

Prevalence and outcomes of D dimer elevation among the COVID-19 patients in tertiary care hospital, Salem

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ABSTRACT

Introduction: The Coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which was initially reported in Wuhan and later spread to the rest of the world.^[1] The incidence of thrombotic events has been reported to be 16% in patients admitted for COVID-19 with an increase in the fibrinogen level and D-dimer level which was associated with mortality. D-Dimer was found to be elevated in severely ill patients admitted in the intensive care unit (ICU) and the dead patients. This study was done to find the prevalence of D-dimer elevation among the COVID-19 patients and its impact on the outcome and to find out the association between the D-dimer elevation and severity of the disease. **Methodology:** A hospital-based cross-sectional study was conducted from August 2020 to September 2020 in a tertiary care hospital in Salem in the Internal Medicine Department. All the COVID-19 patients of both sexes and all age groups were included in the study. The non-COVID pneumonia cases were excluded from the study. The data were collected from the participants after obtaining their written consent to take part in the study and the data were collected using a pretested and pre-validated schedule. Institutional ethical committee clearance was obtained before the start of the study. **Results:** The mean age of the patients was found to be 54.89 ± 14.4 with the minimum age being 14 and the maximum age being 87. The prevalence of the D-dimer elevation was found to be 143 (81.8%). D-Dimer was found to be significant with severe COVID infection. **Conclusion:** The D-dimer levels were found to be more in severe COVID infections compared to mild COVID infections. Furthermore, research is required in this field.

Keywords: COVID-19, D-dimer, pneumonia, saturation

Introduction

In December 2019, a cluster of cases was raised with unknown aetiology in the Wuhan city of China. It mimics pneumonia. On January 9, it was declared that a novel Corona Virus, severe acute respiratory syndrome, SARS-CoV-2 was responsible for this outbreak.^[1] It is transmitted through respiratory droplets and targets the angiotensin-converting enzyme 2 (ACE2) receptor.^[2,3] It has an incubation period of 2–14 days and the clinical spectrum

of the disease varies starting from asymptomatic, mild upper respiratory tract illness, respiratory failure and death.^[1,4] As of May 27, 2019, the globally confirmed cases were 5,488,825 in Europe, America, Africa and South-East Asia and the deaths reported were 349,095.^[5]

About 3.75–68% of COVID-19 patients showed elevated D-dimer and coagulopathy was reported.^[6-8] D-Dimer is found to be the principal breakdown fragment of fibrin and was used as a biomarker for degradation and fibrin formation.^[9] Several studies have shown that it was one of the valuable markers in fibrinolysis and activation of coagulation.^[10] D-Dimer values are reported to be high in patients who are critically ill and who expire due to COVID-19.^[11-14] Micro thrombi were noted mostly

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in the multiple organ systems in COVID-19 patients who were hospitalised but the association between D-dimer and severity of COVID-19 infection is not clear. This study was done mainly to find out the prevalence of the elevation of D-dimer and its impact on the COVID patients' outcomes.

Methodology

A cross-sectional study was done in a tertiary care teaching hospital, Salem, Tamil Nadu, by the Internal Medicine Department. The study was conducted from August 2020 to September 2020. All the patients who were tested positive through reverse transcriptase-polymerase chain reaction (RT-PCR) during this period were included in this study and those patients with a history of cancer, malignancy, chronic liver disease, acute coronary syndrome, recent trauma or surgery within a month and pregnancy were excluded from the study. Investigations like complete blood count, renal parameters, liver function test, lactate dehydrogenase (LDH), serum ferritin and D-dimer level, electro cardio gram (ECG) and chest computerized tomography (CT) scan were done for all patients. For this study purpose, the severity of the disease was classified based on the nature of their treatment—whether they recovered in room air which is taken as a mild disease, those who needed any non-invasive techniques like an oxygen mask, rebreathing mask, high-flow nasal oxygen was considered as a moderate disease and patients in the ICU and who expired was considered as severe.

Data were collected after obtaining written consent from the participants or their attendees in case of severely morbid patients. A pre-designed and pretested schedule containing sociodemographic details like name, age, sex, comorbid status, presentation at the time of admission, symptoms, saturation and pulse rate were collected. The institutional ethical committee clearance was obtained before the start of the study.

Statistical analysis

After collecting the data, it was entered in MS Excel. Statistical analysis was done in SPSS 23. Continuous data with normal distribution were expressed in terms of mean \pm standard deviation and compared by an independent sample *t*-test. The categorical variables were expressed in terms of numbers (percentages) and compared by the Chi-square test. The association between the categorical variables was done by the Spearman test.

