Original Article

Correlation between D-dimer and HRCT in Covid-19

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Abstract:

Background: To retrospectively determine the correlation between CT severity score & D-dimer. **Methodology:** This is retrospective original research of 227 patients (IPD & OPD) during April 1 to May 31, 2021 for Covid-19. Patients CT severity scores, HRCT Thorax findings, D-dimer, Platelet count and Demographic variables were recorded. The correlation between CT severity score & D-dimer were determined. **Results:** Between the mentioned dates, 227 patients are taken into study which includes 146 Males & 81 Females. Mean of CT severity score was 6.7, D-dimer was 0.46mg/l. Higher CT score is seen in males (mean -7.1) as compare to females (mean -6.12). D-dimer are seen higher in males (mean =0.52mg/l) as compare to females (median=0.37mg/l). The study of 227 patients has shown positive correlation between CT score & D-dimer (r=0.38, p<0.05). Males showed relatively stronger positive correlation (r=0.4, p<0.05) than females (r=0.3, p<0.05). Patients with age less than equal to 45 has shown relatively stronger positive correlation between CT score & D-dimer (r=0.4, p<0.05) than patients with age more than 45 (r=0.35, p<0.05). **Conclusion:** Pulmonary lesion induced by SARS-CoV-2 infection was associated with raised inflammatory response, impairment in exchange of gases, and end organ damage. In study, we can conclude that lung lesion may exert important role in COVID-19 pathogenesis & clinical presentation.

Keywords: Covid-19, CT severity score, D-dimer, HRCT Thorax.

Introduction:

Since the outbreak of coronavirus disease 2019 worldwide, studies from different countries have shown elevated levels of D-dimer in patients with SARS-COV-2 (Severe acute respiratory system-Covid -2).[1,2] In further studies it is demonstrated that a higher level of D-dimer was associated with in-patient mortality.[3,4] The suggested mechanism behind that is hypercoagulable state, which could be reflected by an elevated level of D-dimer, might lead to thrombosis, resulting in poor outcomes. However, the coagulation results from local and systemic inflammation caused by the coronavirus. Also, D-dimer is known as biomarker of inflammation.[5] Therefore, D- dimer level may be associated with the severity of inflammation rather than directly related to hypercoagulable state in patients with SARS-COV-2 pneumonia.

Chest computed tomography (CT) involvement extend is the most visual parameter, which could reflect the severity of inflammation.[6]

Methodology:

- Study design and participants: Patients were enrolled randomly from all Inpatient and Outpatient departments in a tertiary care center from April 1 to May 31, 2021 for Covid-19. All patients were diagnosed with COVID-19 based on positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) quantitative RT-PCR using throat swab samples.

- **Data collection:** Demographic, HRCT Thorax, Laboratory data were collected from electronic data record and evaluated by two researchers. D-dimer test was done on MISPA NANO fully automatic machine. HRCT scan was done on 16 slice GE Light speed CT machine. HRCT (High resolution computed tomography) thorax scans were done at 140 kV and 9mAs. Scans were evaluated at WL: 450, WW: 1500.

- **Definition:** CT severity score is the percentage of lung involvement by Covid-19. Depending upon the number of lobes and percentage of each lobe involved with GGOs (Ground glass opacities) on HRCT, a CT Severity score is proposed as (for percentage of each lobe involved as):

   1. < 5% involvement
   2. 5%-25% involvement
   3. 26%-49% involvement
   4. 50%-75% involvement
   5. > 75% involvement.

Sum of all lobar score is done and total severity score is calculated. Range is 0 to 25. Severity was further categorized as

   Mild= <9

   Moderate=9 to 15

   Severe = >15

D-dimer level are obtained from standard laboratory procedures, Normal range = 0-0.50 mg/l.

- **Statistical Analysis:** Continuous variables were described as means and standard deviations or medians and interquartile ranges (IQR), depending on variable distributions. Continuous variables were analyzed by Student's t test or the Mann-Whitney U test as appropriate. The correlation between the continuous variables was tested by Spearman correlation analysis and t test for significance. In all the analyses, the significance level was defined as $p < 0.05$.

Results:

1) Demographic characteristic:

   Table 1: Demographic Characteristics of Patients

		Total Patients (n=227)
Age	Mean (range)	43.969 (16-82)
	Age (SD)	14.383
	=45 years	123 (33.21)
	>45 years	104(56.58)
Sex	Male –	146 (44.3)
	Female -	81 (43.2)

Total of 227 patients were enrolled in our study which includes, 146 (64.31%) were male and 81 (35.6%) were female. The mean age was 43 ± 14.2 years; with a range of 16-82 year. 123 (54.18%) of participants were ≤ 45 years and 104 (45.81%) were > 46 years of age.

