Original Research Article

Serum D-Dimer Level and Chest CT Scoring in SARS-Cov-2 Virus Patients - It's Relevance in Prognostication and Severity of the Disease

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Abstract

Background: COVID -19 has wide range of presentation, from asymptomatic infection to severe viral pneumonia and death. D-dimer >1μg/ml is one of the risk factors for mortality. CT chest plays an important role in early detection and monitoring of disease. *Objectives:* 1. To compare D-dimer value and CT chest findings in Covid-19 patients. 2. To study platelet count, PT, aPTT and CRP in Covid-19 patients. *Methodology:* RT-PCR confirmed Covid- 19 patients admitted in hospital investigated with D-dimer and CT chest were included in the study. Case details retrieved from medical records. Venous blood collected and plasma processed in coagulation analyser for PT, aPTT, INR and D-dimer. Platelet count was performed using auto analyser. CT findings were retrieved from radiology software (PACS). Statistical tests used were mean, percentage and Fisher's exact test (SPSS Version 20). *Results:* During study period of January-June 2021, 38 patients were included. Mean age was 51.1±15.6 years and M:F ratio 2.8:1. 65.8% patients had comorbidities (25/38). D-dimer elevated in 60.5% (23/38) patients. CT showed 10.53%, 28.94%, 60.53% of patients had affected lungs of <15%, 15%-49% and ≥50% of the total area and showed significant association with D- dimer (P=0.018). 17.4% (4/23) patients with elevated D-dimer did not survive. 15.8% (6/38) patients had low platelet, 23.7% (9/38) had abnormal PT, 70.3% had abnormal aPTT and 89.5% (34/38) had elevated CRP. There was no significant correlation between platelet, PT, aPTT, CRP and D-dimer. *Conclusion:* D-Dimer is elevated in COVID -19 patients and shows significant association with lung involvement and can be used as prognostic marker.
Keywords: D-dimer, Covid-19, CT chest.

INTRODUCTION

In December 2019 in Wuhan (Hubei, China) the first case of Corona Virus Disease-2019 (COVID -19) was reported [1, 2]. The number of cases has increased rapidly in China and progressed worldwide. On March 12th the WHO declared COVID-19 as a pandemic disease due to rapidly increase in number of cases [2].

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) typically spreads via respiratory droplets and following close contact with patients with COVID-19 infection causes COVID -19 [3]. The disease has a wide range of presentation ranging from asymptomatic infection, mild respiratory disease to even severe viral pneumonia that can be complicated by respiratory failure and death [4]. Therefore, for clinical diagnosis and treatment of COVID 19 early identification of the disease and its severity is very important to circumvent its grave complications [3]. For disease confirmation, nasopharyngeal swab RT-PCR test has been the gold standard [5].

D-dimer is a marker for inflammation in addition to hypercoagulable state [6].

The severity of inflammation can be reflected by extent of CT chest involvement as a visual parameter [6]. In adult patients with covid 19 D- dimer value of

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more than 1 µg/ml is one of the risk factors for mortality [7]. A positive correlation between elevated D- dimer levels and mortality in patient with COVID-19 has been recently reported by Zhou *et al.,* [4].

For the quick assessment of pulmonary involvement in COVID-19 patients, Yang and his colleagues developed a scoring system that depends on the degree of opacification of lungs on CT chest. It was a modern adaptation of the scoring system used in SARS – Cov -1 patient [8]. For early detection and also for managing and monitoring the course of the disease, non-contrast high-resolution CT chest imaging plays an important role [5].

Present study was done with an aim to analyse the association between the D -dimer value and CT chest findings in COVID 19 positive patients. Also to see its relationship with parameters: Prothrombin time (PT), activated partial thromboplastin time (aPTT), platelet count and C – reactive protein (CRP).

METHODOLOGY
The study was conducted at a tertiary care hospital in North Karnataka. All hospitalized RT – PCR confirmed COVID 19 positive patients with D dimer and CT scan performed during the study period from 1st Jan- 31st June 2021 were enrolled for the study. Patient detected to be COVID-19 positive by Rapid Antigen Test, without RT-PCR was excluded.

The demographic characteristics, detailed medical history, laboratory parameters, and radiological findings of COVID-19 positive patients confirmed by RT-PCR were retrieved from the medical records department and electronic medical records.

Blood samples were drawn by peripheral venipuncture under aseptic precautions from all RT-PCR confirmed COVID-19 positive patients, and collected in a plain vacutainer tube, properly labeled and the plasma obtained after centrifugation were processed in the automated coagulation analyser (Erba ECL 760) for various hematological parameters which are : Prothrombin time (PT), activated partial thromboplastin time (aPTT) and D-dimer. The values of these parameters were noted down. Platelet counts were obtained from automated haematological analyser (Sysmex XN 1000).

