Original Research Article

Estimation of D-dimer levels in COVID-19 patients and its correlation with age and gender

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ABSTRACT

Background: COVID-19 patients show some kind of abnormal coagulation parameters, related to thrombotic disorders, which can act as marker of the disease. One such marker is D-dimer, which is a widely used fibrin degradation product test used for initial diagnosis of thrombotic disorders. D-dimer levels from patients coming in OPD of sub-district hospital Bishnah, Jammu were analyzed to estimate the degree of this relation to its severity, age and gender.
Methods: A retrospective study was conducted on the D-dimer data, collected from the patients coming in OPD of sub-district hospital Bishnah, Jammu, from March 2019 to March 2020. Randomly selected 134 patients infected with COVID-19, with known age and gender and confirmed by RT-PCR were included in the study.
Results: Out of these 134 patients, 76 were males (56.72%) and 58 were females (43.28%). 41.04% patients belonged to the age group 51 to 70 years; 92 patients had elevated levels of D-dimer levels, 52 (38.8%) patients showed D-dimer levels four-folds the safe level, >1000 ng/ml and a significant number of females (70.7%) were found to be with elevated D-dimer levels. Women were found to be at a higher risk of developing thrombotic disorders than men. There was slight relation of thrombotic disorders such as D-dimer with postmenopausal age of women as well.
Conclusions: This study has shown a clear guidance that women and older individuals are at a higher risk of developing thrombotic disorders during COVID-19 infection.

Keywords: COVID-19, D-dimer, Thrombotic disorders, Women

INTRODUCTION

In December 2019 the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the disease it caused, now known as coronavirus disease 2019 (COVID-19), were initially reported in Wuhan, China and rapidly spread throughout world. A number of patients were reported to present with severe infections at the time of admissions itself. As on the date of writing this article, COVID-19 has infected 199,162,000 globally, with 4,243,700 mortalities, and still growing.[1] No one can ignore this huge toll on humanity in terms of mortality, economic losses and subsequent stress.

Pathological studies conducted at the beginning of this pandemic indicated to abnormal coagulation parameters, which further indicate thrombotic disorders which need to be managed as soon as possible.[2,3] Radiological findings are confirmatory diagnosis in these cases but the risks involved like the spread of infections, can make pathological findings the basis to start the treatment. One such marker is D-dimer, which is a widely used fibrin degradation product test used for initial diagnosis of thrombotic disorders.[4] Some studies have indicated that a four-fold increase in its levels is a strong indicator of mortality in active COVID-19 cases.[5,6] Increasing odds of in-hospital deaths have found associated with increased D-dimer levels. In this study we have retrospectively analysed D-dimer data level from patients coming in OPD of sub-district hospital Bishnah, Jammu, designated as a tertiary COVID care centre, to estimate the degree of this relation to its severity, age and gender.

METHODS

This observational study was conducted retrospectively on the D-dimer data, collected from the patients coming in OPD of sub-district hospital Bishnah, Jammu, Jammu and Kashmir, India from March 2019 to March 2020. These values and been measured using Abbott architect. Since the data, available in the labs, comprised of both covid as well as non-covid patients. Patients, infected with COVID-19, with mentioned age and gender and confirmed by RT-PCR were selected randomly and included in the study and those with omission of age and gender data were excluded from the study. Out of the total data collected for 250 such patients, only 134 matched the criteria. Observed threshold of the machine used to measure D-dimer levels in ng/ml was 10,000. Data for which results showed excess value was removed. Samples reporting a value less than 100 were converted to value equal to 100 ng/ml. Names of the patients after completing the above procedure were removed from data to maintain anonymity. The final data set comprised of only three parameters, age, gender and D-dimer levels (in ng/ml). These values had been measured using Tulip diagnostics' Turbodyne SC machine.

The normal value of D-dimer level was taken as 250 ng/ml.[7] The data set was divided into three subsets as follows: age and D-dimer level (irrespective of gender); age of males and D-dimer level; age of females and D-dimer levels.

