ORIGINAL ARTICLE

Study of Correlation between Plasma D-dimer and Chest CT Severity Score in Covid-19

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Abstract:

Background and objectives: covid -19 is caused by SARS-CoV-2 which severely affects the alveolar vascular endothelium leading to covid pneumonia. The direct damaging effects of virus along with inflammation triggered by the virus leads to hypercoagulability in covid-19 patients. This predisposes the patient to DIC, ARDS, increased oxygen requirement, thus, poor prognosis. D-dimer is a biomarker of hypercoagulability and inflammation. Chest CT severity score visually scores the lung lesions in percentage of lung tissue affected. Aims and objectives: estimation of plasma D-dimer levels and its' correlation with Chest CT severity score in covid-19 patients. Material and Method: This is hospital based single centre retrospective study consisting of 91 covid-19 patients admitted in our hospital from19 July 2022 to 25 august 2022 after being diagnosed clinically and confirmed by RT-PCR. We divided the patient into three groups depending on Chest CT severity score and compared the mean plasma D-dimer levels. Results: We found the plasma D-dimer levels were significantly increased in covid-19 patients as compared to the normal proposed level of <500 ng/ml .The plasma D-dimer levels in patients ranged from 49 to 8815 ng/ml. The mean level of plasma D-dimer of all patients was 3629±1819 ng/ml.The three groupshad mean plasma D-dimer levels 453±508, 2705±1256, 5642±1824 respectively(p <0.0001). The plasma D-dimer levels showed significant positive correlation with Chest CT severity score in three groups (p<0.0001 and r<0.8455, r <0.6818, r <0.6753respectively).Conclusion: Plasma D-dimer levels are significantly increased in covid-19 patients suggestive of hypercoagulable state. The plasma D-dimer levels correlated well with Chest CT severity score in covid-19 patients which in turn reflects the disease severity. Hence, estimation of plasma D-dimer levels may predict the severity of infection and further risk estimation.

Introduction:

On December 31, 2019, China informed WHO about the cases of pneumonia of unknown cause in Wuhan city of China. The infective agent was identified as novel coronavirus. Later on, International Committee on Taxonomy of Viruses, (ICTV) had named this virus as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1-3]Coronavirus belongs to RNA virus family. But the case fatality rate of this new virus is high as compared to other members of the family. Recently, World Health Organization (WHO) named this virus as COVID-19 virus disease (coronavirus disease 2019). The clinical features of COVID-19 disease are very broad, ranging from asymptomatic infection, mild upper respiratory tract illness, respiratory failure, complications and death[4]. The most common complication seen in the patients of Covid-19 is related to lungs. These complications may be pneumonia or significant procoagulant events, including life-threatening pulmonary embolism (PE), in these patients. [5] Some studies shows that the case fatality rate of this disease is high in elderly patients. [6] Hence it is very important to diagnose the disease early and should be treated to improve the patient outcome. But, very less knowledge is available about the pathophysiology of Covid-19 disease. High resolution computed tomography (HRCT) of chest and plasma D dimer levels are important diagnostic tools for the diagnosis of covid-19 disease and its severity. [7] D-dimer is a fibrin degradation product(FDP). It is a small protein fragment that is present in blood after degradation of blood clots by fibrinolysis. During fibrinolysis plasmin degrades the fibrin monomers, cross-linked fibrin polymers and possibly fibrinogen into fibrinogen degradation products (FDPs).D-dimer is so named as it is formed by cross-linking two fibrin 'D' domains(ends) and released into circulation. [8] D-dimer reflects the accelerated fibrinolysis and its sensitivity in diagnosing thrombosis is 95% hence ,it has been widely used in screening of thrombosis. [9] Healthy individuals have low levels of circulating D-dimer. Increase D-dimer

