	98.5	0.056	0.058	82.5	47.6	0.501	0.721
WBC(u L)	0.593	59.3	14.12	0.057	0.114	57.5	57.1	0.480	0.705
LYMPH(ul)	0.438	43.8	0.75	0.058	0.288	47.5	47.6	0.324	0.551
Ferritin(ng\ml)	0.612	61.2	1322.5	0.055	0.055	67.5	57.1	0.504	0.721
D-dimer(ng\ml)	0.733	73.3	1314.0	0.050	0.000**	80.0	65.5	0.635	0.831

* p-value ≤ 0.05 ** p-value ≤ 0.01

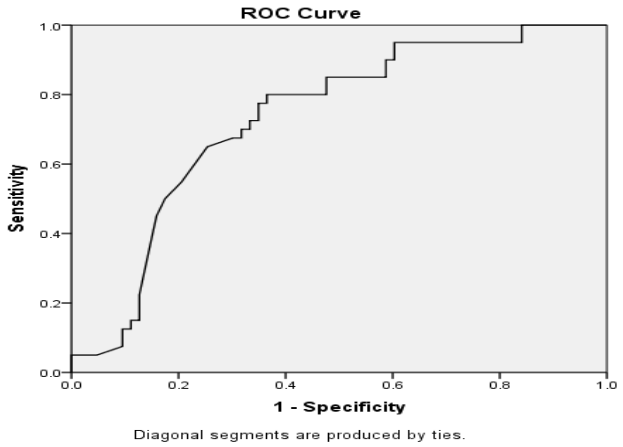

Figure 1. The ROC curve for D-dimer in non-survivors patients with COVID-19

Discussion

The current findings showed that there was an increase 101 (62 survivors patients, 39 non-survivors patients) in CRP levels in COVID-19 patients with a range of ≥ 5 mg\L which can be seen in Table 1. These findings support the theory that the SARS-CoV2 virus might cause an increase in CRP production, which is mediated by elevated Angiotensin II activity, and that this contributes to the severity of COVID-19 (Choirunisa et al., 2023). The current results showed that no significant difference in the non-survivors (194.29 ± 23.005) and survivors patients (182.91 ± 27.83) in CRP levels, was in agreement with (Dhindsa et al., 2021). Our present study showed that the levels of CRP increased in all patients with COVID-19 but it was not a good marker of survival, might be because the half-life of CRP was little (19 hours) and its concentration decreased.

One essential feature of cytokine storm syndrome is hyperferritinemia, which directly suppresses the immune system and increases inflammation. In COVID-19 individuals, fatal outcomes from cytokine storm syndrome have been described, indicating the severity of the illness. The severity of COVID-19 and the poor prognosis, virally driven hyperinflammation linked to elevated ferritin levels is the likely cause of mortality (SOGANI et al., 2022).

The current findings showed that 96 (57 survivors patients, 39 non-survivors patients) of the enrolled patients have high levels of ferritin, and found significant differences in serum ferritin between non-survivors group (1777.8 ± 126.02) which is higher than the survivor's group (1182.7 ± 142.45) of the patient, which in turn is higher than the normal level. This result was in agreement with (SOGANI et al., 2022). There have been reports of COVID-19 patients being hypercoagulable. Thrombotic consequences and coagulopathies, such as

venous thromboembolism (VTE) and disseminated intravascular coagulopathy (DIC), and pulmonary embolism are frequent in COVID-19 patients with significant death rates, and they most likely represent cytokine storm-induced coagulation cascade activation, or perhaps superinfection and organ dysfunction (Wool & Miller, 2021).

The current study found 101 (61 survivor patients, 40 non-survivors patients) with COVID-19 with was high level of D-dimer. D-dimer levels were significantly difference between non-survivors group (3985.42 ± 1224.95) which is higher than the survivors group (1857.50 ± 291.21) of patients which was higher than the reference range. This result was in agreement with the studies of other studies (Santos-Poleo et al., 2020; Han et al., 2020).

D-dimer is a fragment produced when plasmin cleaves fibrin during clot breakdown. A high D-dimer level might suggest a prothrombotic state, increased fibrinolysis, bleeding, and thrombotic events, and indicate cytokine storm, and tissue damage (Ali et al., 2022).

Thromboembolic complications have been found to be associated with low platelet counts, increased prothrombin time, and high D-dimer levels. Therefore, high D-dimer levels is likely to be associated with persistent clotting disorders, acute myocardial infarction, pulmonary embolism, and microthrombotic formation which may be the cause of respiratory failure, DIC, and death (Chan, 2020; Luo et al.,2020). Elevated D-dimer level has been shown to be associated with mortality in COVID-19 patients (Huang et al., 2020; Lim et al., 2020).

The optimal cut-off level for D-dimer to predict in COVID-19 patients as D-dimer mortality found that D-dimer had more sensitivity and specificity than other biomarkers in non-survivors patients with COVID-19 (Soni et al., 2020; Zhang et al., 2020; Naymagon et al., 2020; Cheng et al., 2020). So, these results made D-dimer more useful in detecting non-survival in COVID-19 (sensitivity 80% and specificity 65.5%) which can be seen in Table 3 and Fig.1.