MS-excel 2010 was used for analysis of data. For all subsets, MS-excel was used to draw a scatter plot with age on x-axis and D-dimer levels (in ng/ml) on y-axis. A linear trendline was predicted with y-intercept at 250 ng/ml. Equation of the line and co-efficient of determination (R2) was calculated. To provide correlation between variables in each subset, co-relation (r) and p value using Pearson's coefficient was determined. P<0.05 was considered significant.

RESULTS

The final data set obtained comprised of 134 patients out of which, maximum number of patients (55 or 41.04%) belonged to the age group 51 to 70 years (Table 1). Out of the total 134 patients and 92 patients with elevated levels of D-dimer levels, 52 (38.8%) patients showed D-dimer levels four-folds the safe level, >1000 ng/ml (Table 2).

Out of 134 patients, 76 were males (56.72%) and 58 were females (43.28%). Numbers of males with elevated D-dimer levels (above 250 ng/ml) were 51 (67.1%), while numbers of females with elevated D-dimer levels were 41 (70.7%) (Table 3).

Scatter plot and linear equation (trendline), plotting age against D-dimer levels, irrespective of gender, is shown in Figure 1. Equation of line in first subset is,

$$y = 26.10x + 9.424,$$

where,

y is value of D-dimer in ng/ml,

x is age is years.

The slope of line is positive and the coefficient of determination $R^2 = 0.070$.

Scatter plot and linear equation (trendline), plotting age against D-dimer levels, in males and excluding all females, is shown in Figure 2. Equation of line in first subset is,

$$y = 24.05x + 118.6,$$

where,

y is value of D-dimer in ng/ml,

x is age is years.

The slope of line is positive and the coefficient of determination $R^2 = 0.046$.

Scatter plot and linear equation (trendline), plotting age against D-dimer levels, in females and excluding all males, is shown in Figure 3. Equation of line in first subset is,

$$y = 28.21x - 109.2,$$

where,

y is value of D-dimer in ng/ml,

x is age is years.

The slope of line is positive and the coefficient of determination $R^2 = 0.115$; R=0.3405; p=0.008913 (significant).

Scatter plot and linear equation (trendline), plotting age against D-dimer levels, for all such patients having D-dimer levels above 250 ng/ml, is shown in Figure 4. Equation of line in first subset is,

$$y = 22.69x + 669.6,$$

where,

y is value of D-dimer in ng/ml,

x is age is years.

The slope of line is positive and the coefficient of determination $R^2 = 0.045$.

Table 1: Distribution of patients as per age groups.

S. No.	Age groups (in years)	No. of patients
1.	11 to 30	22
2.	31 to 50	40
3.	51 to 70	55
4.	>70	17
5.	Total	134

Table 2: Data set of 134 COVID-19 infected individuals with D-dimer levels.

S. No.	D-dimer levels	No. of patients
1.	<250	42
2.	>250, ≤500	21
3.	>500, ≤1000	19
4.	>1000, ≤2000	25
5.	>2000, ≤4000	10
6.	>4000	17

Table 3: Data set of COVID-19 infected individuals with gender.

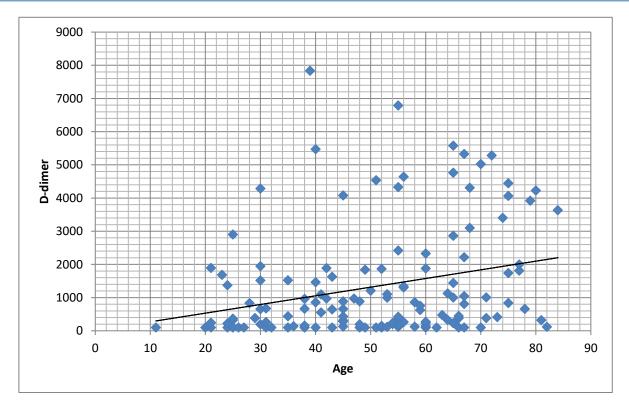| Gender	D-dimer level ≤250	D-dimer level >250	Total	P value
No. of males	25	51	76	
No. of females	17	41	58	0.297
Total	42	92	134	