levels are seen in covid-19 patients as the SARS-CoV-2 induces cytokine storm triggering the coagulation cascade causing disseminated intravascular coagulation(DIC).[10]On autopsy lungs of covid-19 patients showed the presence of fibrinous thrombi, endothelial tumefaction and megakaryocytes in small pulmonary arteries and capillaries.[11]The coagulopathy results from local and systemic inflammation caused by corona virus. Hence, D-dimer is also a marker of inflammation along with hypercoagulable state.[12] Estimation of plasma D-dimer levels is a sensitive test to diagnose thrombotic states including pulmonary embolism and DIC.[13]Also, some studies found that very high D-dimer levels are associated with poor prognosis.[14,15]Therefore increased D-dimer levels in covid-19 patients might be helpful in identifying those with severe disease, pulmonary complications and thrombo-embolism. This would assist in early treatment that might reduce covid-19 morbidity and mortality.[16] Chest CT severity score ranges from 0 to 25 based on the visual imaging of pulmonary lesions. Higher CT score indicate more severity and is associated with poor outcome. Chest CT score could be used as an imaging tool for diagnosis of severity of SARS-CoV-2 pneumonia.[17,18] In this study we have tried to correlate the chest CT severity score with plasma D-dimer levels. To find the correlation more effectively, we have divided the covid-19 patients into three groups based on their chest CT score as Group-I, Group-II and Group-III. Then the mean plasma D-dimer level in each of the above groups is compared for significance. To correlate the chest CT severity score with plasma D-dimer levels in covid-19 patients and to achieve this aim our objectives are- The patients of covid-19 disease were divided into 3 groups as Group I, II and III. Estimation and comparison of the mean plasma D-dimer levels in the groups and Finding the correlation between plasma D-dimer level and Chest CT severity score in the groups.

Material and Methods:

Our study is a single centre, retrospective, descriptive cross-sectional study conducted in Dr. Shankarrao Chavan Government Medical College, Nanded from 19 July 2022 to 25 August 2022.The study was conducted in the Department of Biochemistry in collaboration with the Department of Radiology. A total of 91 covid-19 patients admitted in the hospital from April 2021 to June 2021withconfirmed RT-PCRalong with D-dimer and Chest CT scan done within 24 hourswere included in the study. The patients whose D-dimer and Chest CT scan not done within 24 hours were excluded from the study. All these patients were divided into 3 groups for comparison based on Chest CT severity score as Group-I - chest CT score ranges from 0 to 8 (n=42), Group-II - chest CT score ranges from 9 to 16 (n=39) and Group-III - chest CT score ranges from 17 to 25(n=10). D-dimer level estimation of patients coinciding with Chest CT on same day (within 24 hours) were taken into consideration. D-dimer was estimated by automated chemiluminescence. The normal range of D-dimer is 220 -500 ng/ml.[19] HRCT chest was done by the radiology department of our hospital. The Chest CT severity score index (0 to 25) by Chang et al[20] (devised for assessment of ARDS patient with SARS in 2005) was used to assess the lung involvement in covid 19 patients. Each of the five lung lobes were visually scored and given a score from 1 to 5 as 1 =< 5% lobar involvement, 2 = 5 to 25% lobar involvement, 3 = 26 to 50 % lobar involvement,4= 51 to 75 % lobar involvement and 5 => 75 % lobar involvement The summation of individual lobar scores represents the final score out of 25. The data was analyzed using SPSS software. The chest CT severity score and plasma D-dimer levels were compared in the 3 groups using one way ANNOVA. The correlation between Chest CT severity score and plasma D-dimer levels were done using Pearson's correlation coefficient. The p value >0.05 was taken statistically significant

Results:

The present study is a comparative and correlative study. The plasma D-dimer levels and Chest CT severity scores were compared within above 3 groups. Also correlation between plasma D-dimer levels and Chest CT severity score was done in each group. The age group of patients ranges from 16 to 78 years. Out of 91patients,56 were male patients and 35 were female patients. The plasma D-dimer levels in patients ranged from 49 to 8815 ng/ml. The mean level of plasma D-dimer was 3629±1819ng/ml.The mean plasma D-dimer levels in patients of Group I,II and III (Table1) were 453±508, 2705±1256, 5642±1824 respectively.

