Corelation of D dimer value with the severity of covid 19

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Abstract

The famous pandemic of Covid -19 , known for its high level of contagion and huge amount of cases has no plan to end anytime soon .Coagulation abnormalities have been observed in approximately 60–70% of hospitalized patients. The ultimate pattern of coagulation abnormalities observed in patients hospitalized due to covid 19 is high levels of D-dimer. D-dimer and other laboratory biomarkers can be used to predict the patients profile who are at risk of unfavorable evolution of COVID-19 .This study was aimed to evaluate the correlation of elevated D-dimer with the severity of COVID-19.and its association with thromboembolic complications .

Materials and Methods : The clinical data of 256 Covid PCR positive patients was collected from the hospitals' patients record files of Aga Khan hospital and Chugtai Lab. The coagulation parameters including D-dimer, and other laboratory parameters including ferritin, CRP and Lfts were analyzed and compared among patients with non-severe infection and those with severe infection.

Results: Out of 256 patients 218 patients were severe having elevated D-dimer levels(> 0.5 µg/ml and O2 saturation <94% and 38 patients were non severe having O2 saturation>94% and D dimer <0.5. other coagulation parameters were deranged for all the severe patients.

Conclusion: Severity of covid 19 is associated with coagulation abnormalities.Patients with severe Covid-19 have higher D-dimer levels, and D-dimer within normal range indicats non severe Covid-19 infection. A D-dimer > 0.5 µg/ml is associated with severe infection in patients with COVID-19.

Keywords: COVID-19, D-dimer, coagulation abnormalities, unfavorable evolution marker,severe covid infection,

Introduction

Coronavirus Disease 2019 (COVID-19), a respiratory sickness, brought on by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), has overran the entire world in 2019 and 2020(2).Coronaviruses belongs to Coronaviridae family and Nidovirales order. They are enveloped RNA viruses and contain positive-sense single-stranded RNA (+ssRNA). These viruses generally infect humans and animals and they cause hepatic, respiratory, enteric and neurological diseases

(3).Coronavirus have many variants and some variants are categorized as Variants of concern that includes Delta (B.1.617.2 lineage) variant, which is highly transmissible and Omicron variant (B.1.1.529 lineage) known for its high infectivity(4).Globally, as of 29 March 2023, there have been 761,402,282 confirmed cases ofCOVID19,including 6,887,000 deaths, reported to WHO (5).According to current evidence, SARS-CoV-2 is transmitted from person to person when the infectious particles are released from the respiratory tract of an infected individual and reach the respiratory tract of a susceptible individual(6). The cell surface receptor angiotensin-converting enzyme 2 plays the major role in the entry of the novel coronavirus inside the body(7).

COVID-19 is predominantly a respiratory illness, but it can have its affect on multiple organ systems including hepatic, gastrointestinal, neurological, cardiac, and renal systems(8). The covid -19 infection has an incubation period of almost 4–5 days, which can extend as long as 14 days (9, 10). The most frequent and typical symptoms of COVID-19 are fatigue, fever, and dry cough(10, 11). Clinically, most of the patients infected with COVID-19 experience moderate to mild symptoms (81%). Nevertheless, approximately 14% of covid-19 patients develop pneumonia for which sometimes ventilation is required in an intensive care unit (ICU), and 5% of the infected patients progress to more critical manifestations including septic shock, acute respiratory distress syndrome (ARDS), and multiple organ dysfunction or organ failure(11), leading to several laboratory abnormalities, such as thrombocytopenia, hypercoagulative state,

leukopenia, and increased levels of D-dimer, which often causes admission to the intensive care unit (ICU) (12, 13).

Coagulopathies and Thrombotic complications that includes Disseminated intravascular coagulopathy are commonly present in COVID-19, likely showing the activation of the coagulation cascade caused by cytokine storm or viremia, or can be due to organ dysfunction and superinfection (13). Coagulation abnormalities such as hypercoagulation, thrombocytopenia, venous thrombosis (TV) and disseminated intravascular coagulation (DIC) have been observed in approximately 60–70% of hospitalized patients. The autopsies showed that in almost 58% of patients the cause of death was a pulmonary embolism or venous thrombosis, while DIC was reported in 70% of the patients who died from COVID-19(1).

