D-Dimer Biomarker for Hospitalized COVID-19 – Pneumonia Patients and Mortality Outcome

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Abstract:
Introduction: Coronavirus Disease 2019 (COVID-19) is a respiratory condition that has the potential to result in thrombotic diseases. High D-dimer value is a prospective marker for undesirable prognosis in COVID-19. **Aim of the study:** Establishing D-dimer optimum cut-off value and using it as a predictor of mortality at admission. **Materials and methods:** A cross section record-based study was done on (252) COVID-19 pneumonia cases at Al-Bashir hospital, Amman, Jordan. Demographic, clinical, laboratory data and outcomes were extracted from the patients' files. **Results:** Higher D-dimer group showed significantly higher death rate (76.6%). For the D-Dimer level, the Roc curve resulted in a 2.25 µg/ml cut-off point for predicting patient mortality where Specificity is 61%, sensitivity 84.21%, and AUC 79.5 % (Area Under Curve). a high D-Dimer level at admission, patients with renal disease, and shorter period of hospitalization were associated with high odds of mortality rates by multivariate regression. **Conclusion:** High admission D-Dimer value was a predictive of high mortality rate, especially in individuals with comorbid conditions.
Keywords: Covid-19**,** Cut-off value, D-dimer, Mortality, Pneumonia.

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INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 that causes coronavirus disease 2019 (COVID-19) was initially identified in Wuhan, the capital of China's Hubei province, in December 2019 [1]. Although COVID-19 predominantly affects the respiratory system, it can also have an impact on the digestive, hepatic, cardiac, neurological, and renal systems. [1–3].

Disseminated intravascular coagulopathy (DIC), and other thrombotic consequences and coagulopathies, are frequent in COVID-19; this is probably due to the coagulation cascade being activated by viraemia or a cytokine storm, or it might also be a result of superimposed infection and multiorgan failure [4].

D-dimer, a breakdown product of fibrin, is often used as a biological marker for different thrombotic disorders. Its normal value is often recognized to be below 0.5 µg/ml; however it can be higher with aging and during pregnancy. D-dimer levels increase when community-acquired pneumonia gets worse [5].

After the COVID-19 pandemic broke out, D-dimer was shown to be a predictive of COVID-19 patients' sequels. Numerous studies [6–9] have suggested that the D-dimer fibrin may be useful in predicting the illness severity on the day of patient arrival. The D-dimer cut-off value used in published research varies significantly, and it appears that there is still no agreement on the appropriate cut-off point to predict severity or death. [10].

Aim of the study was to assess the D-dimer level on admission as a predictive of mortality among hospitalized COVID-19 pneumonia cases.

MATERIALS AND METHODS

Al-Bashir Hospital which considered one of the biggest general hospitals affiliated with the Jordanian Ministry of Health, sited in Amman, with a high health services rate and resources in the Kingdom. It was one of the main isolation hospitals for Covid-19 cases in the Kingdom [11-13].

A cross-sectional study was carried out on calculated sample size of (252) adult patients admitted and discharged alive or dead to the Al-Bashir hospital (inpatient wards and ICU) with a preliminary diagnosis of Covid-19 pneumonia by Reverse transcription polymerase chain reaction (RT-PCR). This based on the proportionate mortality rate of COVID-19 in Jordan was 17.09% during the interval of April till December 2020 according to **Khader and Al Nsour** [14]**;** and the admission rate of Covid-19 cases during the same period was 4500 patients. Using an online open epi program at 97% confidence interval and 3% confidence limit.

The study was a record-based study where patients' records which fulfilled the inclusion criteria were included in the study. The sample units were collected by simple random sampling using the hospital's electronic system.

Inclusion criteria: adult patients aged 18 and older and symptomatic cases with COVID-19 pneumonia

Exclusion criteria: patients without documented admission D-dimer level, concomitant infections, presence of deep venous thrombosis or pulmonary embolism (DVT/PE), or prior use of anticoagulants and cases without documented definite outcome (dead or alive). Demographic, laboratory, clinical data, and outcomes were gathered from the patients' records.

Patients' demographic data included sex, age, and comorbidities.

