

Original Article

# D-dimer Levels to Predict in-Hospital Mortality in ICU Patients with COVID-19

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## ABSTRACT

**Objectives:** Coronavirus disease 2019 (COVID-19) is a recently described infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causing various intensive care unit (ICU) admissions and deaths. Common laboratory values may provide key insights into patients with COVID-19, and may predict the morbidity and outcome. The aim of this study was to evaluate the relation of elevated D-dimer levels on mortality of patients admitted to ICU with COVID-19.

**Material and Methods:** All ICU patients with laboratory confirmed COVID-19 were retrospectively enrolled in Sevenstar Hospital, Nagpur from 27 July, 2020, to 30 October, 2020. D-dimer levels on admission, on Day 3 and Day 5, were collected in all ICU patients and death events were collected. The subjects were divided into two groups discharged and expired. Then, the D-dimer levels between two groups were compared to assess the predictive value of D-dimer level and mortality in hospitals.

**Results:** A total of 101 eligible patients were enrolled in the study. Thirty-one deaths occurred during hospitalisation. Patients who expired had on admission D-dimer levels of  $2729 \pm 3243$  ng/mL while those discharged had D-dimer values of  $973 \pm 1553$  ng/mL ( $P < 0.007$ ). D-dimer of expired patients on Day 3 was  $3206.5 \pm 3338.8$  and of discharged patients was  $828.8 \pm 1268.8$  ( $P = 0.001$ ). D-dimer of expired patients on Day 5 was  $5184.5 \pm 3386.1$  versus discharged patients was  $588.7 \pm 645.5$  ( $P < 0.0001$ ). Number of Days in ICU for patients who expired was  $14.22 \pm 6.7$  while for those who survived  $7.6 \pm 5.9$ .

**Conclusion:** We conclude that SARS-CoV-2 infected patients with increasing trend of D-dimer (from admission to day 5) have worse clinical outcomes (all-cause mortality), and thus, measurement of D-dimers on admission and its trend can guide clinical decision-making.

**Keywords:** Acute respiratory distress syndrome, Coronavirus disease 2019, D-dimer

## INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), Outbreak of pneumonia in Wuhan City, Hubei Province, China, in December 2019, spread rapidly throughout world, areas or territories. SARS-CoV-2 is a novel positive-sense RNA virus with 79% homology with (SARS-CoV) and 50% homology with Middle East respiratory syndrome coronavirus;<sup>[1]</sup> however, it is far more infectious than either.

The D-dimer is a by-product of the blood clotting and breakdown process that can be measured through analysis of a blood sample. D-dimer is released when a blood clot begins to break down.<sup>[2]</sup> Recently, several studies reported that elevated D-dimer levels are positively associated with the severity of COVID-19. A meta-analysis also demonstrated that increased

D-dimer values are related to higher risk of severe SARS-CoV-2 infection.<sup>[3]</sup> To better predict the prognosis of COVID-19, the aim of this study was to investigate the role of changes in D-dimer values.

## MATERIAL AND METHODS

### Study design and participants

This retrospective cohort study initially enrolled 101 patients meeting the inclusion criteria from 27 July, 2020, to 30 October, 2020, from the Sevenstar Hospital, Nagpur. The inclusion criteria were as follows: Adult patients (males and non-pregnant females) with laboratory-confirmed COVID-19 admitted to ICU. D-dimer levels on admission, day 3 and day 5, were collected. Patients were divided into discharged and expired categories. Trend of D-dimer analysed in both categories.

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## Data collection

Demographic, clinical and laboratory data were obtained from medical records using a data collection form.

## Statistical analysis

For Statistical analysis, collected data was entered in MS excel and was further analyzed using SPSS version 24.0 software. Descriptive statistics of variables were obtained using mean, median, mode, standard deviation and range. Unpaired t test was used to determine the level of association between two independent samples.