2) HRCT Thorax scan results:

HRCT Thorax scans were evaluated by 2 experienced radiologists. CT Severity score was calculated for each patient. (Range= 0 -25). Mean score was 6.7 (± 5.63). Based on the CT severity score, 96 patients were in mild (<9), 59 were in Moderate (9-15) and 19 were in severe (>15) category.53 Patients showed no signs of lung involvement on HRCT.

3) D-dimer level results

Normal range of D-dimer is 0-0.50mg/L. Total 182 patients had D-dimer within normal limits. Median was 0.28. Interquartile range (IQR) was 0.15-0.46.SD was 0.73. (Table 2)

   Table 2: Characteristics of CT severity score & D-dimer

Parameters		CT Severity Score	D-dimer (mg/L)
Total- n (227)	Mean	6.7	0.46
	Median	6	0.28
	IQR	2-11	0.15-0.46
Male (n=146)	Mean	7.15	0.52
	Median	7	0.26
	IQR	2-12	0.13-0.48
Female (n=81)	Mean	6.12	0.37
	Median	5	0.29
	IQR	0-10	0.17-0.40

4) Correlation analysis:

Correlation between CT Score and D-dimer shows positive correlation (r=0.38) (p-value < 0.05). Results negative correlation in severe CT severity score.

   Table 3: Correlation between D-dimer and CT severity score

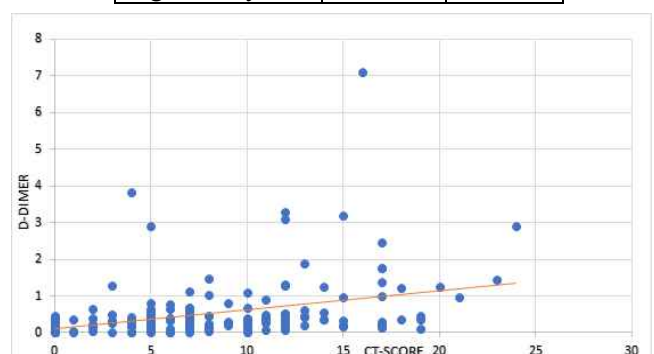| Parameters	r	*p*-value
Total (n-227)	0.38767	<0.05
Male (n-146)	0.41828	<0.05
Female (n-81)	0.31482	<0.05
Age = 45 years	0.43321	<0.05
Age > 45 years	0.34608	<0.05

Image 1: (CT scan axial section, Lung window) =43-year-old male with D-dimer level 0.27 mg/l showing minimal involvement (CT severity score 5). Image 2: (CT scan axial section, Lung window) =56-year-old male with D-dimer level 3.12 mg/l with extensive lung involvement (CT severity score 15).

Discussion:

In our study population median D-dimer level is 0.28mg/l, this value is lower than reported by Zhou et al.(0.8mg/l)[2] in Wuhan and one reported by Cummings et al.(1.6mg/l)[4], whose study population were all critically ill patient.

As Baseline level of the D-dimer varies greatly with patient to patient, dynamic evaluation of D-dimer level may be of higher significance.[7]

Zhang et al showed that the D-dimer value greater than 2 μg/ml at the admission was independent risk factor for the mortality and can identify patient with poor prognosis at early stage.[3] Huang and colleagues showed D-dimer levels on admission were higher in patients needing critical care support than those who did not require it (median, 0.5 μg/mL).[8]

Two factors have been attributed the elevated D-dimer level. Firstly, virus infections are usually accompanied by an aggressive pro-inflammatory response and insufficient control of an anti-inflammatory response. It might induce the dysfunction of endothelial cells, resulting in excess thrombin generation.[9,10]

Second, the hypoxia found in severe Covid-19 can stimulate thrombosis through not only increasing blood viscosity, but also a hypoxia-inducible transcription factor-dependent signaling pathway.[9]

In our study we found positive correlation between D-dimer and CT severity score (Image 1 & 2). Recently it's proved that CT severity score could be as assessing tool for assessing severity of SARS-COV-2 pneumonia.[11,12]

Previously Wang et al[13] have shown that D-dimer level may be associated with severity of inflammation prior to coagulation, on the basis of time point match between D-dimer level and CT-scan time. Inflammation results in severe lung injury which aggravates coagulation and leads to poor outcome and even death.

Conclusion:

Pulmonary lesion induced by SARS-CoV-2 infection was associated with raised inflammatory response, impairment in exchange of gases, and end organ damage. In study, we can conclude that lung lesion may exert important role in COVID-19 pathogenesis & clinical presentation. According to our findings it can be concluded that D-dimer can be used as a bio marker for COVID pneumonia by paralleling with inflammation which can be seen in chest CT score.

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