Clinical and laboratory data:

Admission D-dimer, within 24 hours after admission, blood samples were obtained and forwarded to the medical lab. Within two hours of sample collection, the measurement was performed. D-dimer was measured by Immunofluorescence Quantitative Analyzer (Getein Biotech Inc., China) with reference range of less than 0.5 µg/ml. Oxygen saturation using pulse oximetry (SpO2) on admission. During the hospital stay Low molecular weight heparin (LMWH) was administered to all patients, also steroids, remdesivir (when indicated) and supplemental oxygen therapy via either (nasal cannula, simple face mask, non-rebreathing mask, high flow nasal cannula or non-invasive ventilation). The patients' outcome was reported as: The first outcome was either survival–discharged (when the PCR became negative, resolving the symptoms and SpO2 more than 94%) or non-survival (pneumonia complications). The duration of hospitalization was the second outcome variable. All data was obtained using conventional measuring units by a standardized data collecting form.

Ethical and administrative approval: The study was approved by Al-Bashir hospital ethics committee affiliated to Jordanian ministry of health **(No. MOH/REC/2022/195)** after addressing the officials in the ministry of health to help us to check the records and approved by Mut'ah university faculty of medicine ethics committee **(NO. 492022)**. Ethical considerations were taken through the whole study including coded numbers for each participant was used to guarantee privacy.

Statically analysis: Continuous variables were expressed as median (IQR). Categorical variables were presented as frequency and percent. The difference between the two groups was determined using the Mann-Whitney U test for continuous variables. The chi-square test of association was used for testing the association among categorical variables. The receiver operator characteristics (ROC) curve was used to determine how the D-dimer predicted inpatient mortality. The ROC curve was used to compute the sensitivity, specificity, and area under the curve. The value correlating to the point on the curve that was closest to the top-left of the ROC graph was used to calculate the ideal cut-off value for D-dimer. Two groups of patients were constructed depending on this cut-off value. The variables included in the univariate, and multivariate logistic regression model fulfilled the condition- omnibus test of the model coefficient was statistically significant at the 5% level of significance. The software Jamovi version 2.3.16 was used for statistical analysis.

RESULTS

Table (1) shows the baseline demographics, laboratory data and outcome of the study sample. The sample included 252 patients with covid-19 pneumonia admitted to the hospital, 134 (53.2%) of whom were men, and 118 (46.8%) were women. The median age of the study sample was 64 years old. Deaths accounted for 152 (60.3%) patients of the study sample.

Higher D-dimer group showed significantly higher death rate (76.6%) p <0.001. On admission, the levels of D-dimer, total white blood cells count (WBCs) and CRP were significantly higher among high D-dimer group with P-value (<0.001, 0.015, 0.025) respectively, while the admission Spo2% was significantly higher in low D-dimer group (p <0.001).

Table (1): Baseline demographics, laboratory data and outcome of study sample

Characteristic	Groups Gro			Total patients (N= 252)
	Lower D-Dimer (D-Dimer <2.25) N (%) 85 (33.7%)	Higher D-Dimer (D-Dimer≥2.25) N (%) 167 (66.3%)	P	
Age (years)	60(49-71)	65(53-73)	0.062	64 (49-73)
Sex Male Female	 21 (24.7 %) 64 (75.3%)	 113 (67.7%) 54 (32.3%)	 <0.001*	 134 (53.2%) 118 (46.8%)
Patient outcome (dead)	24(28.2%)	128 (76.6%)	<0.001*	152 (60.3%)
D-Dimer level (µg/mL)	1.2 (0.46- 1.7)	5(3.2-8.1)	<0.001*	3.2 (0.46-8.1)
Spo2 % at admission	89 (81-91)	83 (77-88)	<0.001*	86 (77-91)
Hospital stays (days)	10 (7-15)	9 (5-15)	0.5	9 (5-15)
Platelet level (10^3/mm^3)	212(152-283)	221 (160-293)	0.218	216 (152-293)
CRP (mg/L)	15 (7 -27)	21 (10.8-34)	0.025*	18.7 (7-34)
Level of WBC at admission (10^3/mm^3)	8.1(5.7-12.6)	10.3 (6.95-14.8)	0.015*	9.95 (5.7-14.8)
Numbers of patients with High ferritin level No (%)	9 (10.6%)	16 (9.6%)	0.8	25 (9.9%)

* Significant values (p <0.05), CRP: C-reactive protein, WBCs: White blood cells, Spo2: Oxygen saturation using pulse oximetry.