Table 1: Mean plasma D-dimer levels in covid 19 patients

	Chest CT severity score range	Mean plasma D-dimer ng/ml	p-value
Group I	0 to 8	453±508	
Group II	9 to 16	2705±1256	<0.0001
Group III	17 to 25	5642±1824	

In our study we found that the mean plasma Dimer levels were significantly high in covid 19 patients 3629±1819ng/ml with respect to proposed normal

range(< 500 ng/ml). Similar findings were observed by Zhou et al[21] and Cummings et al[22]with mean D-dimer levels 800 ng/ml and 1600 ng/ml respectively. Also Zhou et al found 18-fold increased mortality risk in patients with D-dimer > 1000 ng/ml. Tang et al[23] and Wang et al[24,25] concluded that patients with higher levels of D-dimer, 3000ng/ml and mean 4380 ng/ml respectively, had poor prognosis compared to those with lower levels. Huang et al[26] reported higher ICU admission rate in patients with high plasma D-dimer levels. Zhang et al[27] found that patients with higher mean D-dimer levels (> 4000 ng/ml) suffered from severe forms of covid -19.Agapakis et al [12] found a significant correlation between the inflammatory marker D-dimer and severity of community acquired pneumonia leading to increased need of hospitalization. A meta-analysis of 18 studies with 3682 patients reported a high D-dimer level in patients with severe versus non-severe covid -19 infection.[28]A subgroup of four studies showed a 2-fold and 4-fold higher risk of critical illness and deaths in patients with plasma D-dimer levels > 500 ng/ml.[28] The Pathogenic mechanism of SARS-CoV-2 is due to binding of virus envelop glycoprotein to ACE2 receptors on alveolar epithelial cells and vascular endothelium.[29,30,31] The SARS-CoV-2 triggers intense activation of inflammatory response and coagulation pathways resulting in intense pro-coagulative phase.[32]As a result micro-thrombosis formation eventually leads to DIC,ARDS and multiorgan failure in covid 19 patients.[33] D-dimer significantly increases in covid -19.[34]D-dimer is produced during fibrin breakdown and hence serves as marker of fibrinolytic activity. In the patients of sepsis and critical illness close relation between pro-inflammatory cytokines and marker of coagulation cascade activation, D-dimer, has been demonstrated.[35,36] Pro-inflammatory cytokines may be involved in endothelial injury, activation of coagulation and inhibition of fibrinolysis in sepsis.[37] D-dimer is also an marker of inflammation.[12]Elevated baseline D-dimer levels are associated with inflammation in covid-19 patients.[34]D-dimer levels significantly correlated with inflammation and fall to normal level as inflammation subsides signifying that inflammation is one of the causes of coagulation activation in covid-19 patients.[34]SARS-COV infection also dysregulates the urokinase pathway further contributing to severe lung injury and alteration in systemic haemostatic balance.[38]In addition to hypercoagulable state the patients with Covid-19 might have increased blood viscosity due to high fever and excessive sweating.[23]There is also evidence to suggest that D-dimer may itself participate in pathogenesis of ARDS

by inducing acute pulmonary dysfunction and a direct pro-coagulant effect.[39] The Chest CT severity score ranged from 0 to 22 in the study patients. The median value of Chest CT severity score was 9. We found that plasma D-dimer levels showed significant positive correlation with chest CT severity score (table 2, Fig1, Fig2,Fig3). The plasma D-dimer levels increased with the increase in visible radiological lung lesions as depicted by the chest CT severity score. The plasma D-dimer levels and Chest CT severity score showed significant positive correlation in all 3 groups.

Table 2: Correlation of plasma D-dimer and Chest CT severity score.

| Covid 19 patients	Pearson's correlation efficient (r value)
Group I	0.8455
Group II	0.6818
Group III	0.6753

**Figure 1: Correlation between Plasma D-dimer and Chest CT severity score in Group I**
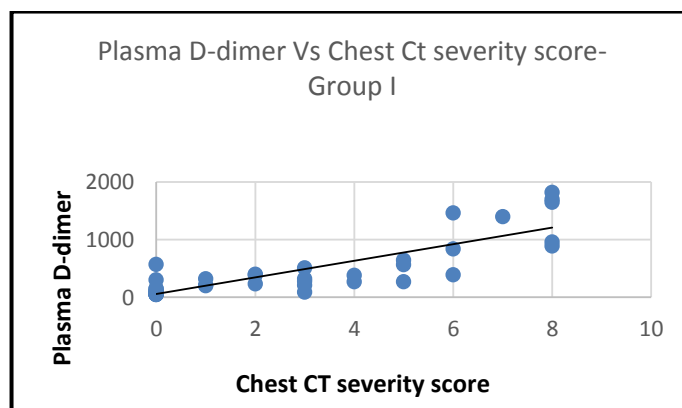
Wang et al[40]observed that chest CT severity score ranged between 8 to 15 (mean 12) in patients with plasma D-dimer levels > 7000 ng/ml whereas patients with D-dimer levels < 7000ng/mlhad CT score ranging between 6 to 13 (mean 8). Jin Zhu et al[41] divided the patients in two groups, mild and severe, depending on clinical and radiological findings. The mean plasma D-dimer levels in the two groups were 965± 854 ng/ml and 3273± 7053 ng/ml respectively. The increase in plasma D-dimer was consistent with the aggravation of chest CT lesions. Jin Zhu et al also reported that the chest CT results correlated with D-dimer levels and these were significantly increased in critically ill patients. G. Saeed et al[42] divided the patients into three groups based on clinical findings as mild, moderate and severe with mean D-dimer levels <1000 ng/ml, 1000- 3000 ng/ml and