4 Conclusion

The high level of D-dimer in the non-survivors group, it may be due to the incidence of pulmonary embolism is highly observed in COVID-19 patients as D-dimer is the degradation of a blood clot. D-dimer biomarkers should be included in future studies to predict the mortality in the patients diagnosed with COVID-19 disease.

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References

Aditianingsih, D., Soenarto, R. F., Puiantana, A. M., Pranata, R., Lim, M. A., Raharja, P. A. R., ... & Meyer, M. (2022). Dose response relationship between D-Dimer level and mortality in critically ill COVID-19 patients: a retrospective observational study. *F1000Research*, *11*.

Ali, A. M., Rostam, H. M., Fatah, M. H., Noori, C. M., Ali, K. M., & Tawfeeq, H. M. (2022). Serum troponin, D-dimer, and CRP level in severe coronavirus (COVID-19) patients. *Immunity, inflammation and disease*, *10*(3), e582.

Becker, R. C. (2020). COVID-19 update: Covid-19-associated coagulopathy. *Journal of thrombosis and thrombolysis*, *50*(1), 54-67.

Chan, K. H., Slim, J., & Shaaban, H. S. (2020). Pulmonary embolism and increased levels of d-dimer in patients with coronavirus disease. *Emerging Infectious Diseases*, *26*(10), 2532-2533.

Cheng, A., Hu, L., Wang, Y., Huang, L., Zhao, L., Zhang, C., ... & Liu, Q. (2020). Diagnostic performance of initial blood urea nitrogen combined with D-dimer levels for predicting in-hospital mortality in COVID-19 patients. *International journal of antimicrobial agents*, *56*(3), 106110. https://doi.org/10.1016/j.ijantimicag.2020.106110

Choi, G. J., Kim, H. M., & Kang, H. (2020). The potential role of dyslipidemia in COVID-19 severity: an umbrella review of systematic reviews. *Journal of Lipid and Atherosclerosis*, *9*(3), 435.

Choirunisa, C. E., Widhyasih, R. M., & Fajrunni'mah, R. (2023). Correlation of C-Reactive Protein (CRP) Levels with D-Dimer Levels in COVID-19 Patients. *Jurnal Ilmu dan Teknologi Kesehatan*, *11*(1), 126-139.

Demelo-Rodríguez, P., Cervilla-Muñoz, E., Ordieres-Ortega, L., Parra-Virto, A., Toledano-Macías, M., Toledo-Samaniego, N., ... & Galeano-Valle, F. (2020). Incidence of asymptomatic deep vein thrombosis in patients with COVID-19 pneumonia and elevated D-dimer levels. *Thrombosis research*, *192*, 23-26. https://doi.org/10.1016/j.thromres.2020.05.018

Dhindsa, S., Zhang, N., McPhaul, M. J., Wu, Z., Ghoshal, A. K., Erlich, E. C., ... & Diwan, A. (2021). Association of circulating sex hormones with inflammation and disease severity in patients with COVID-19. *JAMA network open*, *4*(5), e2111398-e2111398.

Di Gennaro, F., Pizzol, D., Marotta, C., Antunes, M., Racalbuto, V., Veronese, N., & Smith, L. (2020). Coronavirus diseases (COVID-19) current status and future perspectives: a narrative review. *International journal of environmental research and public health*, *17*(8), 2690.

Gungor, B., Atici, A., Baycan, O. F., Alici, G., Ozturk, F., Tugrul, S., ... & Barman, H. A. (2021). Elevated D-dimer levels on admission are associated with severity and increased risk of mortality in COVID-19: A systematic review and meta-analysis. *The American journal of emergency medicine*, *39*, 173-179. https://doi.org/10.1016/j.ajem.2020.09.018

Han, H., Yang, L., Liu, R., Liu, F., Wu, K. L., Li, J., ... & Zhu, C. L. (2020). Prominent changes in blood coagulation of patients with SARS-CoV-2 infection. *Clinical Chemistry and Laboratory Medicine (CCLM)*, *58*(7), 1116-1120.

Huang, I., Pranata, R., Lim, M. A., Oehadian, A., & Alisjahbana, B. (2020). C-reactive protein, procalcitonin, D-dimer, and ferritin in severe coronavirus disease-2019: a meta-analysis. *Therapeutic advances in respiratory disease*, *14*, 1753466620937175.

Lim, M. A., Pranata, R., Huang, I., Yonas, E., Soeroto, A. Y., & Supriyadi, R. (2020). Multiorgan failure with emphasis on acute kidney injury and severity of COVID-19: systematic review and meta-analysis. *Canadian journal of kidney health and disease*, *7*, 2054358120938573.

Luo, W. R., Yu, H., Gou, J. Z., Li, X. X., Sun, Y., Li, J. X., ... & Liu, L. (2020). Histopathologic findings in the explant lungs of a patient with COVID-19 treated with bilateral orthotopic lung transplant. *Transplantation*, *104*(11), e329-e331.