The different comorbidities present in both patients' groups were displayed in **(Table2),** about 73.8% of the total patients (n =252) had comorbidities**.** The most prevalent comorbidities in all studied patients were hypertension (38.9%), Diabetes mellitus (34.1%) and chronic renal illnesses (27.8%) respectively. The higher D-dimer group had more prevalent comorbidities than the lower D-dimer group with high statistical significance between both groups (P <0.001). Also, high D-dimer group had statistically significant higher prevalence of systemic hypertension (45.5%) and chronic kidney diseases (33.5%), p-value (0.003 and 0.004) respectively than the other group.

Table (2): The associated comorbidities in both Low-level D-Dimer group and High-level D-Dimer group

Comorbidities No (%)	Low D-Dimer (D-Dimer<2.25) N (%) 85 (33.7%)	High D-Dimer (D-Dimer≥2.25) N (%) 167 (66.3%)	P	Total (252)
Comorbidities (present)	49 (57.6%)	137 (82%)	<0.001*	186 (73.8%)
DM	26 (30.6%)	60 (35.9%)	0.39	86(34.1%)
Hypertension (Yes)	22 (25.9%)	76 (45.5%)	0.003*	98(38.9%)
Cardiac diseases Ischemic heart diseases (IHD) Atrial fibrillation (AF) Heart failure (HF)	 6 (7.1%) 0 2 (2.4 %)	 15 (9%) 5 (3%) 3 (1.8%)	 0.391	 21(8.3%) 5 (2%) 5 (2%)
Chronic kidney diseases	14 (16.5%)	56 (33.5%)	0.004*	70(27.8%)
Asthma	1 (1.2%)	4 (2.4%)	0.51	5 (2%)
Cancer	0	5 (3%)	0.62	5 (2%)
Autoimmune diseases	2 (2.4%)	4 (2.4 %)	0.2	6 (2.4%)
Hypothyroidism	2 (2.4%)	5 (3%)	0.77	7 (2.8%)
Neurological diseases (cerebrovascular stroke, Alzheimer, and epilepsy)	7 (8.2%)	14 (8.4%)	0.44	21 (8.3%)

* Significant values (p <0.05), DM: Diabetes mellitus.

In the univariate and multivariate logistic regression analysis, the patients were divided into two categories: dead and living (**Table 3**). Age, diabetes mellitus, high blood pressure, heart disease, kidney disease, a high D-Dimer level upon admission, the length of the hospital stays, and platelet levels were all linked to mortality in a univariable analysis. A high D-Dimer level at admission was connected to higher odds of mortality when the previous factors were

incorporated in the multivariate model [OR 7.74 (95% CI 4.03-14.8), P <0.001]. Also, renal patients had more chance for death than those without renal disease [OR 3.42 (95% CI 1.48-7.89), P = 0.004], Additionally, patients with a shorter period of hospital staying were associated with greater odds of death than patients with a longer period of hospital staying [OR 0.94 (95% CI 0.90-0.98), P = 0.003].

Table (3): The univariable and multivariable logistic regression analysis for risk factors associated with mortality among COVID-19 patients.

	Univariable OR (95% CI)	P value	Multivariable OR (95% CI)	P value
Age (Years)	1.023 (1.007-1.04)	0.006	1.008 (0.98-1.02)	0.42
Comorbidities (present vs not present)				
DM	1.86 (1.06-3.23)	0.028	1.32 (0.62-2.76)	0.46
HTN	3 (1.71-5.25)	<0.001	1.88 (0.90-3.90)	0.9
Cardiac disease	2.48 (1.08 -5.27)	0.032	1.50 (0.55-4.08)	0.42
Renal disease	5.13 (2.53-10.40)	<0.001	3.42 (1.48-7.89)	0.004
Cancer	3.92 (0.00-Inf)	0.98		
D-dimer on admission (High vs Low)	8.34 (4.61-15.1)	<0.001	7.74 (4.03-14.8)	<0.001
Length of hospitalization (days)	0.96 (0.93-0.99)	0.029	0.94 (0.90-0.98)	0.003
Platelet level	1 (1-1)	0.042	1 (0.99-1.005)	0.114

DM: Diabetes mellitus, HTN: Hypertension

A ROC (Receiver operator characteristic) curve **(Figure1)** analysis was done to discriminate the cut-off point value between dead and alive covid-19 patients based on D-Dimer level. For the D-Dimer level, the Roc curve resulted in a 2.25 µg/ml cut-off point for predicting patient mortality where Specificity is 61%, sensitivity 84.21%, and AUC 79.5 % (Area Under Curve).

