Research Article

Role of 'Serial D-Dimer Level' in predicting Severity and outcome in COVID-19 pneumonia: A Prospective multicentric Observational Study of 1000 cases in Tertiary Care Setting in India

 Shital Patil,[1] Abhijit Acharya,[2] Gajanan Gondhali,[3] Ganesh Narwade[4]

[1]Department of Pulmonary Medicine, MIMSR Medical College, Latur India
[2]Department of Pathology, MIMSR Medical College, Latur India
[3]Department of Internal Medicine, MIMSR Medical College, Latur India
[4]Department of Pulmonary Medicine, MIMSR Medical College, Latur India

Abstract

Objectives: Covid-19 pneumonia is heterogeneous disease with variable effect on lung parenchyma, airways and vasculature.

Methods: Multicentric, prospective, observational and interventional study included 1000 covid-19 cases confirmed with RT PCR. All cases were assessed with HRCT thorax, oxygen saturation, inflammatory marker as D-Dimer at entry point and follow up. Age, gender, Comorbidity and use BIPAP/NIV and outcome as with or without lung fibrosis were key observations. In selected cases, lower limb venous doppler and CT pulmonary angiography to rule out DVT or PTE. Statistical analysis is done by using Chi square test.

Results: CT severity score at entry point with D-Dimer level has significant correlation.[p<0.00001] D-Dimer level has significant association with duration of illness prior to hospitalization.[p<0.00001] Comorbidities have significant association with D-Dimer level. [p<0.00001] D-Dimer level has significant association with oxygen saturation.[p<0.00001] BIPAP/NIV requirement has significant association with D-Dimer level.[p<0.00001] Timing of BIPAP/NIV requirement during hospitalization has significant association with D-Dimer level.[p<0.00001] Follow-up D-Dimer titer during hospitalization as compared normal & abnormal to entry point level has significant association with post-covid lung fibrosis, deep vein thrombosis and pulmonary thromboembolism.[p<0.00001].

Conclusion: D-Dimer has documented very crucial role in covid-19 pneumonia in predicting severity of illness and assessing response to treatment during hospitalization.

Keywords: Covid-19 pneumonia, D-dimer, lung fibrosis, deep vein thrombosis, pulmonary embolism, inflammatory marker

Cite This Article: Patil S, Acharya A, Gondhali G, Narwade G. Role of 'Serial D-Dimer Level' in predicting Severity and outcome in COVID-19 pneumonia: A Prospective multicentric Observational Study of 1000 cases in Tertiary Care Setting in India. EJMA 2022;2(2):73–80.

The current pandemic of coronavirus disease 2019 (covid-19) caused by SARS-CoV-2, originally emerged from China, has documented 274,628,461 confirmed cases and 5,358,978 deaths globally, and 34,752,164 confirmed cases 478,007 deaths in India.[1] The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Task Force on covid-19 has been established to synthesize up-to-date information on the epidemiology, pathogenesis, and laboratory diagnosis and monitoring of covid-19, as well as to develop practical recommendations on the use of molecular, serological, and biochemical tests in disease diagnosis and management.[2,3]

Covid-19 pneumonia is heterogeneous disease with variable effect on lung parenchyma, airways and vasculature leading to long term effects on lung functions. Although Lung is the primary target organ involvement in corona virus disease-19 (covid-19), many patients were shown pulmonary and extrapulmonary manifestations of diseases variably during first and second wave, which occurred as resultant pathophysiological effects of immune activation pathway and direct virus induced lung damage. In covid-19 pneumonia pathophysiology constitutes different pathways like immune activation, inflammatory, thrombogenic and direct viral affection to lungs and extrapulmonary tissues. Covid-19, the pandemic disease caused by infection with the novel virus, SARS-CoV-2 (severe acute respiratory syndrome coronavirus-2) can now be added to the already extensive list of conditions that may be associated with elevated D-dimer. The discovery that D-dimer may be elevated in covid-19 was first reported by physicians in Wuhan, China where the epidemic started. A study of 191 patients with covid-19, who were hospitalized in Wuhan during January 2020 at the outset of the pandemic, revealed that D-dimer was elevated in many of these patients and the magnitude of the elevation was greatest in those who did not survive.[4]

