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A Study of D-Dimer Levels with and without Co-Morbidities as a Prognostic Marker for Disease Severity in COVID-19 Patients

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Abstract: ***Background: A novel coronavirus COVID-19 pandemic called SARS-CoV-2 is defining global health crisis of our time and has resulted in the outbreak of respiratory illness. Coagulation system is active in critically ill patients and D-dimer levels co-relate with activation of pro-inflammatory cytokine cascade. As COVID-19 is caused by severe respiratory syndrome coronavirus 2, increased D-dimer were reported in corona like infections due to activation of Coagulation by respiratory viruses. Elevated D-dimer following anticoagulation for thrombotic event indicates increased risk of recurrent thrombosis. Objectives: To assess the levels of D-Dimer in COVID-19 patients with and without co-morbidities. Methodology: This is an observational study done for about 40 confirmed cases of COVID-19 in the month of August 2020to September 2020. D-dimer values were determined in an age groups 30-60years including male and female patients with and without co-morbidities like Diabetes, Hypertension. Results: In my study population of 40 patients – 50%i. e., 20 patients were with co-morbidities and 50% i. e., 20 patients were without co-morbidities. Among patients with co-morbidities, D-dimer levels observed were <500 ng/ml in about 5%, 500-1000 ng/ml in 55%, and >1000 ng/ml in 40% when compared with that of patients without co-morbidities, D-dimer levels observed were <500 ng/ml in 90%, 500-1000 ng/ml in 10% and >1000 ng/ml in 0%. p value is estimated as (p=0.007) which is statistically significant. Conclusion: We have come to conclusion that D-dimer levels were markedly elevated in COVID-19 patients with co-morbidities when compared with that of COVID-19 patients without co-morbidities.***

Keywords: COVID-19, SARS-COV-2, Severe Respiratory Syndrome Coronavirus-2, Comorbidities, Diabetes, Hypertension, Cytokine Cascade

1. Introduction

Coronavirus disease (COVID-19) is caused by severe acute respiratory syndrome coronavirus-2 (SARS-COV-2) (1). A novel coronavirus COVID-19 pandemic called SARS-CoV-2 is defining global health crisis of our time and has resulted in the outbreak of respiratory illness. Inflammatory markers are often elevated in patients with COVID-19 notably C-reactive protein (CRP), D-dimer, procalcitonin (PCT), Lactate dehydrogenase (LDH), Erythrocyte Sedimentation rate (ESR), and ferritin. Multiple prior studies have found correlations between various biomarkers and clinical outcomes in patients with COVID-19 (2, 3, 4, 5, 6, 7, 8). However; the clinical utility of these various biomarker for risk stratification and determining prognosis among patients with COVID-19 is evolving and still-ill defined. Various data published about D-dimer around the world, studies about severity of COVID-19 and relation of D-dimer to severity are scanty in India. My study emphasizes on role of D-dimer in assessing severity of COVID-19 with and without comorbidities like diabetes and hypertension and pointing towards prognosis of disease. D-dimer is a byproduct of fibrin degradation. D-dimer constitutes t o adjacent fibrin "D"domain (ends) that are crosslinked and released as intact fragment; hence name D-dimer. D-dimer is a product of cross link fibrin; it is considered as sensitive biomarker to rule out venous thromboembolism. It is widely recognised as a biomarker for thromboembolism and as a prognostic marker for critical patients. It is sensitive to intravascular thrombus and may markedly elevated in DIC; acute aortic dissection and pulmonary embolism (9). There is variable rise in D-dimer in active malignancy and indicates increase thrombosis risk in active disease. COVID-19 is a primarily respiratory illness that can cause thrombotic disorders. Although it is well documented that COVID-19 is primarily manifestated as a respiratory tract infection, emerging data indicates that it should be regarded as a systemic disease involving multiple systems including respiratory; gastrointestinal; neurological; hematopoietic; and immune systems (10). COVID-19 is primarily respiratory illnesses that cause thrombotic disorders. SARS-COV-2 infection induces profound inflammatory response which triggers Coagulation cascade (11). As COVID-19 is caused by SARS-COV-2; increased D-dimer were reported in corona like infections due to activation of coagulation by respiratory viruses (12). Coagulation system is active in critically ill patients and D-dimer levels co-relate with activation of pro-inflammatory cytokine cascade (13). Activation of coagulation cascade in COVID-19 patients is associated with hypercoagulable state and adverse outcomes including death. Available evidence shows that an activation of thrombosis may be generated in patients with comorbidities like diabetes and hypertension. Evidence shows that hyperglycemia may produce a pro-thrombotic

status, due to imbalance between pro-coagulation, anti-coagulation and fibrinolysis (14, 15, 16). Elevated D-dimer following anticoagulation for thrombotic event indicates increased risk of recurrent thrombosis (12). COVID-19 being a procoagulant state; this D-dimer has been studied as a biomarker for predicting disease severity. Elevation of D-dimer is a potential biomarker for poor prognosis in COVID-19. Because thrombosis affects the prognosis of people with COVID-19, understanding what contributes to increase the risk for a thrombotic event in this disease is highly relevant. Therefore clarifying the possible link between comorbidities like diabetes and hypertension with thrombosis with specific studies might be very useful for better diagnosing disease severity and prognosis and for better management of COVID-19.