Based on the cut-off point value of 2.25 µg/ml all patients were divided into two groups: Lower D-dimer group (patients with low D-Dimer level < 2.25 µg/mL) (85 patients) and Higher D-dimer group (patients with high D-Dimer level ≥ 2.25 µg/mL) (167 patients).

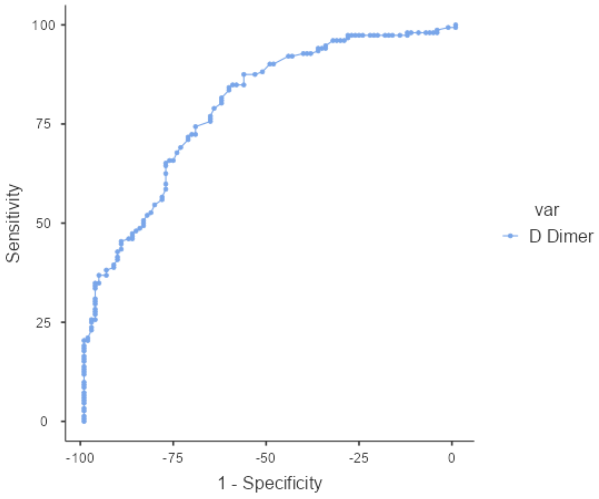

Figure (1): ROC Curve for D-Dimer level as predictor of patients' mortality

DISCUSSION

When plasmin cleaves fibrin to dissolve clots, it produces fragments called a D-dimer. To exclude the diagnosis of thrombosis, d-dimer is utilized as a component of a diagnostic strategy. The levels of plasma D-dimer are also elevated in many physiological and pathological conditions that cause a rise in fibrin formation or breakdown [15]. Arterial and venous thrombosis disseminated intravascular coagulation (DIC), pregnancy, inflammation, malignancy; chronic liver diseases, trauma, postoperative conditions, and vasculitis were common conditions. Infections are more

frequently to blame for D-dimer elevation in patients admitted to the emergency room than Venous thrombosis or PE [16].

D-dimer was not considered to be a helpful marker for bacterial or viral pneumonia before the COVID-19 pandemic, despite some evidence to the contrary [5]. Although, many COVID-19 patients have reported high level of D-dimer with thrombotic conditions. The most often reported cause of D-dimer rise in the literature is cytokine storm due to viremia, in which the proinflammatory cytokines (Interleukines-2, 6, 8, 17, and TNF-α) are insufficiently regulated by the anti-inflammatory factors, the coagulation cascade being overcome [4]. The hypoxia-inducible transcription factor-dependent signaling pathway is activated by hypoxia and results in thrombosis. Elderly and comorbid individuals are the major targets of the illness. The risk of thrombosis may be increased by aging and various comorbidities as diabetes, hypertension, and cardiac diseases [10].

The current study was a retrospective study, its data were collected from the already present hospital records of 252 adult Covid-19 pneumonia patients admitted to Al-Bashir hospital during the interval of April till December 2020, and we aimed to assess the D-dimer level on admission as a predictive of mortality among hospitalized COVID-19 pneumonia cases.