In covid 19 patients, elevated D-dimer levels and fibrinogen levels are the most common biomarkers of dysregulated coagulation functions (14).D-dimer is formed as a byproduct of fibrin degradation, it is widely used as a biomarker to diagnose thrombotic disorders.(15). D-dimer symbolizes activation of fibrinolysis and coagulation. It is formed by the formation and lysis of cross-linked fibrin (16). Normal value of D-dimer is less than 0.5 µg/mL, but this value may increase in older age or in pregnancy. It is observed that its value increases as the covid 19 infection gets worse(15). The elevated levels of D-dimer may indicate that of the COVID-19 infection is advancing towards severity and can be used to foretell the need for more urgent critical care. (17). It is beneficial to precisely identify COVID-19 patients who may have a high risk of

developing a severe infection and to start treating them with various therapies at an early stage of the disease. (18). This study aims to highlight the role of D-dimer in COVID-19 infection by corelating the level of D dimer with the severity of covid 19.

Materials and methods

This retrospective study was conducted in primary care centers for covid 19. Clinical characteristics and other laboratory parameters(feretin,CRP,LFTs) were collected and analyzed for confirmed covid 19 patients. Disease severity was determined by corelating the value of D-dimer between severe and non severe covid-19 patients.

Patient selection: Patients diagnosed with COVID-19 confirmed by Reverse transcription polymerase chain reaction (RT-PCR) were considered for inclusion in the study. Severity was defined by following parameters: suspected respiratory infection or fever, severe respiratory distress, or SpO2 < 94% on room air.

Data collection: The clinical data of 250 Covid PCR positive patients was collected from the hospitals' patients record files of Aga Khan hospital and Chugtai Lab. Patients demographic features like (name, age , sex),D-dimer level on admission, SpO2 on admission, and outcome were recorded for each patient. The data were recorded using standard units of measurements for each variable on a standardize data collection sheet.

Laboratory testing :O2 saturation of each patient was checked using pulse oximeter at the time of admission.Blood samples for each patient were collected within 2 hours of admission and sent to laboratory for assessment of D dimer and other laboratory parameters. D dimer was measured using Wondfo finecare Immunofluorescence Quantitative Analyzer.

Statistical analysis

Statistical analysis was performed on patients data using IBM Statistics and Excel 2019 . To Corelate D-dimer with severitry of Covid -19 two variables were used including O2 saturation and D-dimer value for each patient. Pearson Corelation test was performed on these two variables. Further frequency of severe and non severe patients was checked . severe patients are further analyzed for deranged parameters using cross tabulation.

Results

In this analysis ,there is a negative correlation between O2 saturation and D dimer values .it shows as the O2 saturation was decreasing the D-dimer value was increasing(Table 1) that is showing and inverse relation between O2 and D -dimer. Out of 256 patients 218 patients were severe

having O2 saturation <94% and 38 patients were non severe having O2 saturation>94%.Mean D-dimer of severe patients were 4.7 µg/ml as compared to 0.4 µg/ml for non severe patients.Other laboratory parameters including Ferritin,CRP,Lfts were deranged for all the severe patients.On the other hand non severe patients had these parameters in normal range.

Table 1

Correlations of D-dimer and Covid 19

		Ddimer	oxygen saturation
Ddimer	Pearson Correlation	1	-.827**
	Sig. (2-tailed)		.000
	N	256	256
oxygen saturation	Pearson Correlation	-.827**	1
	Sig. (2-tailed)	.000	
	N	256	256

**. Correlation is significant at the 0.01 level (2-tailed).

Table 2

Mean D-dimer of Severe vs non severe patients

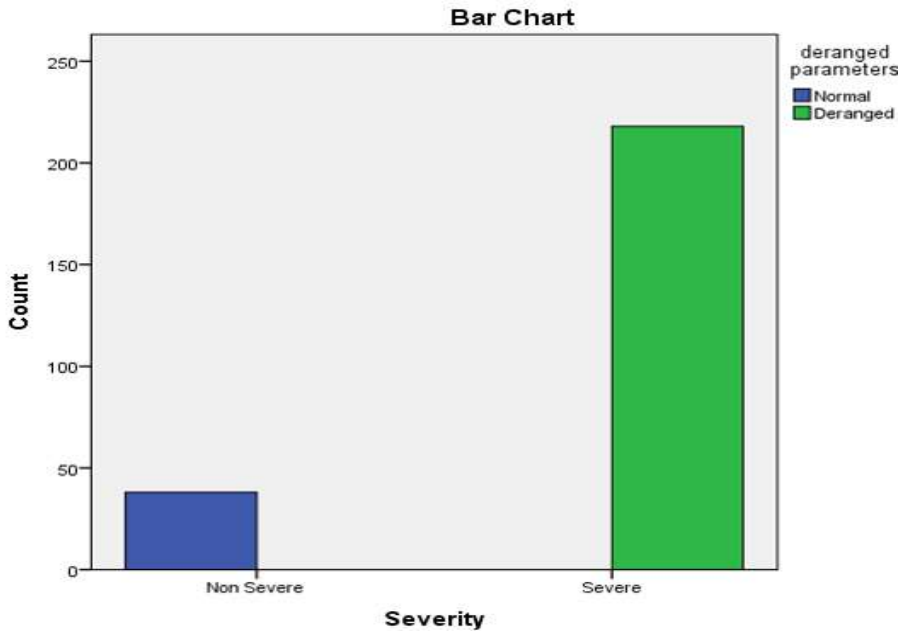
Non Severe	N	Valid	38
		Missing	0
	Mean		.403
Severe	N	Valid	218
		Missing	0
	Mean		4.726

