

A STUDY OF D-DIMER LEVEL & IT'S CORRELATION WITH DEMOGRAPHIC PROFILE OF COVID 19 POSITIVE PATIENTS AT TERTIARY CARE CENTRE, KARWAR

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Abstract

Background: Pro-thrombotic changes are stimulated by Corona Virus as it has an affinity for endothelium and lung structures and this may explain its association with thrombotic events, reduction of pulmonary gas exchange, respiratory distress, and death. D-dimer is a specific marker of the breakdown of a fibrin clot and has been used as a diagnostic and prognostic marker in VTE and other coagulation disorders. So this study was conducted to assess the correlation of the D-Dimer levels with demographic profile and disease severity among COVID-19 patients. **Methods:** This was a Retrospective observational study. Four hundred and twenty (420) covid-19 positive patients were studied at tertiary care hospital KRIMS, Karwar, from July-2021 to December-2021. A citrate sample was collected of all patients who tested positive for the covid-19 disease. Citrated plasma was separated from each sample after proper centrifugation. Hemolysed samples and samples with insufficient quantity were rejected. In such cases, a new sample of the same patient was collected. D dimer test was then carried out from separated citrate plasma. Cut off value for d-dimer is 0.5 [Positive: >0.5 Fibrinogen equivalent units (FEU)/ml]. **Result:** From 420 cases: 290 males and 130 Females affected with peak occurrence in their sixth and seventh decade. A similar distribution pattern was found with a High D-dimer level also. The majority of the patients with elevated d-dimer levels had moderate to severe symptoms and required hospitalization. **Conclusion:** A significant correlation is found between elderly age with elevated d-dimer level, and it was found to be more common in female patients(50.76%). So, d-dimer is one of the most important tests to be carried out in a hospitalized novel corona disease patient for preventing thrombotic events with timely interventions guided by d-dimer level.

Keywords: Covid-19 disease, D-dimer, elder patient, community-acquired pneumonia.

Introduction

Under normal physiological conditions, the hemostatic system maintains the balance between two opposing processes i.e

1) The coagulation process leads to the formation of thrombin, which converts fibre monomer molecules with the release of fibrinopeptides A and B. These fibrin monomer molecules polymerize forming an insoluble fibrin network stabilized by covalent cross-links introduced by the action of the enzyme factor XIIIa, causing the formation of thrombus.

2)The fibrinolytic process leads to the lysis of the crosslinked fibrin by plasmin into a heterogeneous population of fragments released into the blood. These degradation products of cross-linked fibrinogen are called D-Dimer.^{1,2}

D-dimer is a degradation product of cross-linked fibrin resulting from plasmin cleavage. During fibrinolysis plasmin may degrade fibrin monomers, crosslinked fibrin polymers and possibly fibrinogen during systemic fibrinolysis following alpha2 depletion. All these fragments are collectively called fibrin degradation products (FDPs). D-dimer constitutes two adjacent fibrin 'D' domains (ends) that are cross-linked and released as an intact fragment, hence the name D-dimer.^{3,4}

There are two main types of D-dimer assays, each reporting different D-dimer units. The Fibrinogen Equivalent Unit (FEU) reports D-dimer levels based on the molecular weight of fibrinogen (340kDa), whereas the D-Dimer Unit (DDU) reports D-dimer levels based on its molecular weight (195kDa), which is about half that of fibrinogen.⁵ Also, the reporting of the unit is different depending on the manufacturer, resulting in up to 9 different depictions of results, including mg/L, mg/dL, ng/dL, ng/mL, µg/L, µg/mL, µg/dL, mg/mL, and ng/L. In our hospital we used µg/L to measure D-Dimer.⁶

D-dimer is a product of cross-linked fibrin, it is considered a sensitive biomarker to rule out venous thromboembolism. However, D-dimer has low specificity as there are many other conditions with ongoing activation of the haemostatic system in which D-dimer can be elevated such as pregnancy, inflammation, malignancy, trauma, liver disease (decreased clearance), heart disease, sepsis or as a result of haemodialysis, or recent surgery.⁷

Materials and Methods

This was a Retrospective observational study. Information on 420 patients with confirmed COVID-19 reports was retrospectively collected from MRD at tertiary care hospital KRIMS, Karwar during July 2021 to December 2021. The samples for laboratory tests were collected on admission and during the hospital stay. Peripheral venous blood was collected for a routine blood test. Laboratory testing for D Dimer on Citrate sample was performed in hematology and clinical pathology laboratory of hospital. These values had been measured using the MISPA-i3 analyzer machine. Inclusion criteria were defined as patients infected with COVID-19 and had been confirmed by RT-PCR.

MISPA-i3 is an automated Cartridge based specific protein analyzer work on Dual Channel System-Nephelometry and Turbidimetry. For D dimer measurement range of machine is 0.05-15mg/L with biological reference range is 0-0.5mg/L [Fibrinogen equivalent units (FEU) Units].