Fibrin degradation products (FbDP) are a highly heterogeneous group of soluble fragments that appear in the circulation as a result of two simultaneous physiological processes: 1) Coagulation, resulting in the conversion of soluble fibrinogen into insoluble stabilized fibrin by the enzymes thrombin and factor XIIIa, 2) Fibrinolysis, resulting in the dissolution of the fibrin clot by the enzyme plasmin. The D-dimer fragment is the terminal product of this process.[5] A number of subsequent studies conducted around the world have confirmed that D-dimer is elevated in those with severe covid-19 and highest in those who are most critically ill and those who do not survive. Much covid-19 research over the past months has been directed at understanding the significance of D-dimer elevation and the covid-19 related coagulopathy that is presumed responsible for the elevation.[4]

D-dimer has been extensively investigated for the diagnosis, monitoring, and treatment of venous thromboembolism (VTE) for which it is used routinely.[6] D-dimer levels are also elevated in conditions of chronic inflammation, such as active malignancy, rheumatoid arthritis, sickle cell disease, and asthma.[7] In the setting of covid-19, D-dimer has been reported to be higher in subjects who are critically ill or those who expire.[8-12]

In present study, we have utilized D-Dimer as a basic marker in laboratory panel workup in all covid patients and analyzed as 'core marker' for assessment of coagulation status with other markers of inflammation IL-6, CRP and ferritin during follow up in all admitted patients to assess response to therapy and predictor of post-covid fibrosis, which can be promptly evaluated and treated to have successful treatment outcome.

Methods

Multicentric, prospective, and observational study conducted during July 2020 to May 2021, in MIMSR Medical College and Venkatesh Hospital Latur India, included 1000 covid-19 cases confirmed with RT PCR, to find out role of D-Dimer in predicting severity of illness, assessing response to therapy and outcome as post-covid fibrosis & predicting DVT/PTE in covid-19 pneumonia cases admitted in critical care unit. Total 1000 cases were enrolled in study after IRB approval and written informed consent of patient.

Inclusion criteria: Covid-19 patients, confirmed with RT-PCR, above the age of 18 years, hospitalized in the study centers, including those with comorbidities and irrespective of severity and oxygen saturation were included in the study

Exclusion criteria: Those not willing to give consent, not able to perform D-dimer and not willing to remain in follow-up were excluded

All study cases were undergone following assessment before enrolling in study:

1. Covid-19 RT PCR test performed in all cases, if first test results were negative and radiological features clearly documenting pneumonia, we have repeated RT PCR test and enrolled all cases with positive Covid-19 RT-PCR test.

2. HRCT Thorax to assess severity of lung involvement, and categorized as Mild if score <7, moderated if score 8-15 and severe if score >15 or 15-25.

3. Clinical assessment as- vital parameters like heart rate, oxygen saturation, respiratory rate, blood pressure and documentation of respiratory adventitious sounds

4. Laboratory parameters- complete blood counts, liver functions, blood sugar level, renal functions, ECG

5. Viral inflammatory markers like D-Dimer, CRP, IL-6 assessed at entry point and repeated whenever required during course of illness. Normal and abnormal parameter readings were considered as per pathological laboratory standard.

6. Entry point D-Dimer titer was utilized as assessment tool of severity of illness with clinical parameters

7. If D-Dimer analysis was normal at entry point, then D-Dimer titer was repeated on day of discharge from hospital or done during hospitalization if clinical course deteriorates.

8. If D-Dimer analysis was abnormal at entry point, we repeated on every 72 hours as follow up to assess severity, progression of illness and also titer level utilized to assess response to medical treatment.

9. In selected cases, with abnormal D-dimer or persistent tachycardia, subjected to lower limb venous doppler to rule out DVT, and or CT Pulmonary angiography to rule out pulmonary thromboembolism.

10. Follow-up HRCT thorax was done after twelve weeks or 3 months of discharge from hospital for analysis of post covid lung fibrosis in selected cases with abnormal D-Dimer level at discharge and required BIPAP/NIV during hospitalization and cases required oxygen supplementation at home.

D-Dimer titer assessment:

Normal values: Normal values 70-470 mg/dL

Interpretation of results:

1. Normal: D-Dimer value up to 470 mg/L

2. Positive: value above 470 mg/dL

3. Significant: two-fold raised D-Dimer level

4. Highly significant: four-fold raised D-Dimer level

5. Follow up significance: values raised or decreased in two-to-four-fold change

The statistical analysis was done using chi-squared test. Significant values of χ^2 were seen from probability table for different degree of freedom required. P value was considered significant if it was below 0.05 and highly significant in case if it was less than 0.001.