2. Materials and Methods

This is an observational study done for about 40 confirmed cases of COVID-19. D-dimer values were determined by CLIA (chemiluminescence immunoassay) using plasma Na, citrate as sample type in an age groups 30-60 years including male and female patients with and without comorbidities like Diabetes and Hypertension.

3. Results and Findings

In my study population of 40 patients-50% (20 patients) were with co-morbidities and 50% (20 patients) without co-morbidities.

Table 1

D-Dimer levels (ng/ml)	Patients with comorbidities	Patients without comorbidities
<500	5%	90%
500-1000	55%	10%
>1000	40%	0%

4. Discussion

In table: 1 Of about 40 patients, D-dimer levels of <500 ng/ml was seen in about 5% in patients wth co-morbidities and about 90% in patients without co-morbidities. D-dimer levels of 500-1000 ng/ml was seen in about 55% in patients with co-morbidities and about 10% seen in patients without co-morbidities, D-dimer levels of >1000 ng/ml was seen in about 40% in patients with co-morbidities and 0% in case of patients without co-morbidities.

Statistical Analysis: Bar Chart

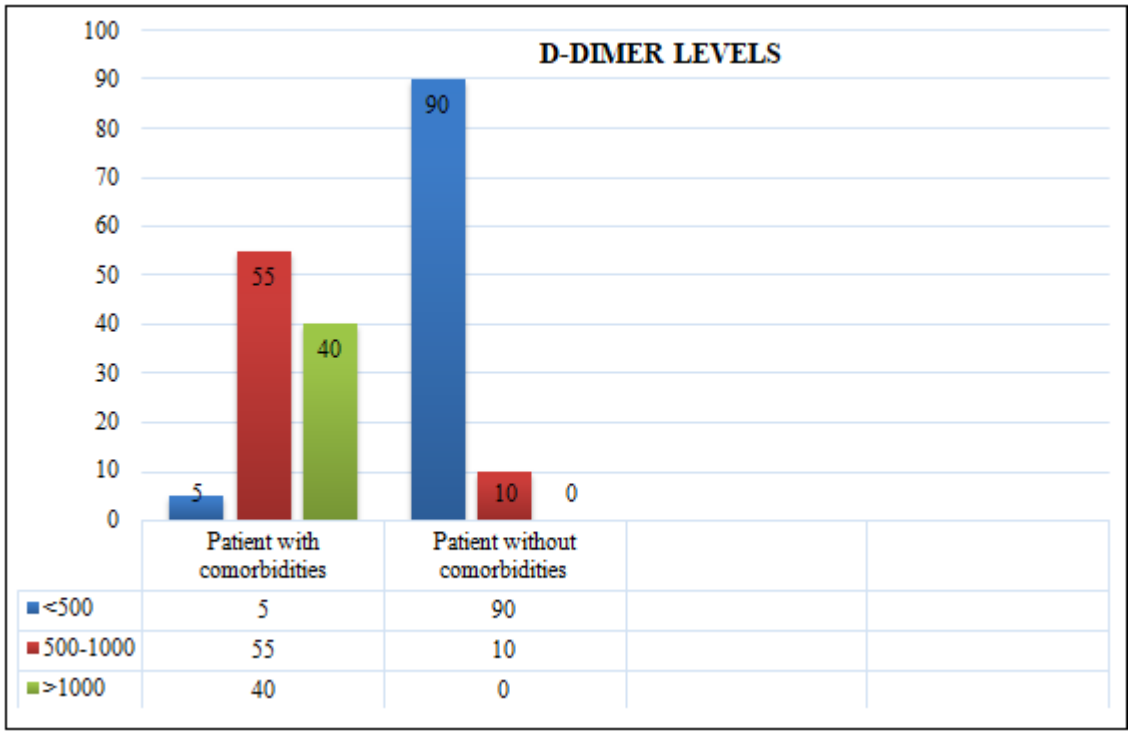

Table 2

	Group-1 COVID-19 With Co-Morbidities	Group-2 COVID-19 Without Co-Morbidities
Mean	1378.5	293.4
SD	1627.1019	96.2663
SEM	363.831	21.5258

In table: 2, Group-1 includes a total of 20 COVID-19 patients with co-morbidities like Diabetes and Hypertension were taken and MEAN, STANDARD DEVIATION, and STANDARD ERROR OF MEAN was estimated to be 1378.5, 1627.1019, and 363.831 respectively and compared with Group-2 with an equal number of 20 COVID-19 patients without co-morbidities were taken and MEAN, STANDARD DEVIATION, and STANDARD ERROR OF MEAN was estimated to be 293.4; 96.2663, 21.5258 respectively.

p value was calculated through unpaired t-test and was observed as p=0.007 which is statistically significant.

p-value	0.007

5. Conclusion

We have come to conclusion that patients with co-morbidities tend to have higher levels of D-dimer and associated with bad prognosis when compared to patients without co-morbidities tend to have low levels of D-dimer and good prognosis.

6. Limitations

1) Small sample size
2) Inflammatory markers such as CRP, FERRITIN, LDH, IL-6have not included in the study

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