According to the ROC curve results of the present study, the cut-off value of D-dimer level was a 2.25 µg/ml for predicting patient mortality with Specificity 61% and sensitivity 84.21%. The optimum D-dimer value at admission for predicting patient mortality was largely varied in different studies, with variable sensitivity and specificity. D-dimer could be a valuable preliminary marker which predicts hospitalized patient mortality, according to **Zhang et al** research [8] in China, which included 343 patients. They reported that 2 µg/ml was the optimum D-dimer cut-off value. According to **Yao et al.** [7], D-dimer levels at admission for hospitalization mortality had an AUC of 0.846 with 88.2% sensitivity and 71.3% specificity, when using the cut-off value of 2.14. However, research from India discovered that 1.44 µg/ml was the ideal admission D-dimer value to predict hospitalization mortality [9]. Additionally, **Poudel et al.** [10] reported that COVID-19 patients' in-hospital mortality was positively correlated with a D-dimer value higher than 1.5 µg/ml on hospital admission, with 70.6% sensitivity and 78.4% specificity. They recommended further research targeted frequent D-dimer measurements during hospitalization which may have a valued predictor than D-dimer at admission alone.

High D-dimer levels were shown to increase the risk of severe illness and death in COVID-19 patients, regarding a published systematic study in 2020, and it was observed that no definite cut-off value had been recognized to anticipate undesirable consequences [17].

In the current study, the AUC of the ROC curve for D-dimer level on hospital admission was 79.5 %. Our results were in concordance with the following studies: **Oualim et al** [18] and **Peiro et al.** [19] were stated an AUC of 0.775 and 0.756 respectively. While the current study AUC value was higher than the AUC values reported by **Soni et al.** [9], **Naymagon et al.** [20]**,** and **He et al.** [21] which were (0.683, 0.694, and 0.661) respectively. On the other hand, The AUC of the ROC curve for admission D-dimer in **Poudel et al.** [10] was higher (0.807), also **Zhang et al.** [8] observed an AUC of 0.89 in their research.

There is a lot of variations across research on COVID-19 and D-dimer. The explanation of our high cut-off value of D-dimer as a predictive of hospitalization mortality among COVID-19 pneumonia cases might be due to the recruited patients in the current study had older age (median age was 64 years), highly prevalent associated comorbidities among all patients (73.8%),all patients included in the study were severe COVID-19 pneumonia according to Spo2 on admission (77-91%) and also we revealed high percentage of deaths among all patients (60.3%). Furthermore, different laboratories utilize various measurement kits, and the efficiency and reliability of the measurement might fluctuate depending on the kits manufacturer. D-dimer units (DDU) or fibrinogen equivalent units (FEU) reporting units differ as well. All of these might lead to errors when interpreting D-dimer readings in COVID-19 [22].

In the current study, higher D-dimer group showed significantly higher death rate (76.6%) than the lower D-Dimer group (28.2%) with p <0.001.Similarly, **Poudel et al.,** [10] demonstrated that 7.9% of patients who had D-dimer value at admission less than 1.5 µg/ml, died during hospital stay, while 42.9% of patients with D-dimer higher than1.5 µg/ml died, with highly statistical significance difference between both patients groups (P <0.001). Increased D-dimer levels were linked to higher mortality during hospitalization, indicating that the test might serve as the only relevant biomarker for prognostic outcome in COVID-19 patients. [7]

About 73.8% of COVID-19 patients had different comorbidities in the present study, The most prevalent comorbidities in all studied patients (n =252) were hypertension (38.9%), Diabetes mellitus (34.1%) and chronic renal illnesses (27.8%) respectively. In agreement with our study: **Yao et al.** [7] reported that about 30% of the COVID-19 patients included in the sample had comorbidities as hypertension and diabetes mellitus (31.5%, 17.7% respectively). **Zhou et al.** [6] stated that about 48% of patients had comorbidity, with

hypertension being the most common 30% of patients, followed by diabetes 19% of patients and coronary heart disease 8% of patients. **Poudel et al.** [10] detected 47.8% of all COVID-19 patients had comorbidity, among patients with D-dimer lower than 1.5 µg/ml at admission, Hypertension was the most common followed by diabetes, hypothyroidism, COPD, chronic renal illness, hyperlipidemia, and coronary artery disease. likely, patients with D-dimer higher than 1.5 µg/ml at admission, the most common comorbidity was Diabetes mellitus followed by Hypertension, chronic obstructive pulmonary disease (COPD), hypothyroidism, Atrial fibrillation, dyslipidemia, and chronic kidney disease (CKD) but without a statistically significant difference between both groups.