CT Chest was given scores, lungs were subdivided into 20 regions, which were then subjectively evaluated and scored from 0 to 2; where 0 represents no involvement of lungs in CT chest , while 1 and 2 represent less than and more than 50% involvement of lungs in CT chest, respectively. The summation of individual scores of 20 regions gave total CT –Severity score (CT-SS score), which ranged from 0 to 40 points.

Statistical analysis was performed using statistical package of social sciences (SPSS) Version 20. Descriptive statistics like mean, median, percentage, Fishers Exact test, Mann- Whitney U test, Spearman's correlation coefficient and Pearson correlation coefficient were calculated. The p value of <0.05 was considered significant.

RESULTS
Total of 38 inpatients between January 1st and June 31 2021 were included in the study.

The mean age of the 38 patients was 51.1 ± 15.6 years, ranging from 22-81years with M:F ratio of 2.8:1. The average time from onset of symptoms to admission was 6.04 ± 4.65 days. Comorbidities were seen in 65.7% (25/38) of the patients, with hypertension and diabetes being the most common. Ten patients had both hypertension and diabetes mellitus. Average length of hospital stay was 19.05 ± 12.5 days.

D-dimer elevation (≥ 0.50 mg/L) was seen in 60.5% (23/38) of the patients. Low platelet count (<1.5 lakh/mm^3) was seen in 15.8% (6/38) of patients, five patients with low platelets had elevated D- dimer. 23.7% (9/38) of patients had elevated PT value and six of these patients had elevated D-dimer. Elevated aPTT value was seen in 70.3% (26/37) of patients, 18 patients of these had elevated D-dimer. There was no significant correlation between platelet, PT, aPTT with D-dimer value. CRP value was elevated in 34/38 (89.5%) of patients out of which 21 patients had elevated D – dimer value. CRP median range was elevated in patients with elevated D – dimer, however did not show significance. The Platelet counts, aPTT, PT, CRP were compared with normal and elevated D – dimer levels (Table No 1).

Table No 1: Platelet count, aPTT, PT, CRP median range in patients with normal and elevated D – dimer levels

	Platelet count (Lakh/mm3) Median(IQ range)	aPTT (s) Median(IQ range)	PT (s) Median(IQ range)	CRP (mg/L) Median(IQ range)
NORMAL D- DIMER (n=15)	1.95 (1.64 - 2.76)	42.8 (35.4–48.1)	14.4 (13.6 –15.2)	35.92(6.26 –64.82)
ELEVATED D- DIMER (n=23)	2.05(1.37–2.99)	46.7 (41.88–53.5)	15.3 (13.6–16.7)	48.71(12.1– 97. 02)
P value	**0.906**	**0.637**	**0.152**	**0.172**

The predominant radiological changes seen on CT chest were ground glass opacity (92%) and interlobular septal thickening (92%) followed by crazy paving pattern (26.3%), consolidation (23.7%) and pleural effusion (5.2%). These findings were more common with patients with elevated D- dimer. However did not show statistical significance (Table No 2).

Table No 2: Radiological findings in Covid 19 patients with normal and elevated D – dimer levels

Radiological findings	No of cases (38)	Normal d dimer (n=15)	Elevated d dimer (n= 23)	P value
Ground glass opacity	35(92%)	12 (80 %)	23(100%)	p= 0.0539
Interlobular septal thickening	35(92%)	12 (80%)	23(100%)	p=0.0539
Crazy paving pattern	10(26.3%)	2(13.3%)	8(34.8%)	p=0.2625
Consolidation	9 (23.7%)	3(20%)	6(26.08%)	p= 1.000
Pleural effusion	2(5.2%)	0(0%)	2(8.7%)	p=0.5092

Majority of patients (23/38, 60.53%) had ≥50% of lung affected followed by 28.94% (11/38) patients with 15- 49% involvement and 10.53% (4/38) patients with <15% involvement. Area of affected lung on CT showed significant association with D-dimer level (P =0.018). D – Dimer levels significantly increased with chest CT staging (Spearman correlation coefficient = 0.362, p= 0.026) (Table No 3, Fig No 1).