Observations and analysis:

In present study, 1000 covid-19 pneumonia cases confirmed by covid-19 RT PCR, males were 650/1000 and females were 350/1000, age >50 were 600 cases and age <50 were 400 cases.

CT severity score at entry point with D-Dimer level has significant correlation in covid-19 pneumonia cases [p<0.00001] (Table 1).

D-Dimer level has significant association with duration of illness in covid-19 pneumonia cases. [p<0.00001] (Table 2).

Significant association in D-Dimer and COIVD-19 pneumonia has been documented with variables like age, gender, diabetes mellitus, IHD, Hypertension, COPD, Obesity [p<0.00001] (Table 3).

D-Dimer level has significant association with oxygen saturation in covid1-19 pneumonia cases. [p<0.00001] (Table 4).

BIPAP/NIV requirement during course of covid-19 pneumonia in critical care setting has significant association with D-Dimer level. [p<0.00001] (Table 5)

Timing of BIPAP/NIV requirement during course of covid-19 pneumonia in critical care setting has significant association with D-Dimer level. [p<0.00001] (Table 6)

Follow-up D-Dimer titer during hospitalization as compared to entry point abnormal D-Dimer has significant association in post-covid lung fibrosis [p<0.00001] (Table 7).

Follow-up D-Dimer titer during hospitalization as compared to entry point normal D-Dimer has significant association in post-covid lung fibrosis [p<0.00001] (Table 8).

Follow-up D-Dimer titer during hospitalization as compared to entry point abnormal D-Dimer has significant association in presence of deep vein thrombosis [p<0.00001] (Table 9).

Follow-up D-Dimer titer during hospitalization as compared to entry point normal D-Dimer has significant association with pulmonary thromboembolism [p<0.00001] (Table 10).

Table 1. Correlation of CT severity (at entry point) and D-Dimer in covid-19 cases (n=1000)

CT severity	Normal D-Dimer (n=320)	Abnormal D-Dimer level (n=680)	Analysis
<8 score (n=300)	190	110	Chi test value
9-15 (n=300)	90	210	224.87 p<0.00001
>15 (n=400)	40	360	

Table 2. Duration of illness (Doi) at entry point during hospitalization and D-Dimer level in covid-19 pneumonia cases (n=1000)

Duration of illness	Normal D-Dimer (n=320)	Abnormal D-Dimer (n=680)	Analysis
<7 days (n=340)	30	310	Chi test value
8-15 days (n=460)	160	300	185.65 p<0.00001
>15 days (n=200)	130	70	

Table 3. Other variables and D-Dimer level in Covid-19 Pneumonia cases (n=1000)

COVID-19 RT PCR positive (n=1000)	D-Dimer level normal (n=320)	D-Dimer level abnormal (n=680)	Chi test value and P value
Age >50 years (n=600)	140	460	χ^2=51.77
Age <50 years (n=400)	180	220	p<0.00001
Male gender (n=650)	190	460	χ^2=6.5
Female gender (n=350)	130	220	p< 0.010
Diabetes mellitus (n=600)	150	450	χ^2=33.77
Without diabetes (n=400)	170	230	p< 0.00001
Hypertension (n=210)	160	50	χ^2=238.55
Without Hypertension (n=790)	160	630	p< 0.00001
COPD (n=150)	100	50	χ^2=97.46
Without COPD (n=850)	220	630	p< 0.00001
IHD (n=200)	110	90	χ^2=60.77
Without IHD (n=800)	210	590	p< 0.00001
Obesity (n=160)	20	140	χ^2=33.28
Without obesity (n=840)	300	540	p< 0.00001

Table 4. Oxygen saturation at entry point and D-Dimer level in Covid-19 pneumonia cases (n=1000)

Oxygen saturation	Normal D-Dimer level (n=320)	Abnormal D-Dimer level (n=680)	Analysis
>90% (n=210)	110	100	Chi test value
75-90% (n=490)	150	340	60.37 p<0.00001
<75% (n=300)	60	240	

Table 5. Correlation of BIPAP use with D-Dimer level in covid-19 pneumonia cases (n=1000)

