



LEVELS OF D-DIMER IN COVID-19 PATIENTS ADMITTED TO A TERTIARY CARE HOSPITAL: A CASE CONTROL STUDY

Medical Science

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ABSTRACT

Background: The COVID-19 pandemic has changed the clinical scenario of the world on an unprecedented scale affecting billions of people across the globe. Various studies have found that D-Dimer levels may be an indication of disease severity and should be used as a key indicator for disease monitoring.

Objective: To compare the level of D-Dimer in COVID-19 patients with the non-COVID-19 patients at the time of hospitalization.

Materials And Method: This case-control study included all consecutive Real Time Reverse Transcriptase-polymerase chain reaction (RT-PCR) positive cases admitted at Jorhat Medical College and Hospital (JMCH), Jorhat, Assam from 1st September 2020 to 1st December, 2020 between the age group of 11 and 90 years. Consecutive Controls of same age group were selected from the non COVID-19 patients admitted at JMCH during the same period. The D-dimer level was determined using Nephelometry.

Result: A total of 240 RT-PCR positive cases and 48 controls were included in the study. The mean D-Dimer value in the COVID-19 patients was 2.242 $\mu\text{g/mL}$ -1 (FEU) while the mean D-Dimer value in the control patients was 1.43 $\mu\text{g/mL}$ -1 (FEU). There was a significant ($p \leq 0.05$) difference between the D-dimer level of the COVID-19 patients and the control patients.

Conclusion: D-Dimer value may be an important indicator for prognosis and assessment as well as management of COVID-19 patients admitted to hospital. However its higher levels are not significantly related with mortality due to COVID-19.

KEYWORDS

INTRODUCTION:

The disease COVID-19 is caused by a human beta corona virus known as SARS-CoV-2, which first originated in the city of Wuhan, China in December 2019 [1–3]. The disease then turned into pandemic and quickly spread to various countries including India and so far millions of positive cases have been reported worldwide with several deaths recorded in different age groups. The WHO declared COVID-19 as a Public Health Emergency of International Concern on 30th January, 2020 [4]. In India, the first positive case of COVID 19 was reported in Kerala on January 30th, 2020 and in Assam the first positive case of COVID-19 was reported on 31st March, 2020 [4]. However, within a few weeks the number of cases increased exponentially. The severity of Covid-19 increases due to the development of acute respiratory distress syndrome (ARDS) with incidence rate of 15.9-29% and sepsis that subsequently leads to death [1–3]. Moreover, another principal cause of death in COVID-19 patients reported is disseminated intravascular coagulation (DIC) [5] that causes a decrease in fibrinogen and an increase in D-dimer levels. DIC may increase the risk of mortality in COVID-19 patients. In fact, D-dimer, has been reported to provide a predictive value about the mortality of COVID-19 patients in comparison to non-COVID sepsis in addition to the complications of DIC [6,7].

D-dimer is a small protein fragment found in blood, produced during the cleavage of cross-linked fibrin clots and has been routinely used as a sensitive biomarker in the evaluation of venous thromboembolism in clinical practice [8]. It has been reported that elevated D-dimer levels in COVID-19 patients are associated with higher mortality [9–12]. D-dimer levels indicate the underlying hypercoagulable state in COVID-19 patients, and anticoagulant therapy for hospitalized COVID-19 patients with elevated D-dimer level showed a significant decline in risk of mortality [9,13–16]. Therefore, it is important to evaluate the levels of D-dimer in the hospitalized COVID-19 patients in order to recommend strategies for thromboprophylaxis.

In the present study, we hypothesized that the D-dimer level in patients

with COVID-19 disease is elevated compared to non-COVID-19 patients.

METHOD AND MATERIALS:

Study Design And Participants

We conducted a retrospective case control study for 3 months in Jorhat Medical College and Hospital, Assam, India which was one of the COVID-19-designated hospitals during the pandemic, and collected clinical data from patients with diagnosed COVID-19 between September 1, 2020 and December 1, 2020. Study population was divided into two groups of which the Case group consists of symptomatic COVID-19 patients admitted to the hospital and the Control group comprised of the non-COVID-19 patients (age and sex matched, age between 11 and 90) admitted during the same period.

There were 288 total patients and among them 240 were COVID-19 positive and the rest 48 were non-COVID patients. The diagnosis and treatment of COVID-19 was performed as per the guidelines recommended by the Government of India [17]. Laboratory diagnosis of COVID-19 are confirmed by RT-PCR amplification of open reading frame 1ab (ORF1ab) and nucleocapsid protein gene (N gene) fragments from the viral nucleic acid isolated from naso-pharyngeal and pharyngeal swab samples.

Data Collection

Clinical data included demographic information (gender, age, Date of admission, comorbidities), and outcome (survival or death at hospital discharge). Coagulation function test included D-Dimer test of all the patients during the time of hospitalization. The D-Dimer test was performed using Nephelometry and the result is shown in FEU (Fibrinogen Equivalent Unit).