Table No 3: Area of affected lung on CT (Chest CT Stage) with normal and elevated D – dimer levels

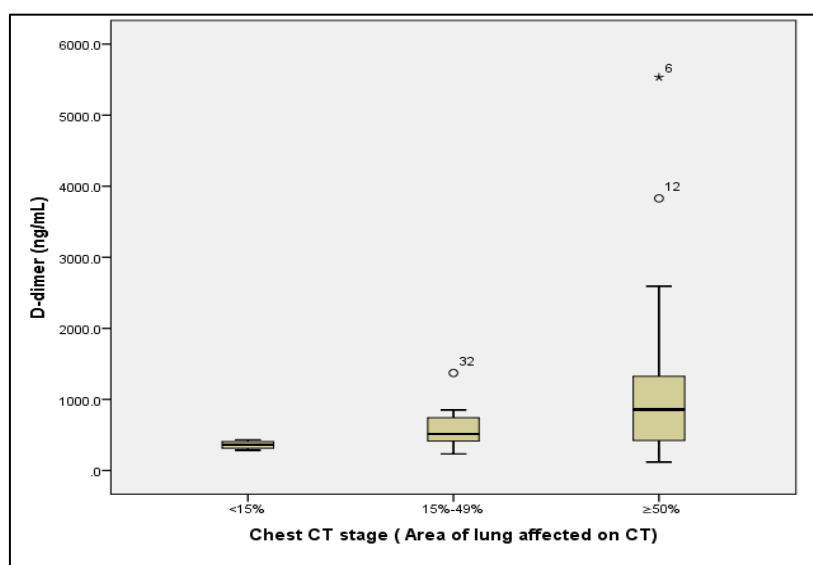| Area of affected lung on CT (Chest CT Stage)	All patients (n = 38)	Normal D- dimer (n =15)	Elevated D- dimer (n=23)	P value
<15%	4 (10.53 %)	4 (26.7%)	0	0.018
15%-49%	11 (28.94%)	5 (33.3%)	6 (26.1%)	Fisher
≥50%	23 (60.53%)	6 (40%)	17 (73.9%)	Extract test

Fig. No 1: Graph showing distribution of D dimer values with Chest CT stage (Area of lung affected on CT)

Among total cases majority (13/38, 34.2%) had CT-SS between 19-30 (Table No 4). The D- dimer values showed weak positive correlation with CT Severity Scores (Pearson correlation coefficient = 0.344, p = 0.035) (Fig No 2).

Table No 4: CT Severity score between Covid 19 patients with normal and elevated D– dimer levels

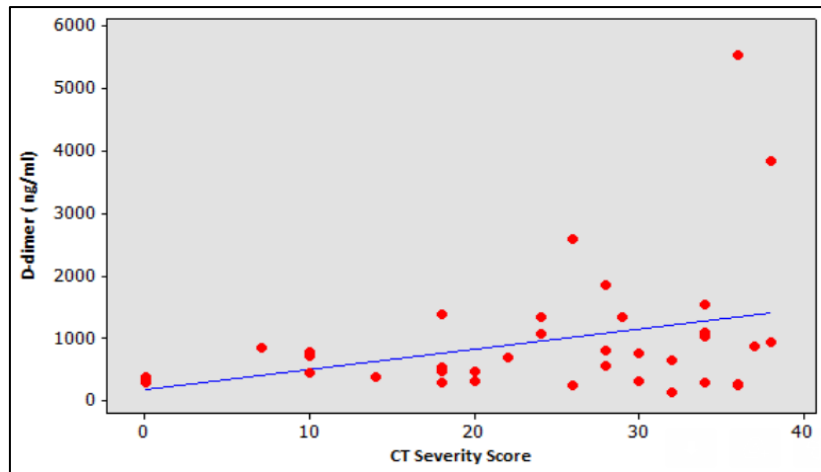| CT – Score	All patients (n = 38)	Normal D- dimer (n =15)	Elevated D- dimer (n=23)
No abnormalities (n=3)	3 (7.9%)	3(20%)	0
1-18 (n= 10)	10(26.3%)	4 (26.67%)	6 (26.1%)
19- 30 (n= 13)	13(34.2%)	4 (26.67%)	9 (39.1%)
>30 (n= 12)	12 (31.6%)	4 (26.67%)	8 (34.8%)

Fig. No 2: Graph showing distribution of D -dimer values with CT Severity Scores.