BIPAP/NIV	Normal D-Dimer (n=320)	Abnormal D-Dimer level (n=680)	Analysis
BIPAP/NIV required (n=600)	155	445	Chi test value 26.21 p<0.00001
BIPAP/NIV not required (n=400)	165	235	

Table 6. BIPAP/NIV initiation time at entry point and D-Dimer level covid-19 pneumonia cases (n=600)

BIPAP used (n=600) with duration of illness	Abnormal D-Dimer level (n=290)	Four-fold raised D-Dimer level (n=310)	Analysis
Entry point <1days (n=180)	110	70	Chi test value 31.30 p<0.00001
3- 7 days (n=310)	150	160	
After 7 days (n=110)	30	80	

Discussion

Correlation of CT Severity (at entry point) and D-Dimer in Covid-19 Cases

In present study, CT severity score at entry point with D-Dimer level has significant correlation in covid-19 pneumonia cases, score <8, 8-15 and >15 documented normal and abnormal D-Dimer level as in 190/110, 90/210 and 40/360 respectively of total 1000 study cases [p<0.00001] We observed that CT severity is best visual assessment and indirect marker of inflammation which can be collaborated with D-dimer, and as CT severity score increases, D-dimer level also increases, which is a marker of coagulation abnormality. Numerous studies[13-16,18,20] have documented similar observation.

Duration of Illness (Doi) at Entry Point During Hospitalization and D-Dimer Level in COVID-19 Pneumonia Cases (n=1000)

In present study, D-Dimer level has significant association with duration of illness in covid-19 pneumonia cases, Doi <7 days, 8-15 days and >15 days of onset of symptoms documented normal and abnormal D-Dimer levels in 30/310, 160/300 and 130/70 cases respectively [p<0.00001] As duration of illness in COVID-19 pneumonia increases, ongoing inflammation increases and having abnormal D-Dimer level due to abnormal coagulation cascade stimulation. Studies by various author[14-18,20,26] have documented similar observation. We have also documented that; entry point abnormal D-Dimer with other inflammatory markers like CRP and IL-6 with duration of illness more than a week or 7 days is predictor of prolonged hospital stay with requirement of ventilatory requirement in intensive care unit. Similar observation has been documented in various studies.[21-25]

Table 7. Abnormal D-Dimer level at entry point (n=680) and follow up and its correlation with post-covid lung fibrosis

Post-covid Covid pneumonia fibrosis	D-Dimer titer increased/abnormal at entry point (n=400)	D-Dimer titer fourfold increased during follow up (n=280)	Analysis
Pulmonary fibrosis present (n=210)	40	170	Chi test value 198.45 p<0.00001
Pulmonary fibrosis absent (n=470)	360	110	

Table 8. Normal D-Dimer level (n=320) at entry point and follow up and its correlation with post-covid lung fibrosis

Post-covid Covid pneumonia fibrosis	D-Dimer normal at entry point and remained less than fourfold (n=120)	D-Dimer titer fourfold increased during follow up (n=200)	Analysis
Pulmonary fibrosis present (n=40)	5	35	Chi test value 12.19 p<0.00048
Pulmonary fibrosis absent (n=280)	115	165	

Table 9. Abnormal D-Dimer level at entry point (n=680) and its correlation with follow up titer with deep vein thrombosis

DVT (Deep Vein thrombosis)	D-Dimer titer increased/abnormal at entry point (n=400)	D-Dimer titer fourfold increased during follow up (n=280)	Analysis
DVT present (n=210)	40	170	Chi test value 198.45 p<0.00001
DVT absent (n=470)	360	110	

Table 10. Normal D-Dimer level (n=320) at entry point and its correlation with follow up titer with pulmonary thromboembolism

PTE (Pulmonary embolism)	D-Dimer normal at entry point and remained less than fourfold (n=120)	D-Dimer titer fourfold increased during follow up (n=200)	Analysis
PTE present (n=40)	5	35	Chi test value 12.19 p<0.00048
PTE absent (n=280)	115	165	

Correlation of BIPAP use with D-Dimer Level in Covid-19 Pneumonia Cases (n=1000)

In present study, BIPAP/NIV requirement during course of covid-19 pneumonia in critical care setting has significant association with D-Dimer level; cases received BIPAP/NIV during hospitalization were documented normal and abnormal D-Dimer level in 155/445, 165/235 cases respectively [p<0.00001] We have documented positive correlation with hypoxia and resulting in need of ventilatory support during hospitalization with abnormal D-Dimer level. Similarly various authors[14,20-25] have observed that abnormal or high D-dimer is predictor of poor outcome and these patients require aggressive interventions like BIPAP/NIV, mechanical ventilation or ECMO in due course and persistent high level denotes higher chances of mortality.