Statistical Analysis

Statistical analysis was performed in R. Differences in the quantitative variables were analyzed using Welch's t-test. Statistically significant value was set as p value < 0.05 was considered

RESULTS:

A total of 240 symptomatic hospitalized patients with equal number of males and females were taken. Median age was calculated to be 49.5 years. The mean length of stay was 17 days for the COVID-19 patients. The mean D-dimer level was 2.242 in COVID-19 patients and 1.43 in control patients. The highest mean D-dimer ($4.008 \mu\text{g mL}^{-1}$) was observed in the age group 71-80 and lowest mean d-dimer ($1.248 \mu\text{g mL}^{-1}$) was observed in the age group of 31-40 in case of COVID-19 patients. There was a significant ($p \leq 0.05$) difference between the D-dimer level of the COVID-19 patients and the control patients. The details of patients and the result of d-dimer test are shown in Figure 1. Among the COVID-19 patients 221 (92.08 %) patients survived at hospital discharge, while 9 (3.75%) died due to COVID-19 and the rest 10 (4.17%) died due to comorbidities. The mean D-dimer level of the deceased patients was $2.87 \mu\text{g mL}^{-1}$.

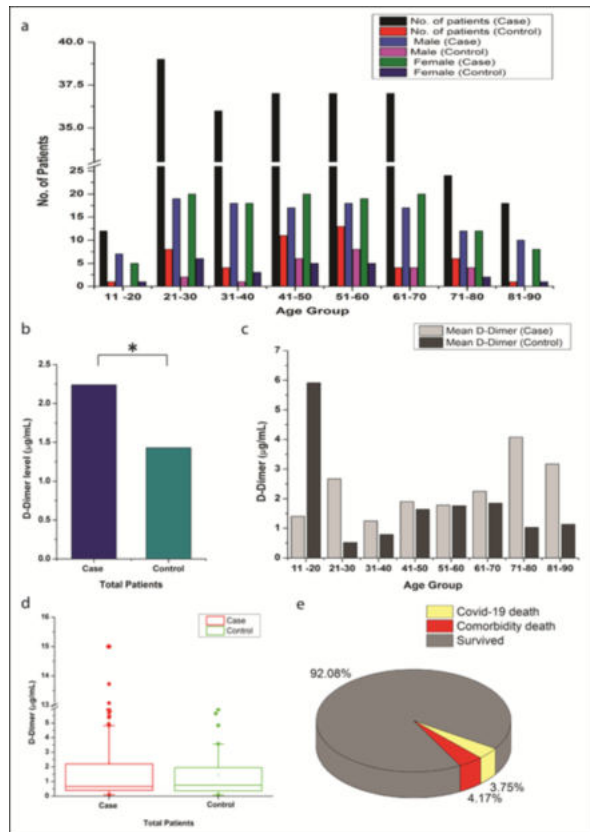


Figure 1: The details of patients and the result of d-dimer test. (a) Details of patients (case and control) included in the present study; (b) Mean D-Dimer of cases vs. control; (c) D-Dimer level in different age group; (d) D-Dimer in levels of all patients; (e) Pie chart showing the deceased and survived patients.

DISCUSSION:

COVID-19 causes severe illness and sustained person-to-person transmission, making it a concerning and serious public health threat. It is important for health professionals to be aware of this disease so that coordinated, timely, and effective actions can be taken to help prevent poor health outcomes [18]. D-Dimer is a specific degradation product that is produced in hydrolysis of fibrin [8]. It may reflect the effects of a particular infection on coagulation. Some studies reported increase in D-Dimer levels in patients with pneumonia, with an indication of the blood hypercoagulable state and the presence of thrombosis [19,20]. D-Dimer of critically ill patients with COVID-19 was found to be significantly increased, with frequent clotting disorders and microthrombotic formation in peripheral blood vessels [21].

In the present study, we assessed the D-Dimer value of the COVID-19 patients after hospitalization and it was found that the D-dimer level was significantly higher in the COVID-19 patients than the patients in the control group. The results of D-Dimer level of the present study corroborates with the results published earlier [22,23]. The high D-Dimer levels seen in some patients of the control group might be due to

associated underlying disease of the patients. In the deceased patients, the D-Dimer value was not significantly higher than those in survival group.

It was postulated that patients with elevated D-Dimer value are likely to have a higher risk of mortality. High D-Dimer is likely to be associated with persistent clotting disorders, microthrombus formation, pulmonary embolism and acute myocardial infarction in long-stay leading to mortality [24]. However, if a large amount of thrombus forms in the body but it is not dissolved, the increase in d-dimer may be mild. Specifically, in the suppressed fibrinolytic type DIC caused by sepsis, the increase in D-Dimer level was relatively mild even in severe cases [25]. However, there was no direct correlation seen between high D-Dimer levels and mortality.

Limitation Of The Study:

The present study is only concerned with the evaluation of D-dimer level in Covid-19 patients. To gain more insight into the clinical picture and the associated prognosis benefit, other biomarkers should be assessed. More detailed and representative data are needed to verify the association of d-dimer level with morbidity. In addition, as JMCH was declared as dedicated COVID-19 hospital during the pandemic period, less number of non COVID-19 patients were admitted during that period. Therefore, the number of patients taken as control was less than that of the patients included in the cases.

CONCLUSION:

D-Dimer value may be an important indicator for prognosis and assessment as well as management of COVID-19 patients admitted to hospital. However its higher levels are not significantly related with mortality due to COVID-19. Further studies are needed to analyze the cause of D-Dimer changes in order to provide potential treatment for the COVID-19 infection and decrease mortality.

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