In the univariate and multivariate logistic regression, the patients were divided into two categories: dead and living (**Table 3**). Age, diabetes mellitus, high blood pressure, heart disease, kidney disease, a high D-Dimer level upon admission, the length of the hospital stays, and platelet levels were all associated to mortality in a univariable analysis. High admission D-Dimer value was linked with increased odds of mortality when these factors were involved in the multivariate regression model [OR 7.74 (95% CI 4.03-14.8), P 0.001] and patients with renal disease have a higher mortality risk compared to those without renal disease. [OR 3.42 (95% CI 1.48-7.89)].

Age, SOFA score, qSOFA score, ISTH-DIC score, CURB-65, lymphocytopenia, and increased D-dimer all showed an association with mortality in a univariable test by **Yao et al.** [7]. Admission D-dimer more than 2mg/L was the sole predictor attributed with higher chances of death [OR 10.17 (95% CI 1.10-94.38)] when these factors were involved in the multivariate logistic model**.** In **Zhou et al.** [6] **study,** multivariable regression showed increasing odds of in-hospital death associated with older age (odds ratio 1.10, 95% CI 1.03–1.17, per year increase; p=0·0043), higher Sequential Organ Failure Assessment (SOFA) score (5.65, 2.61–12.23; p<0·0001), and d-dimer greater than 1 µg/mL (95% CI 18.42, 2.64–128.55) on admission. Also, Results of univariate Cox regression utilizing high D-dimer level at admission (greater than 1.5 µg/ml), sex, age and significant comorbid conditions (hypertension, diabetes, chronic renal illness) were assessed by **Poudel et al.** [10]. When studied independently, only age and admission D-dimer exhibited significant hazard ratios. However, after adjusting for sex, age, the occurrence of diabetes, hypertension, and chronic renal illnesses, the hazard ratio for D-dimer was 6.823 (95% CI 3.105-14.991). Furthermore, retrospective research done on 1065 patients hospitalized in the United States stated that every 1 µg/ml rise in D-dimer at admission was linked to a hazard ratio of 1.06 (95% CI 1.04-1.08) for all-cause deaths [20].

High D-dimer levels at admission among COVID-19 patients were generally agreed to be the common variable associated with higher odds of mortality based on our results and those of the prior research. As a result, patients with high admission D-dimer levels may be identified as being at higher risk for in-hospital mortality, and clinicians may be informed of patients who might benefit from intensive care and early intervention [7].

No patient had a proven PE/DVT in either the current research or **Yao et al.,** [7] study, which recommend the utilization of D-dimer in COVID-19 as a marker for more conditions other than thromboembolism.

CONCLUSION

With high sensitivity and specificity, the ideal D-dimer cut-off value at admission was 2.25 µg/ml which predict the mortality of COVID-19 patients. Greater death rates were associated with higher D-Dimer values at admission, particularly in people with comorbid illnesses. In order to determine the COVID-19 prognosis, D-dimer may be utilized as a preliminary test to be combined with other common laboratory assays.

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Authors' contribution: SMS, HSS, and AH contributed to the planning of the work, drafting of the work, reporting, literature review, revision of the manuscript, approval of the final version of the manuscript, and agreed to all aspects of the work. AAZ contributed to statistical analysis of the work, revision of the manuscript, approval of the final version of the manuscript, and agreed to all aspects of the work. MA, MA, MA, and MD contributed to drafting of the work, and data collection.

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REFERENCES

1. Zhou P, Yang X-L, Wang X-G, Hu B, Zhang L, Zhang W, et al. (2020) A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 579: 270–273. https://doi.org/10.1038/s41586-020-2012-7 PMID: 32015507
2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. (2020) Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 395: 497–506.