>3000ng/ml respectively. They found the D-dimer levels showed significant positive correlation with Chest CT severity score.

Figure 2: Correlation between Plasma D-dimer and Chest CT severity score in Group II
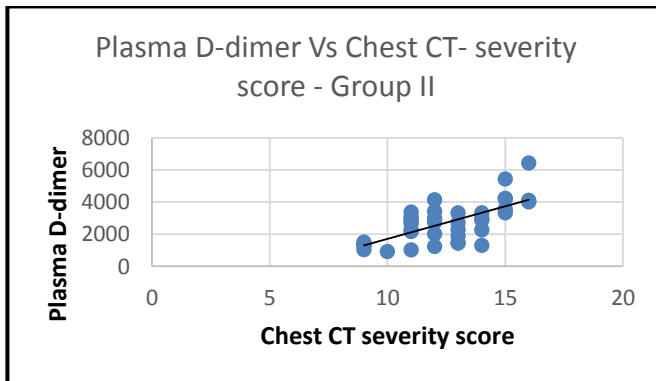
Figure 3: Correlation between Plasma D-dimer and Chest CT severity score in Group III
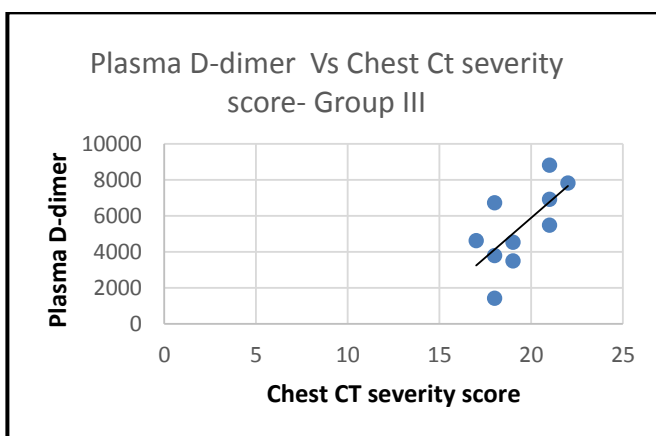
They also reported higher Chest CT severity score and plasma D-dimer levels were associated with increased oxygen requirement and poor prognosis. Inamdar et levels and Hs-CRP levels. Yilmaz et al[45]found that Chest CT score significantly co-related with plasma D-reflected by chest CT lesions, oxygenation index and clinical staging. The increase in oxygen requirement

with increased Chest CT severity score suggests the D-dimer can be used as aprognostic indicator as higher levels are seen in critical cases. However, it is not clear whether the increase is due to direct effect of the virus al[43]and Francone et al[44]found that Chest CT score significantly positively co-related with plasma D-dimer dimer levels and serum ferritin levels at the time of admission, thereby predicting radiologic severity and disease severity. A recent study has proved that Chest CT severity score could be used as an imaging tool for direct damage by virus causing inflammation of alveolar walls, limiting the oxygen exchange leading to ARDS, pulmonary fibrosis and eventually death.[48,49,50] assessing the severity of SARS-COV-2 pneumonia.[46,47] Yumen Yao et al7 found that there is significant co-relation between D-dimer levels and disease severity as or the systemic inflammatory response.[7]This may also be due to referral of critically ill patients to higher centers.[7]Plasma D-dimer can be used as an early marker of disease severity before Chest CT or as a complement to CT and clinical staging.[7,38]D-dimer could be a biomarker for severity of the SAR-COV -2 pneumonia provided that the timepoint of D-dimer estimation and Chest CT scan are matched(same day/within 24 hours).[40]

Conclusion:

Covid -19 patients showed abnormal increase in plasma D-dimer levels. Severity of covid-19 is predicted well by Chest CT severity score which positively correlated with biochemical marker plasma D-dimer. Hence, D-dimer may predict severity of covid infection which further predicts the ICU admission, oxygen requirement and prognosis. This is especially important at the peripheral centers with non-availability of radiological imaging. But considering the limitations of our study with respect to sample size, retrospective nature and exclusion of co-morbidity correlation in the study we suggest a study with larger sample size.