Results

The mean age of the study participants was found to be 52.8 ± 14.4 years with a minimum age of 14 years and maximum age of 87 years. Male (76.1%) predominance is noted in our study; 94 (54.3%) have comorbidities like diabetes, hypertension, asthma, hypothyroidism and cardiovascular disease [Table 1].

The baseline characteristics of the study participants reveal that when age increases the D-dimer value also increases and is found to be statistically significant. Breathlessness was noted

more in patients with increased D-dimer and also was found to be statistically significant. Saturation was noted to drop more in patients with a high level of D-dimer and their association was also found to be statistically significant.

In our study, around 81.3% (143) showed elevation in their D-dimer levels [Figure 1].

In our study, the D-dimer level markedly increased with moderate and severely ill patients. The increase was also found to be statistically significant [Table 2].

When the association between the severity of the disease and D-dimer levels were taken, it was found to be statistically significant and they have a good correlation of .72 [Table 3].

Discussion

Baseline characteristics

D-Dimer is usually not present in human blood plasma. It is present only when the coagulation system has been activated. The commonly used laboratory coagulation indicators include D-dimer, prothrombin time and activated partial thromboplastin time (APTT).^[14] For exogenous and endogenous coagulating systems, PT and APTT are used for the early diagnosis of disseminated intravascular coagulation. D-Dimer is elevated due to fibrinolytic solubilisation of fibrin and it indicates a hyper coagulating state and secondary fibrinolysis in the body.^[15,16]

In our study, the mean age was 52.8 ± 14.4 which was lesser than the report of Yumeng Yao *et al.*'s^[17] study done in Wuhan where the mean age was 63 ± 13.5 . In our study, diabetes (34.1%) was the most common comorbidity followed by hypertension (26.4%) which is vice versa to Yumeng Yao *et al.*'s^[17] study.

In our study, the mild cases were 65 (36.9%), moderate 91 (51.7%) and those in severe were 20 (11.4%) which is similar to the Yumeng Yao *et al.* study.^[17] The D-dimer elevation was found in 143 (81.8%) in our study which was higher compared to the above study where it was 74.6% and Chen N *et al.*^[6] and Wu J's studies. This may be due to higher referrals of critically ill patients referred to our hospitals from other periphery centres.

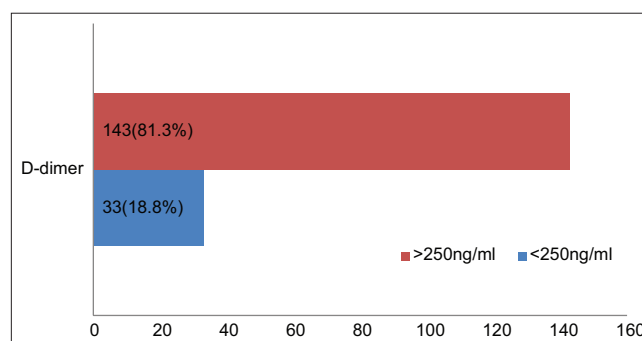


Figure 1: Prevalence of elevation of D-dimer in the study participants

Table 1: Baseline characteristics of the study participants (n=176)

Characteristics	D-Dimer (<250 ng)	D-Dimer (>250 ng)	P
Age			
<60 years	28 (84.8)	95 (66.4)	0.03
>60 Years	5 (15.2)	48 (33.6)	
Sex			
Male	26 (78.8)	106 (76.1%)	0.377
Female	7 (21.2%)	37 (25%)	
Clinical features			
Fever	21 (63.6)	90 (62.9)	0.554
Yes	12 (36.4)	53 (37.1)	
No			
Cough			
Yes	21 (63.6)	84 (58.7)	0.378
No	12 (36.4)	59 (41.3)	
Throat pain			
Yes	1 (3)	6 (4.2)	0.610
No	32 (97)	137 (95.8)	
Body pain			
Yes	10 (30.3)	56 (39.2)	0.229
No	23 (69.7)	87 (60.8)	
Breathlessness			
Yes	1 (3)	14 (9.8)	0.036
No	32 (97)	129 (90.2)	
Headache			
Yes	4 (12.1)	19 (13.3)	0.560
No	29 (87.9)	24 (86.7)	
Loose stools			
Yes	4 (3)	14 (9.8)	0.185
No	32 (97)	129 (90.2)	
Loss of taste			
Yes	3 (9.1)	10 (7)	0.454
No	30 (90.9)	133 (93)	
Loss of smell			
Yes	1 (3)	5 (3.5)	0.687
No	32 (97)	138 (96.5)	
Loss of appetite			
Yes	1 (3)	1 (0.7)	0.813
No	32 (97)	142 (99.3)	
Comorbidity Diabetes			
Yes	8 (24.2)	52 (36.4)	0.130
No	25 (75.8)	91 (63.6)	
Hypertension			
Yes	8 (24.2)	39 (27.3)	0.454
No	25 (75.8)	104 (72.7)	
Asthma			
Yes	1 (3)	5 (3.5)	0.687
No	32 (97)	138 (96.5)	
Hypothyroidism			
Yes	1 (3)	6 (4.2)	0.282
No	32 (97)	137 (95.8)	
Cardiovascular			
Yes	1 (3)	7 (4.9)	0.227
No	32 (97)	136 (95.1)	
Presentation at the time of admission Saturation			
<90	4 (12.5)	50 (43.9)	0.007
>90	29 (87.5)	93 (56.1)	