https://doi.org/10.1016/S0140-6736(20)30183-5 PMID: 31986264
3. Guan W-J, Ni Z-Y, Hu Y, Liang W-H, Ou C-Q, He J-X, et al. (2020) Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 382: 1708–1720. https://doi.org/10.1056/NEJMoa2002032 PMID: 32109013
4. Wool GD, Miller JL. (2021) The Impact of COVID-19 Disease on Platelets and Coagulation. Pathobiology. 88: 15–27. https://doi.org/10.1159/000512007 PMID: 33049751
5. Querol-Ribelles JM, Tenias JM, Grau E, Querol-Borras JM, Climent JL, Gomez E, et al. (2004) Plasma d dimer levels correlate with outcomes in patients with community-acquired pneumonia. Chest.126: 1087–1092. https://doi.org/10.1378/chest.126.4.1087 PMID: 15486368
6. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. (2020) Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 395: 1054–1062. https://doi.org/10.1016/S0140-6736(20)30566-3 PMID: 32171076
7. Yao Y, Cao J, Wang Q, Shi Q, Liu K, Luo Z, et al. (2020) D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study. J Intensive Care. 8: 49. https://doi.org/10.1186/s40560-020-00466-z PMID: 32665858
8. Zhang L, Yan X, Fan Q, Liu H, Liu X, Liu Z, et al. (2020) D-dimer levels on admission to predict in-hospital mortality in patients with Covid-19. J Thromb Haemost. 18: 1324–1329. https://doi.org/10.1111/jth.14859 PMID: 32306492
9. 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 Metab Syndr Clin Res Rev.14: 2245–2249. https://doi.org/10.1016/j.dsx.2020.11.007 PMID: 33395786.
10. Poudel A, Poudel Y, Adhikari A, Aryal BB, Dangol D, Bajracharya T, et al. (2021) 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 16(8): e0256744. https://doi.org/10.1371/journal.pone.0256744.
11. https://jordantimes.com/news/local/-bashir-public-hospital-working-tirelessly-offer-better-services-citizens (accessed January, 2022)
12. https://www.usaid.gov/jordan/fact-sheets/al-bashir-hospital-new-emergency-building (accessed January, 2022)
13. https://jo.usembassy.gov/emergency-department-at-al-bashir-hospital-will-provide-high-quality-care-for-jordans-most-vulnerable/ (accessed January, 2022)
14. Khader Y and Al Nsour M (2021) Excess Mortality During the COVID-19 Pandemic in Jordan: Secondary Data Analysis. JMIR public health and surveillance, 7(10), e32559. https://doi.org/10.2196/32559
15. Linkins LA, Takach S (2017) Review of D-dimer testing: good, bad, and ugly. Int J Lab Hematol. 39(S1):98–103.
16. Lippi G, Bonfanti L, Saccenti C, Cervellin G (2014) Causes of elevated D-dimer in patients admitted to a large urban emergency department. Eur J Intern Med. 25(1):45–8.
17. Shah S, Shah K, Patel SB, Patel FS, Osman M, Velagapudi P, et al. (2020) Elevated D-dimer levels are associated with increased risk of mortality in coronavirus disease 2019: a systematic review and meta-analysis.Cardiol Rev. 28(6), 295-302 https://doi.org/10.1097/CRD.0000000000000330 PMID: 33017364
18. Oualim S, Abdeladim S, El Ouarradi A, Bensahi I, Hafid S, Naitlho A, et al. (2020) Elevated levels of D-dimer in patients with COVID-19: prognosis value. Pan Afr Med J. 35 (suppl 2). https://doi.org/10.11604/pamj.supp.2020.35.2.24692 PMID: 33282060
19. Peiró ÓM, Carrasquer A, Sa´nchez-Gimenez R, Lal-Trehan N, del-Moral-Ronda V, Bonet G, et al. (2021) Biomarkers and short-term prognosis in COVID-19. Biomarkers. 26: 119–126. https://doi.org/10.1080/1354750X.2021.1874052 PMID: 33426934
20. Naymagon L, Zubizarreta N, Feld J, van Gerwen M, Alsen M, Thibaud S, et al. (2020) Admission D-dimer levels, D-dimer trends, and outcomes in COVID-19. Thromb Res. 196: 99–105. https://doi.org/10.1016/j.thromres.2020.08.032 PMID: 32853982
21. He X, Yao F, Chen J, Wang Y, Fang X, Lin X, et al. (2021) The poor prognosis and influencing factors of high D-dimer levels for COVID-19 patients. Sci Rep. 11: 1–7. https://doi.org/10.1038/s41598-021-81300-w PMID: 33414495
22. Favaloro EJ, Thachil J (2020) Reporting of D-dimer data in COVID-19: some confusion and potential for misinformation. Clin Chem Lab Med. 58: 1191–1199. https://doi.org/10.1515/cclm-2020-0573 PMID: 32432563.