Sources of supports: Nil

Conflicts of Interest: Nil

References

1. Chen N, Zhou M, Dong X et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020; 395(10223):507–513.
2. Huang C, Wang Y, Li X et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395(10223):497–506.
3. Wang D, Hu B, Hu C et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *Journal of American Medical Association* 2020; 323(11):1061–1069
4. Petrilli CM, Jones S, Yang J, Rajagopalan H, O'Donnell L, Chernyak Y, Tobin KA, Cerfolio RJ, Francois F, Horwitz LI. Factors associated with

hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *British Medical Journal* 2020; 369: m1966.

5. Jeffrey S. Berger, Dennis Kunichoff , Samrachana Adhikari , Tania Ahuja, Nancy Amoroso,YindalonAphinyanaphongs , Meng Cao , Ronald Goldenberg , Alexander Hindenburg, James Horowitz, Sam Parnia , Christopher Petrilli , Harmony Reynolds , Emma Simon , James Slater , Shadi Yaghi , Eugene Yuriditsky , Judith Hochman , Leora I. Horwitz. Prevalence and Outcomes of D-Dimer Elevation in Hospitalized Patients With COVID-19.*Arteriosclerosis, Thrombosis, and Vascular Biology* 2020;40: 2539–2547.

6. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020; 323(13):1239-1242.

7. Yumeng Yao, Jiatian Cao, Qingqing Wang, Qingfeng Shi, Kai Liu, Zhe Luo, Xiang Chen, Sisi Chen, Kaihuan Yu, Zheyong Huang and Bijie Hu. D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study. *Journal of Intensive Care* 2020; 8:49-60

8. Input from Drs. Morayma Reyes Gil, Aggie Lee, Nigel Key, Dan Sabath, Cindy Leissinger, Oksana Volod, Geoff Wool, Lisa Baumann Kreuziger. COVID-19 and D-dimer: Frequently Asked Questions (Version 1.0; last updated April 20, 2020)

9. Linkins LA, Bates SM, Lang E, Kahn SR, Douketis JD, Julian J, et al. Selective D-Dimer Testing for Diagnosis of a First Suspected Episode of Deep Venous Thrombosis: A Randomized Trial. *Annals of Internal Medicine*2013;158(2):93-100.

10. Liu B, Li M, Zhou Z, Guan X, Xiang YJ. Can we use interleukin- 6 (IL-6) blockade for coronavirus disease (2019). (COVID-19)- induced cytokine release syndrome (CRS)? Journal of *Autoimmunity* 2020; 111(102452): 1-8.

11. Dolhnikoff M, Duarte-Neto AN, de Almeida Monteiro RA, Ferraz da Silva LF, Pierre de Oliveira E, Nascimento Saldiva PH, et al. Pathological evidence of pulmonary thrombotic phenomena in severe COVID-19. *Journal of Thrombosis and Haemostasis* 2020; 18:1517–1519.

12. DimitriosI.Agapakis, dionissiostsantilas, panagiotis psarris, eleniV.Massa, panagiotiskotsaftis, konstanti nostziomalos, apostolosi.Hatzitolios.Coagulation and inflammation biomarkers may help predict the severity of community-acquired pneumonia. *Respirology* 2010; 15: 796–803.

13. Olson JD. D-dimer: an overview of hemostasis and fibrinolysis, assays, clinical applications. *Advances in Clinical Chemistry* 2015; 69:1–46.

14. Guan W, Ni Z, Hu Y et al. Clinical characteristics of 2019 novel coronavirus infection in China. *medRxiv Journal of Emergency Medicine* 2020; 58(4):711-712.

15. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *Journal of Thrombosis and Haemostasis* 2020; 18(4):844–847.