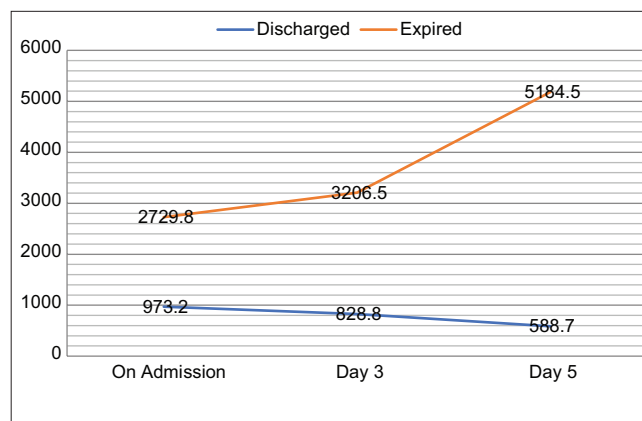
## RESULTS

A total of 101 COVID-19 patients (77 males and 24 females) were included in the study. All patients admitted to ICU were classified into two groups as discharged group  $n = 70$  and expired group,  $n = 31$ . The overall mean age was  $58.83 \pm 15.32$  years. The mean age was – years in the discharged group and – years in the expired group. Approximately two-thirds of the patients had underlying diseases (63%), including hypertension (48%), diabetes (34%), cardiovascular disease (4%), hypothyroidism (9%), cerebrovascular disease (1%), chronic obstructive pulmonary disease (COPD) (2%) and bronchial asthma (2%). There was no history of other diseases in these patients. The mean length of hospital stay was  $13.3 \pm 6.0$  days and mean length of ICU stay was  $9.67 \pm 6.8$ .

Laboratory data within 5 days of admission demonstrated that the mean serum D-dimer levels on admission were  $1512.36 \pm 2341.8$ , on day 3 was  $1542.2 \pm 2363.6$  and on day 5 was  $1967.45 \pm 2851.2$ . Patients who expired had on admission D-dimer levels of  $2729 \pm 3243$  ng/mL while those discharged had D-dimer value of  $973 \pm 1553$  ng/mL ( $P < 0.007$ ). D-dimer of expired patients on Day 3 was  $3206.5 \pm 3338.8$  and of discharged patients was  $828.8 \pm 1268.8$  ( $P = 0.001$ ). D-dimer of expired patients on Day 5 was  $5184.5 \pm 3386.1$  versus discharged patients was  $588.7 \pm 645.5$  ( $P < 0.0001$ ). Number of Days in ICU for patients who expired was  $14.22 \pm 6.7$  while for those who survived  $7.6 \pm 5.9$ . Most of the D-dimer values measured in the death cases showed increasing trend after the patients were admitted [Figure 1].

## DISCUSSION

Here, we report on 101 patients with laboratory-confirmed SARS-CoV-2 infection requiring ICU admission in Sevenstar hospital, Nagpur. Of the 101 patients in this cohort, 31 (30.7%) died. In our study, we demonstrated that in patients diagnosed with COVID-19, D-dimer elevation on admission and increasing trend was associated with both increased disease severity and in-hospital mortality. D-dimers are one of the fragments produced when plasmin cleaves fibrin to break down clots. The assays are routinely used as part of a diagnostic algorithm to exclude the diagnosis



**Figure 1:** Trend D-dimer value in Covid-19 patients admitted in ICU (Discharged vs Expired).

of thrombosis. However, any pathologic or non-pathologic process that increases fibrin production or breakdown also increases plasma D-dimer levels.<sup>[4]</sup> The results showed that mean serum D-dimer levels were approximately 3 times higher in expired group in comparison to discharged group along with it the trend of D-dimer was increasing in expired group and decreasing in discharged group. We also observed that need for ventilatory support was higher in expired group 29 (93.5%) with significant difference ( $P < 0.0001$ ). In our study, D-dimer levels on admission and its increasing trend were not found to be a strong predictor of mortality.

Comorbidities such as diabetes mellitus, hypertension, coronary artery disease, malignancy, COPD and bronchial asthma were seen. The mortality showed a strong association with underlying disease 20 (64%) of 31 patients had comorbidities.

## CONCLUSION

This study demonstrates that D-dimer may be an indicator of disease severity and may contribute to determining the severity of patients with COVID-19. In addition, serial D-dimer measurements may be useful in predicting the prognosis. Additional investigation is needed to further illustrate the mechanisms by which increased D-dimer is synthesised and released in patients infected with SARS-CoV-2.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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