In our study, the D-dimer level is increased in COVID-19 patients and in disease progression. Similar results are also seen in Bilian

Yu *et al.*'s^[18] study in China and also in Hui DS *et al.*^[19] and Snijders D *et al.*'s^[20] studies.

The mortality rate of our study was 4.6% which was lesser than Zhou's *et al.*^[8] and Yumerang Yao's studies. In the present study, a significant correlation was noted between the D-dimer level and disease severity. We know that diffuse alveolar damage with cellular fibromyxoid exudates; hyaline membrane formation, pulmonary oedema and interstitial mononuclear inflammatory infiltrates were noted in the pathology of COVID-19 patients. In one of the recent studies done by Paranjpe I *et al.*,^[21] they stated that anticoagulant therapy for the elevated D-dimer level has reduced the risk of mortality mainly among the patients who required mechanical ventilation.

It was used as a marker for hypercoagulability in the past. In severe COVID-19 disease patients, the D-dimer level is markedly elevated and it is shown in many studies.^[22] Among the comorbidities, diabetes has been noted to be associated with the severity of the disease. In ICU, patients with diabetes were two times more than in the wards.^[23-25]

COVID-19 is a recent disease which is evolving day by day. The more we get to know about the disease the more we change the treatment. At present, we do not have very clear guidelines regarding the initiation, dosing and duration of anticoagulants in the COVID-19 patients. More studies like this will help in understanding the thromboembolic complications of COVID-19 and help in framing clear guidelines for anticoagulation in patients with COVID that can be easily and confidently used by primary care physicians.

Conclusion

To summarise, this study was done to find the prevalence of D-dimer elevation among the COVID-19 patients and its impact on the outcome and to find out the association between the D-dimer elevation and severity of the disease. A hospital-based cross-sectional study was conducted in a tertiary care hospital in Salem in the Internal Medicine Department. All COVID-19 patients of both sexes and all age groups were included in the study. In this study, the mean age of the patients was found to be 54.89 ± 14.4 with a minimum age of 14 and maximum age of 87. The prevalence of the D-dimer elevation was found to be 143 (81.8%). D-Dimer was found to be significant with severe COVID infection.

Patients suffering from COVID-19 markedly have a high level of D-dimer. In those with critically ill patients, the elevation was found to be significant. So, D-dimer can be used as a prognostic marker for inpatient treatment in hospitals. And for those elevated levels anticoagulant therapy is needed.

Limitation

Our study was done in a single centre and our mortality rate was lesser compared to several studies done in other countries. There

Table 2: Association between the D-dimer level and the severity of the disease

Severity of the disease	D-Dimer (<250 ng)	D-Dimer (>250 ng)	Mean±SD	P
Mild	16 (48.5)	49 (34)	2.200±0.81	0.034
Moderate	14 (42.4)	77 (53)	2.439±0.71	
Severe	3 (9.1)	17 (13)	2.650±0.67	

Table 3: Correlation between the D-dimer level and the severity of the disease

Spearman's rho	Severity of the disease	D-Dimer levels
Severity of the disease		
Correlation coefficient	1.000	0.720
Sig (two-tailed)	176	0.003
n		176
D-Dimer levels		
Correlation coefficient	720	0.000
Sig (two-tailed)	0.003	176
n	176	

Correlation is significant at the 0.01 level.

is no systematic approach to rule out pulmonary embolism or deep vein thrombosis for those with elevated D-dimer levels. Later, we generally do not take the D-dimer value for monitoring the patients suffering from COVID-19.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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