16. Panagiotis Paliogiannis, Arduino Aleksander Mangoni, Paola Dettori, Gheyath K. Nasrallah, Gianfranco Pintus and Angelo Zinellu. D-Dimer Concentrations andCOVID-19 Severity: A SystematicReview and Meta-Analysis. *Frontiers in Public Health* 2020; 8(432):108-112.

17. Yang, R. et al. Chest CT severity score: An imaging tool for assessing severe COVID-19. *Radiology and Cardiothoracic Imaging*2020; 2(2): 200047.

18. Zhao, W., Zhong, Z., Xie, X., Yu, Q. & Liu, J. Relation between chest CT findings and clinical conditions of coronavirus disease (COVID-19) pneumonia: A multicenter study. *American Journal of Roentgenology* 2020; 214: 1072–1077.

19. Nitin Chopra, Pradeep Doddamreddy, Hermanjeet Grewal, and Pratap C Kumar. An elevated D-dimer value: a burden on our patients and hospitals.*International Journal of General Medicine* 2012; 5: 87–92.

20. Yeun-Chung Chang [1] , Chong-Jen Yu, Shan-Chwen Chang, Jeffrey R Galvin, Hon-Man Liu, Cheng-Hsiang Hsiao, Ping-Hong Kuo, Kuan-Yu Chen, Teri J Franks, Kou-Mou Huang, Pan-Chyr Yang. Pulmonary sequelae in convalescent patients after severe acute respiratory syndrome: evaluation with thin-section CT Radiology. *Radiology* 2005; 236(3):1067-1075.

21. Zhou F, Yu T, Du R, 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: 1054–1062.

22. Cummings, M. J. et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: A prospective cohort study. Lancet 2020; 395(10239):1763-1770.

23. Tang N, Li D, Wang X, et al. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *Journal of Thrombosis and Haemostasis* 2020; 18: 844–847.

24. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, *China. Journal of American Medical Association*2020; 323: 1061–1069.

25. Wang L, He W, Yu X, et al. Coronavirus disease 2019 in elderly patients: characteristics and prognostic factors based on 4-week follow-up. *Journal of Infection*2020; 80: 639–645.

26. Yin S, Huang M, Li D, et al. Difference of coagulation features between severe pneumonia induced by SARS-CoV2 and non-SARS-CoV2. *Journal of Thrombosis and Thrombolysis* 2020; 6:395(10239): 1763-1770.

27. Zhang JJ, Dong X, Cao YY, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan.China *Allergy* 2020; July75(7):1730-1741.

28. Shah S, Shah K, Patel SB, Patel FS, Osman M, Velagapudi P, Turagam MK, Lakkireddy D, Garg J. Elevated D-Dimer Levels are Associated with Increased Risk of Mortality in COVID-19: A Systematic Review and Meta-Analysis. *medrxiv* Cardiology in review 2020; 28(6):295-302.

29. Zhang H, Penninger JM, Li Y, et al. Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor : molecular mechanisms and potential therapeutic target. *Intensive Care Medicine* 2020; 46: 586–590.

30. Wan Y, Shang J, Graham R, et al. Receptor recognition by the novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS coronavirus. *Journal of Virology* 2020; 94 (e00127):20.

31. Zhang Y, Cao W, Xiao M, et al. Clinical and coagulation characteristics in 7 patients with critical COVID-2019 pneumonia and acro-ischemia. *China Journal of Hematology* 2020; 41: 302–307.

32. Liu PP, Blet A, Smyth D, et al. The science underlying COVID-19: implications for the cardiovascular system. *Circulation American Heart Association*2020; 142: 68–78

33. Vidali S, Morosetti D, Cossu E, et al. D-dimer as an indicator of prognosis in SARS-CoV-2 infection: a systematic review. *European Open Respiratory Journal* 2020; 6: 0260-2020.

34. Bilian Yu1, Xin Li, Jin Chen, Mingqi Ouyang, Hong Zhang, Xinge Zhao, Liang Tang, Qin Luo, Min Xu, Lizhen Yang, Guxiang Huang,Xianling Liu, Jianjun Tang. Evaluation of variation in Ddimer levels among COVID19 and bacterial pneumonia: a retrospective analysis. *Journal of Thrombosis and Thrombolysis* 2020; 50(3)548-557.