D-dimer values were significantly higher in non survivors compared to survivors (p =0.010). Non survivors median D-dimer was 2426 (951.75 – 5107.3) ng/mL and survivors median D-dimer was 533.9 (299.5 – 910.75) ng/mL (Fig No 3). Four patients succumbed to disease and all these cases had elevated D dimer levels.
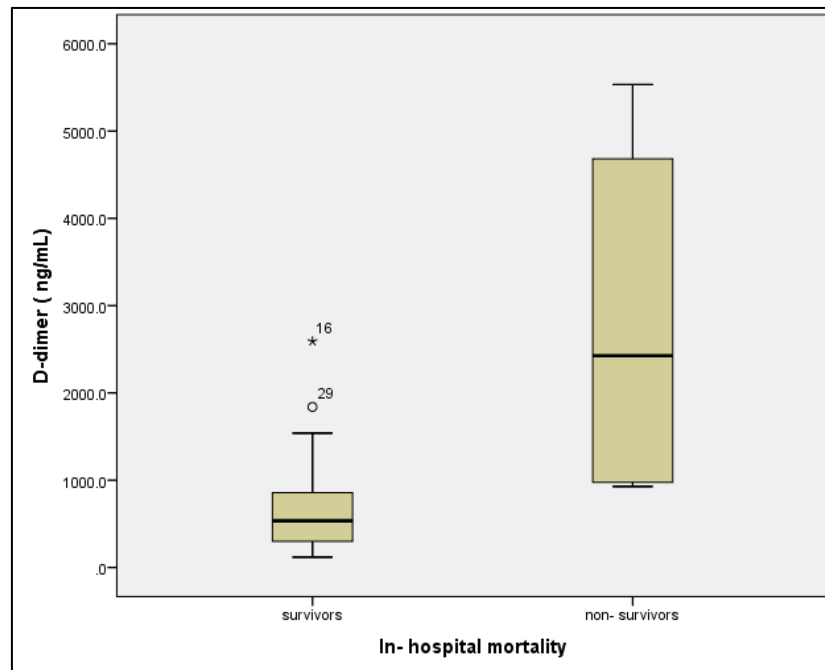

Fig. No 3: Graph showing distribution of D- dimer levels among patients who survived and died during hospitalization

DISCUSSION

In the present study mean age was 51.1±15.6 years, ranging from 22 – 81 years. Maximum number of cases was seen in 7th decade.

Comorbidities were seen in 65.7% (25/38) of the patients, with diabetes (16/38, 42%) and hypertension (17/38, 44.7%) being the most common and the same was observed in study done by Yao Y *et al.,* (58.06 %) (hypertension- 31.5%, diabetes-17.7%) and Wang L *et al.,* (34.8%) (Hypertension- 20.9%, diabetes -4.7%).

Elevated D-dimer level were seen in 60.5% (23/38) patients, similar finding was seen in study done by Yao Y *et al.,* (74.6%). D – Dimer elevation signifies hyperfibrinolysis state and increased inflammatory burden induced in COVID 19 [7]. Patients diagnosed with COVID-19 showed elevated D-dimer levels on day one of admission and was associated with increased in-hospital mortality [7].

70.3 % of patients had elevated aPTT value with median (IQ range) of 46.7 (41.88–53.5) s in patients with elevated D – dimer value. In study done by Yao *et al.,* median (IQ range) (27.3 (25.45-29.85) s)

of aPTT in patients with elevated D - dimer was increased. However it was less compared to present study. CRP was elevated in 34/38 (89.5%) of patients with median (IQ range) of 48.71(12.1– 97. 02) mg/L s in patients with elevated D – dimer value. In study done by Yao *et al.,* and Wang L *et al.,* median (IQ range) (48.4 (10.98-92.25) mg/L and 35.8 (5-95.6) mg/L, respectively) of CRP in patients with elevated D - dimer was elevated similar to present study.

The predominant radiological change seen was ground glass opacity (92%), same was observed by Yao *et al.,* (54%) and Wang L *et al.,* (98.7%). 73.9% of patients with elevated D –dimer showed ≥50% of lung involvement. In patients with normal D –dimer value 40% showed ≥50% of lung involvement. Area of affected lung on CT showed significant association with D-dimer level (P =0.018), similar finding was seen in study by Yao *et al.,*

The D- dimer values showed weak positive correlation with chest CT Severity Score (Pearson correlation coefficient = 0.344, p = 0.035). Wang L *et al.,* observed a significant association between D dimer and chest CT Severity Score.

Raised D- dimer was also associated with In-hospital mortality, suggesting that it can be used as a single biomarker for clinical outcomes in patients with COVID -19 [7, 9]. In Zhou *et al.,* study, mortality rate was higher compared to the present study (28.3% vs 10.5 %). The coagulation cascade dysregulation results in worsening of lung pathology [7, 10]. Study done by paranjpe *et al.,* found that treatment with anticoagulant was associated with a reduced risk of mortality [7, 11].

CONCLUSION

D-dimer is commonly elevated in Covid -19 patients and shows significant association with Lung involvement and can be used as a prognostic marker. D-Dimer is a cost effective, easily available test with rapid turnover time.

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Conflicting Interest (if present, give more details): Nil.

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