Correlation of Oxygen Saturation at entry point and D-Dimer Level in Covid-19 Pneumonia Cases (n=1000)

In present study, D-Dimer level has significant association with oxygen saturation in covid-19 pneumonia cases; cases with oxygen saturation >90%, 75-90%, and <75% observed as normal and abnormal D-Dimer level in 110/100, 150/340 and 60/240 cases respectively [p<0.00001] We have documented positive correlation with hypoxia at entry point during hospitalization and abnormal D-Dimer level which is similar to studies by various authors.[14,20] Low Oxygen saturation or hypoxia is independent predictor of poor outcome in covid-19 pneumonia, as hypoxia is trigger for deranged coagulation secondary to increase in hypoxia-inducible transcription factor which will increase D-Dimer level, Numerous studies[21-25] have documented similar observation.

Correlation of BIPAP/NIV Initiation Time at Entry Point and D-Dimer Level Covid-19 Pneumonia Cases (n=600)

In present study, Timing of BIPAP/NIV requirement during course of covid-19 pneumonia in critical care setting has significant association with D-Dimer level; cases received BIPAP/NIV at entry point <1 day, 3-7 days and after 7 days of hospitalization were documented significance in four-fold

raised D-Dimer level in 110/70, 150/160 and 30/80 cases respectively [p<0.00001] We have documented positive correlation with hypoxia and resulting in need of ventilatory support during hospitalization with abnormal D-Dimer level. Cases with high D-dimer would have required BIPAP/NIV early as compared with normal to slightly raised D-Dimer level, which is in correlation with studies[14,20] documented similar observation.

Other important observation in this study:

Correlation of Abnormal D-Dimer level at entry point (n=680) and follow up and its correlation with post-covid lung fibrosis, Deep vein thrombosis and pulmonary Thromboembolism:

In present study, Follow-up D-Dimer titer during hospitalization during hospitalization as compared to entry point abnormal D-Dimer has significant association in post-covid lung fibrosis [p<0.00001] i.e., D-Dimer at entry point to four-fold raised cases in presence or absence of pulmonary fibrosis were 40/170 and 360/110 cases respectively. Follow-up D-Dimer titer during hospitalization as compared to entry point abnormal D-Dimer has significant association in presence of deep vein thrombosis [p<0.00001] i.e., D-Dimer at entry point to four-fold raised cases in presence or absence of deep vein thrombosis were 40/170 and 360/110 cases respectively. We have observed that ongoing inflammation is the key for rise of D-dimer level irrespective of CT severity score as mild cases were also having significant rise in D-Dimer level as compared to advanced CT Severity, thus it will help in predicting progression of disease in due course during hospitalization and aggressive steps to be taken during management of these cases. Numerous studies[20,27-31] have documented similar risk of poor outcome and adverse lung outcome as increased D-Dimer is an indication of severe inflammatory response and resulted in lung fibrosis in follow up of survivors of COVID-19 pneumonia.

Correlation of Normal D-Dimer level (n=320) at entry point and follow up and its correlation with post-covid lung fibrosis, Deep vein thrombosis and pulmonary Thromboembolism:

In present study, Follow-up D-Dimer titer during hospitalization during hospitalization as compared to entry point normal D-Dimer has significant association in post-covid lung fibrosis [p<0.00001] i.e., D-Dimer at entry point to four-fold raised cases in presence or absence of pulmonary fibrosis were 5/35 and 115/165 cases respectively. In this study, a small fraction of nonsevere patients developed into severe cases in the first 2 weeks after symptom onset. Therefore, health care institutions should also pay close attention to the mild patients, identify progressors early, and

provide appropriate treatment to reduce mortality. Follow-up D-Dimer titer during hospitalization as compared to entry point normal D-Dimer has significant association with pulmonary thromboembolism [p<0.00001] i.e., D-Dimer at entry point to four-fold raised cases in presence or absence of pulmonary thromboembolism were 5/35 and 115/165 cases respectively. Authors in various studies[14, 15,17,19,-25] have documented similar observation.