The information included demographic details; laboratory findings were collected. Patients' details were kept confidential. Patients with a positive result of SARS-CoV-2 by real-time

RT-PCR as per World Health Organization guidelines were considered as confirmed COVID-19 cases. D-dimer values that the laboratory had reported are used for analysis. In case of the repeated testing highest value of D Dimer has been included in data for all the patients included in the study. This study has been approved by institutional ethical committee of KRIMS, Karwar.

Statistical Analysis

All the data analysis was performed using IBM SPSS ver. 20 software. Frequency distribution was performed to obtain the tables. All the data are expressed as numbers and percentages.

Results

Out of a total of 420 cases, the majority were males i.e.290 (69%) compared to females 130(31%). (Table 1)

Table 1: Gender distribution of Covid 19 patients.

S.No	Gender	N	%
1	Male	290	69
2	Female	130	31

Total patients: 420

Table 2: Age distribution of covid 19 patients.

S.No	Age	Male (%)	Female (%)
1	18-30	16 (5.51%)	8 (6.5)
2	31-40	44 (15.17)	16 (12.30)
3	41-50	52 (17.93)	17 (13.07)
4	51-60	64 (22.09)	34 (26.15)
5	61-70	72 (24.82)	40 (30.76)
6	>70	42 (14.48)	15 (11.53)

Table 3. D-dimer level in Males & Females in different Age groups.

S.No	Age group	Males (%)	Females (%)
1	18-30	2 (1.58%)	3 (4.54%)
2	31-40	13 (10.31%)	5 (7.57%)
3	41-50	16 (12.70%)	4 (6.06%)
4	51-60	27 (21.19%)	16 (24.24%)
5	61-70	33 (26.19%)	24 (36.36%)
6	>70	35 (27.78%)	14 (21.21%)

The majority of the COVID-19 patients had an age between 61-70 years (24.82%). The table-wise distribution between gender is given in table 2. Out of a total of 420 cases, 192 (45.71%) patients had (>0.5 FEU) high D dimer. Of these 192 cases with high D-dimer, the majority were male [126 (65.62%)] followed by the female [66 (34.42 %)]. Out of the total 290 male cases, 126 (43.44%) had a high d dimer level, while out of 130 females, 66 (50.76%) had a high d dimer level (Table 3). It has been observed that the total number of female cases is

lower than the male case the however higher proportion of female patients had high D dimer levels than male patients who had high d dimer levels. The majority of the COVID-19 patients having high D-dimer levels had an age between 61-70 years (26.66%) followed by 51-60 years (23.33%) (Table 2). This highlights that high D-dimer was more prevalent in old age group patients.

In cases with high d dimer (>0.5 FEU) level age, wise distribution concerning gender showed the highest number of cases with high d dimer (>0.5 FEU) in male patients in above 70 years age(27.78% group while in females it is observed in 61-70 years age group(36.36%).

Discussion

D dimer elevation has been reported to be one of the commonest laboratory findings noted in COVID-19 patients requiring hospitalization.⁸ Studies have shown that rising D-dimer levels during hospitalization are associated with the worst long-term outcomes⁹. International Society of Thrombosis and Hemostasis interim guidance on recognition and management of coagulopathy recommends PT as the next most crucial test after D-dimer to be performed in patients with COVID-19¹⁰. In our study, out of 420 cases, 69% were males, and 31% were female. High D-dimer was reported in 45.71% of the total cases. A similar study by Soni et al. involving 483 patients mostly comprised of adults and elderly persons where the majority of the patients were male (69.9%) compared to the female (30.1%). D-dimer elevation (0.50 mg/ml) was observed in 80.1% (387/483) of the hospitalized patients⁷. In the present study, 43.44% males and 50.76% females had high d dimer levels. In line with current study findings Sharp, et al. retrospectively analyzed Ddimer levels from patients admitted in tertiary COVID care centers and reported that numbers of males and females with elevated Ddimer levels (above 250 ng/ml) were 68.81% and 73.33%, respectively¹¹. In our study, we found an association between age and elevated D-dimer level. A recently conducted research by He and colleagues also reported that most patients with abnormal D-dimer values were over 60 years old and had a higher average age ($p < 0.001$).¹²

Because COVID-19 mortality rises with age and elderly patients are more prone to experience bleeding events, bleeding scores should be factored into clinical considerations¹³. Women are at a higher risk of developing coagulation-related complications than men, as seen from results drawn for elevated D-dimer levels. Results obtained by Sharp et al. agree to present study findings they obtained a variation in d-dimer level with age in females by a factor of 0.0869 and in males by a factor of 0.0454¹¹. There is certain limitation involved with the study. The study was conducted in a retrospective manner at a single center. There is a scope for a large, multicentre study to consolidate the study outcome. The repeated measurement of D-dimer could be more helpful to assess the prognosis correctly.

Conclusion

COVID 19 patients can have coagulation related complication as the disease progress. D-dimer is a reliable and one of the most essential coagulation parameters to monitor the patients, which significantly correlates with the age and gender of patients.

Conflict of interest: Nil

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