Table 3

Severity * deranged laboratory parameters Cross tabulation

Count

		Deranged laboratory parameters		Total
		Normal	Deranged	
Severity	Non Severe	38	0	38
	Severe	0	218	218
Total		38	218	256



Conclusion

Patients with severe COVID-19 have a higher level of D-dimer than those with non-severe disease, and D-dimer greater than 0.5 μg/ml is associated with severe infection in patients with COVID 19.

References

1. Wichmann D, Sperhake JP, Lütgehetmann M, Steurer S, Edler C, Heinemann A, et al. Autopsy Findings and Venous Thromboembolism in Patients With COVID-19: A Prospective Cohort Study. Annals of internal medicine. 2020;173(4):268-77.
2. Baroiu L, Lese AC, Stefanopol IA, Iancu A, Dumitru C, Ciubara AB, et al. The Role of D-Dimers in the Initial Evaluation of COVID-19. Therapeutics and clinical risk management. 2022;18:323-35.
3. Weiss SR, Leibowitz JL. Coronavirus pathogenesis. Advances in virus research. 2011;81:85-164.
4. Long B, Carius BM, Chavez S, Liang SY, Brady WJ, Koyfman A, et al. Clinical update on COVID-19 for the emergency clinician: Presentation and evaluation. The American journal of emergency medicine. 2022;54:46-57.
5. who. WHO Coronavirus (COVID-19) Dashboard: WHO; 2022 [Available from: https://covid19.who.int/?mapFilter=cases.
6. Leung NHL. Transmissibility and transmission of respiratory viruses. Nature reviews Microbiology. 2021;19(8):528-45.
7. Zhang H, Penninger JM, Li Y, Zhong N, Slutsky AS. Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target. Intensive Care Medicine. 2020;46(4):586-90.
8. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020;579(7798):270-3.
9. Vidali S, Morosetti D, Cossu E, Luisi MLE, Pancani S, Semeraro V, et al. D-dimer as an indicator of prognosis in SARS-CoV-2 infection: a systematic review. ERJ open research. 2020;6(2).
10. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. The New England journal of medicine. 2020;382(18):1708-20.
11. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet (London, England). 2020;395(10223):507-13.
12. Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Biondi-Zoccai G, et al. Cardiovascular considerations for patients, health care workers, and health systems during the COVID-19 pandemic. Journal of the American College of cardiology. 2020;75(18):2352-71.
13. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. jama. 2020;323(13):1239-42.
14. Ge YL, Liu CH, Wang N, Xu J, Zhu XY, Su CS, et al. Elevated Plasma D-Dimer in Adult Community-Acquired Pneumonia Patients is Associated with an Increased Inflammatory Reaction and Lower Survival. Clinical laboratory. 2019;65(1).
15. Querol-Ribelles JM, Tenias JM, Grau E, Querol-Borras JM, Climent JL, Gomez E, et al. Plasma d-dimer levels correlate with outcomes in patients with community-acquired pneumonia. Chest. 2004;126(4):1087-92.
16. 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. Journal of thrombosis and haemostasis : JTH. 2020;18(6):1324-9.
17. Li Q, Cao Y, Chen L, Wu D, Yu J, Wang H, et al. Hematological features of persons with COVID-19. Leukemia. 2020;34(8):2163-72.
18. 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 : JTH. 2020;18(4):844-7.

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. Arteriosclerosis, thrombosis, and vascular biology. 2020;40(10):2539-47.

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