Correlation of Other Variables and D-Dimer Level in Covid-19 Pneumonia Cases

In present study, age of patient i.e., <50 years and >50 years has significant association in covid-19 cases with normal and abnormal D-Dimer level [p<0.00001]. we have also documented gender of included cases has significant association in covid-19 cases with normal and abnormal D-Dimer level [p<0.010] documented significant differences in age, gender, comorbidities, respiratory symptom, neutrophil count, lymphocyte count, eosinophil count, and D-Dimer level. Studies by various author[14,-20,26] have documented similar observation.

In present study, comorbidities as Diabetes mellitus, COPD, Hypertension, IHD and obesity has documented significant association in covid-19 cases with normal and abnormal D-Dimer level at entry point. [p<0.00001] Numerous studies [14-20,26-31] have documented similar observation.

Conclusion

D-Dimer is easily available, and universally acceptable inflammatory marker, which has documented very crucial role in covid-19 pneumonia in predicting severity of illness, and assessing response to treatment during hospitalization. D-Dimer has important role during interventions in intensive care unit, as follow up titers have significant role in step-up or step-down interventions in critical care setting. Correlating D-dimer with variables like duration of illness, oxygenation status and timing of BIPAP/NIV at entry point is important to have satisfactory treatment outcome.

D-Dimer titer has significant associations with predicting progression of pneumonia, as proportionate number of pneumonia cases with mild variety on CT thorax and normal initial D-Dimer has progressed to critical course and we have documented follow up titers has played crucial role with other inflammatory markers, and many times in second week of illness rising titers indicates ongoing coagulation abnormality, worsening of pneumonia, and increased inflammatory burden which will help to target therapy accordingly. D-Dimer follow-up titer can help in predicting progression of covid pneumonia, and assessing risk of post covid lung fibrosis.

Disclosures

Ethics Committee Approval: Venkatesh Chest Hospital & MIMSR Medical college Latur India, 17/07/2020, number: VCC/51/2020.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – S.V.P.; Design – S.V.P.; Supervision – S.P., A.A., G.G., G.N.; Materials – S.P., A.A.; Data collection and/or processing – S.P., A.A., G.G., G.N.; Analysis and/or interpretation – S.P., A.A., G.G., G.N.; Literature search – S.P., A.A.; Writing – S.P., G.G.; Critical review – S.P., G.N.

References

1. Coronavirus disease (COVID-19) weekly epidemiological update and weekly operational update. Available at: https://www.who.int/emergenc aies/diseases/novel-coronavirus-2019/situation-reports. Accessed Dec 24, 2021.

2. Lippi G, Plebani M. The critical role of laboratory medicine during coronavirus disease 2019 (COVID-19) and other viral outbreaks. Clin Chem Lab Med 2020;58:1063–9. [CrossRef]

3. Bohn MK, Lippi G, Horvath A, Sethi S, Koch D, Ferrari M, et al. Molecular, serological, and biochemical diagnosis and monitoring of COVID-19: IFCC taskforce evaluation of the latest evidence. Clin Chem Lab Med 2020;58:1037–52. [CrossRef]

4. Weiss P, Murdoch DR. Clinical course and mortality risk of severe COVID-19. Lancet. 2020 Mar 28;395(10229):1014-1015. doi: 10.1016/S0140-6736(20)30633-4. Epub 2020 Mar 17. PMID: 32197108; PMCID: PMC7138151. [CrossRef]

5. Dempfle Ce. Validation, calibration, and specificity of quantitative D-dimer assays. Semin Vasc Med 2005;5:315–20.

6. Bockenstedt P. D-dimer in venous thromboembolism. N Engl J Med 2003;349:1203–4. [CrossRef]

7. Kabrhel C, Mark Courtney D, Camargo CA, Plewa MC, Nordenholz KE, Moore CL, et al. Factors associated with positive D-dimer results in patients evaluated for pulmonary embolism. Acad Emerg Med 2010;17:589–97. [CrossRef]

8. Levi M, Thachil J, Iba T, Levy JH. Coagulation abnormalities and thrombosis in patients with COVID-19. Lancet Haematol 2020;7:438–40. [CrossRef]

9. Shah S, Shah K, Patel SB, Patel FS, Osman M, Velagapudi P, et al. Elevated D-dimer levels are associated with increased risk of mortality in coronavirus disease 2019: a systematic review and meta-analysis. Cardiol Rev 2020;28:295–302. [CrossRef]

10. 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;18:844–7.

11. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054–62. [CrossRef]

12. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ 2020;368:m1091. [CrossRef]

13. Scherer PM, Chen DL. Imaging Pulmonary Inflammation. J Nucl Med 2016;57:1764–70. [CrossRef]

14. Wang L, Yang L, Bai L, Huang Z, Peng Y. Association between D-dimer level and chest CT severity score in patients with SARS-COV-2 pneumonia. Sci Rep 2021;11:11636. [CrossRef]

15. Saeed GA, Gaba W, Shah A, Al Helali AA, Raidullah E, Al Ali AB, et al. Correlation between chest CT severity scores and the clinical parameters of adult patients with COVID-19 pneumonia. Radiol Res Pract 2021;2021:6697677. [CrossRef]

16. Inamdar AV. Correlation of chest CT severity score with D-dimer levels in patients with COVID-19. Eur Heart J 2021;42:ehab724.1285. [CrossRef]

17. Jesenak M, Brndiarova M, Urbancikova I, Rennerova Z, Vojtkova J, Bobcakova A, et al. Immune parameters and COVID-19 infection - associations with clinical severity and disease prognosis. Front Cell Infect Microbiol 2020;10:364. [CrossRef]

18. Ibrahim AI Mohamed, Hasan HA, Abdel-Tawab M. CT characteristics and laboratory findings of COVID-19 pneumonia in relation to patient outcome. EJRNM 2021;52:28. [CrossRef]

19. Berger JS, Kunichoff D, Adhikari S, Ahuja T, Amoroso N, Aphinyanaphongs Y, et al. Prevalence and outcomes of D-dimer elevation in hospitalized patients with COVID-19. Arterioscler Thromb Vasc Biol 2020;40:2539–47. [CrossRef]

20. Gopala Krishna BS, Krishna PP, Sankar VR, Raghu K, Kumar AS, Srikanth M, et al. laboratory markers versus CT severity score in predicting mortality In Covid 19. Eur J Mol Clin Med 2021;7:1824–31.

21. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al; China Medical Treatment Expert Group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382:1708–20. [CrossRef]

22. Yang W, Cao Q, Qin L, Wang X, Cheng Z, Pan A, et al. Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19): A multi-center study in Wenzhou city, Zhejiang, China. J Infect 2020;80:388–93. [CrossRef]

23. Yuan J, Zou R, Zeng L, Kou S, Lan J, Li X, et al. The correlation between viral clearance and biochemical outcomes of 94 COVID-19 infected discharged patients. Inflamm Res 2020;69:599–606. [CrossRef]

24. Yang AP, Liu JP, Tao WQ, Li HM. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. Int Immunopharmacol 2020;84:106504. [CrossRef]

25. Shoenfeld Y. Corona (COVID-19) time musings: Our involvement in COVID-19 pathogenesis, diagnosis, treatment and vaccine planning. Autoimmun Rev 2020;19:102538. [CrossRef]

26. Poudel A, Poudel Y, Adhikari A, Aryal BB, Dangol D, Bajracharya T, et al. 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;16:e0256744. [CrossRef]

27. Zhang L, Yan X, Fan Q, Liu H, Liu X, Liu Z, et al. D-dimer levels on admission to predict in-hospital mortality in patients with Covid-19. J Thromb Haemost 2020;18:1324–9.

28. 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 Clin Res Rev 2020;14:2245–9.

29. Naymagon L, Zubizarreta N, Feld J, van Gerwen M, Alsen M, Thibaud S, et al. Admission D-dimer levels, D-dimer trends, and outcomes in COVID-19. Thromb Res 2020;196:99–105.

30. Oualim S, Abdeladim S, Ouarradi AE, Bensahi I, Hafid S, Naitlho A, et al. Elevated levels of D-dimer in patients with COVID-19: prognosis value. Pan Afr Med J 2020;35:105.

31. Peiró ÓM, Carrasquer A, Sánchez-Gimenez R, Lal-Trehan N, Del-Moral-Ronda V, Bonet G, et al. Biomarkers and short-term prognosis in COVID-19. Biomarkers 2021;26:119–26.

32. He X, Yao F, Chen J, Wang Y, Fang X, Lin X, et al. The poor prognosis and influencing factors of high D-dimer levels for COVID-19 patients. Sci Rep 2021;11:1830.