Mcgonagle, D. (2020). Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. *The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information*.

Naymagon, L., Zubizarreta, N., Feld, J., van Gerwen, M., Alsen, M., Thibaud, S., ... & Tremblay, D. (2020). Admission D-dimer levels, D-dimer trends, and outcomes in COVID-19. *Thrombosis research*, *196*, 99-105. https://doi.org/10.1016/j.thromres.2020.08.032

Ozen, M., Yilmaz, A., Cakmak, V., Beyoglu, R., Oskay, A., Seyit, M., & Senol, H. (2021). D-Dimer as a potential biomarker for disease severity in COVID-19. *The American journal of emergency medicine*, *40*, 55-59. https://doi.org/10.1016/j.ajem.2020.12.023

Poznyak, A. V., Bezsonov, E. E., Eid, A. H., Popkova, T. V., Nedosugova, L. V., Starodubova, A. V., & Orekhov, A. N.

(2021). ACE2 is an adjacent element of atherosclerosis and COVID-19 pathogenesis. *International Journal of Molecular Sciences*, *22*(9), 4691.

Roberts, C. M., Levi, M., McKee, M., Schilling, R., Lim, W. S., & Grocott, M. P. (2020). COVID-19: a complex multisystem disorder. *British Journal of Anaesthesia*, *125*(3), 238-242.

Sakka, M., Connors, J. M., Hékimian, G., Martin-Toutain, I., Crichi, B., Colmegna, I., ... & Frere, C. (2020). Association between D-Dimer levels and mortality in patients with coronavirus disease 2019 (COVID-19): a systematic review and pooled analysis. *JMV-Journal de Médecine Vasculaire*, *45*(5), 268-274. https://doi.org/10.1016/j.jdmv.2020.05.003

Santos-Poleo, Y.D., Perez-Sanchez, L., Ocanto, A., Oquillas-Izquierdo, D., & Rodriguez-Recio, F. (2020). Elevated D-dimer and acute pulmonary thromboembolism in patients with COVID-19. *Journal of Negative and No Positive Results* , *5* (12), 1516-1527.

Schafer, K., Goldschmidt, E., Oostra, D., Fish, J., Russell, T., & Lurie, F. (2022). The clinical significance of ultra-high D-dimer levels. *Journal of Vascular Surgery: Venous and Lymphatic Disorders*, *10*(1), 8-13. https://doi.org/10.1016/j.jvsv.2021.06.011

Shi, S., Qin, M., Shen, B., Cai, Y., Liu, T., Yang, F., ... & Huang, C. (2020). Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA cardiology*, *5*(7), 802-810.

SOGANI, S., PRAJAPAT, R., TOMAR, J., JAIN, S., & BAPNA, A. (2022). STUDY OF D-DIMER AND SERUM FERRITIN LEVELS AS PROGNOSTIC BIOMARKERS IN COVID-19 PATIENTS. *Asian J Pharm Clin Res*, *15*(12), 92-94.

Soni, M., Gopalakrishnan, R., Vaishya, R., & Prabu, P. (2020). D-dimer level is a useful predictor for mortality in patients with COVID-19: Analysis of 483 cases. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, *14*(6), 2245-2249. https://doi.org/10.1016/j.dsx.2020.11.007

Su, L., Ma, X., Yu, H., Zhang, Z., Bian, P., Han, Y., ... & Gai, Z. (2020). The different clinical characteristics of corona virus disease cases between children and their families in China–the character of children with COVID-19. *Emerging microbes & infections*, *9*(1), 707-713.

Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2021). The COVID-19 pandemic. *International Journal of Health Sciences*, *5*(2), 6-9.

Tang, N., Li, D., Wang, X., & Sun, Z. (2020). Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *Journal of thrombosis and haemostasis*, *18*(4), 844-847.

Trimaille, A., Thachil, J., Marchandot, B., Curtiaud, A., Leonard-Lorant, I., Carmona, A., ... & Morel, O. (2020). D-dimers level as a possible marker of extravascular fibrinolysis in COVID-19 patients. *Journal of Clinical Medicine*, *10*(1), 39.

Wijayanto, M. A., Myrtha, R., Rahayu, D., & Lukas, G. A. (2023). Can D-dimer predict length of hospital stay in COVID-19 survivors? A cross-sectional study. *Jurnal Keperawatan Padjadjaran*, *11*(2), 112-117.

Wool, G. D., & Miller, J. L. (2021). The impact of COVID-19 disease on platelets and coagulation. *Pathobiology*, *88*(1), 15-27.

Yu, H. H., Qin, C., Chen, M., Wang, W., & Tian, D. S. (2020). D-dimer level is associated with the severity of COVID-19. *Thrombosis research*, *195*, 219-225. https://doi.org/10.1016/j.thromres.2020.07.047

Zhang, L., Yan, X., Fan, Q., Liu, H., Liu, X., Liu, Z., & Zhang, Z. (2020). D-dimer levels on admission to predict in-hospital mortality in patients with Covid-19. *Journal of thrombosis and haemostasis*, *18*(6), 1324-1329. https://doi.org/10.1111/jth.14859

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