35. 23. Pettila V, Hynninen M, Takkunen O, Kuusela P, Valtonen M. Predictive value of procalcitonin and interleukin 6 in critically ill patients with suspected sepsis. *Intensive Care Medicine* 2002; 28(9):1220–1225.

36. Gunther A, Mosavi P, Heinemann S, Ruppert C, Muth H, Markart P, Grimminger F, Walmrath D, Temmesfeld-Wollbruck B, Seeger W. Alveolar fibrin formation caused by enhanced procoagulant and depressed fibrinolytic capacities in severe pneumonia. Comparison with the acute respiratory distress syndrome. *American Journal of Respiratory and Critical Care Medicine* 2000; 161(2 Pt 1):454–462

37. Bone RC, Grodzin CJ, Balk RA. Sepsis: a new hypothesis for pathogenesis of the disease process. *Chest* 1997; 112(1):235–243

38. Gralinski LE, Bankhead AR, Jeng S et al. Mechanisms of severe acute respiratory syndrome coronavirus-induced acute lung injury. *Microbiology- American Society for Microbiology*2013; 4(4): e00271–e00313.

39. Manwaring D, Curreri PW. Cellular mediation of respiratory distress syndrome induced by fragment D.*AnnalsChirurgiae Et Gynaecologiae* 1981; 70:304–307.

40. Lan Wang, Ling Yang, Lang Bai, Zhixin Huang & Yong Peng. Association between Ddimerlevel and chest CT severity score in patients with SARSCOV2 pneumonia. *Scientific Reports* 2021; 11:11636.

41. Zhu J, Chen C, Shi R, Li B. Correlations of CT scan with high-sensitivity C-reactive protein and D-dimer in patients with coronavirus disease 2019. *Pakistan Journal of Medical Sciences*2020;36(6):1397-1401.

42. Ghufran Aref Saeed , Waqar Gaba, Asad Shah, Abeer Ahmed Al Helali,EmadullahRaidullah, Ameirah Bader Al Ali, Mohammed Elghazali, Deena Yousef Ahmed, Shaikha Ghanam Al Kaabi, and Safaa Almazrouei. Correlation between Chest CT Severity Scores and the ClinicalParameters of Adult Patients with COVID-19 Pneumonia. *Hindawi Radiology Research and Practice* 2021;10(2):1155-1161.

43. A.V. Inamdar. – The Digital ExperienceCoronary Artery Disease, Acute Coronary Syndromes, Acute Cardiac Care –Acute Coronary Syndromes, Pathophysiology and Mechanisms, Thrombosis, Platelets, and Coagulation. *India European society of cardiology Congress* 2021: European Heart Journal / e-poster/article 42- supplement 1/ehab 724.1285.

44. Francone M, Iafrate F, Masci GM, Coco S, Cilia F, Manganaro L, Panebianco V, Andreoli C, Colaiacomo MC, Zingaropoli MA, Ciardi MR. Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis. *European Radiology*2020; 3012: 6808–6817

45. Yang, R. et al. Chest CT severity score: An imaging tool for assessing severe COVID-19. *Radiology and Cardiothorasic Imaging* 2020; 2(2):e200047:1

46. Zhao, W., Zhong, Z., Xie, X., Yu, Q. & Liu, J. Relation between chest CT findings and clinical conditions of coronavirus disease (COVID-19) pneumonia: A multicenter study. *American Journal of Roentgenology* 2020; 214: 1072–1077.

47. Atakan Yilmaz a, Ramazan Sabirli b, Murat Seyit a, Mert Ozen a, Alten Oskay a, Vefa Cakmak c,Tarik Goren d, Ibrahim Turkcuer a. Association between laboratory parameters and CT severity in patientsinfected with Covid-19: A retrospective, observational study.Elsevier *American Journal of Emergency Medicine*2021; 42: 110–114.

48. J. B. Prudhomme and L. B. Ware. Acute lung injury and acute respiratory distress syndrome: mechanisms and potential new therapies. *Drug Discovery Today: Disease Mechanisms 2004;1(1):* 123–128.

49. Europa.eu., CORDIS, European Commission, 2020, https:// cordis.europa.eu/article/id/421597-how-covid-19-damages-the -lungs. European vision:2023 ,p- 1-4

50. M. Ackermann, S. E. Verleden, M. Kuehnel et al. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in covid-19. *New England Journal of Medicine* 2020; 383(2):120- 128. 388

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