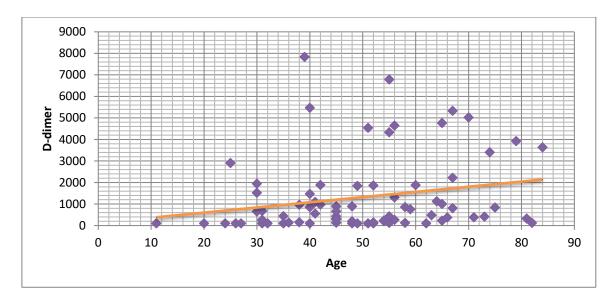**Figure 1: Age and D-dimer levels (irrespective of gender).**

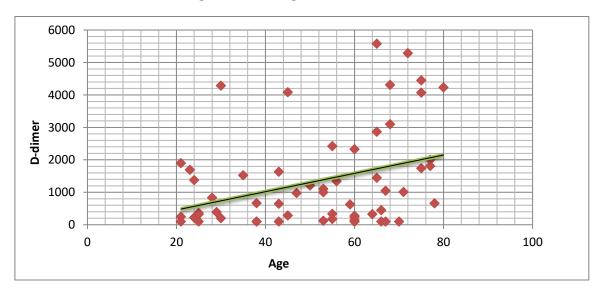**Figure 2: Males' age and D-dimer levels.**

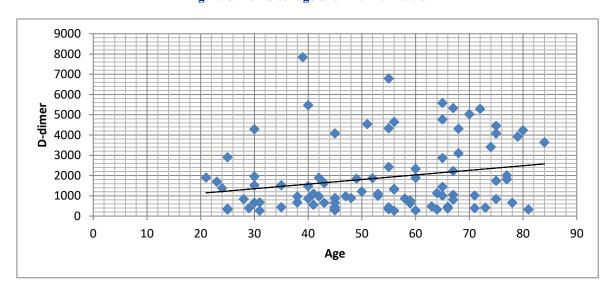**Figure 3: Females' age and D-dimer levels.**

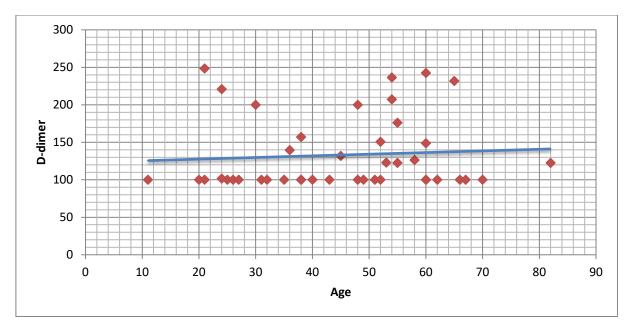**Figure 4: D-dimer levels >250 ng/ml.**

Figure 5: D-dimer levels ≤250 ng/ml.

Scatter plot and linear equation (trend-line), plotting age against D-dimer levels, for all such patients having D-dimer levels below 250 ng/ml, is shown in Figure 5. Equation of line in first subset,

$$y = 0.218x + 123.2,$$

where,

y is value of D-dimer in ng/ml,

x is age is years.

The slope of line is positive and the coefficient of determination R^2=0.005.

DISCUSSION

D-dimer levels in COVID-19 patients increased in our study, consistent with other studies.[6] The trendline plotting for age against D-dimer levels, in females (excluding all males) was positive, with the coefficient of determination R=0.3405, R^2=0.115 and p value at 0.008913 which was very significant. Thus, women were at a higher risk of developing thrombotic disorders than men.

Corelation of most of the subsets indicated positive relation of D-dimer levels with COVID-19 infection and indicated towards more studies like these to be conducted. There was slight relation of thrombotic disorders such as D-dimer with post-menopausal age of women as well as maximum cases of altered D-dimer values were found in women above 50 year of age, which was consistent with the findings of Kline et al.[8]

The primary limitation of the study was that co-morbidities and clinical conditions of the patients were not clinically co-related to the results of the study and therefore future studies in this ongoing pandemic should take care of them.

CONCLUSION

Studies like these are required on an extensive scale, with the continuous rise of COVID-19 cases worldwide, wave after wave, to help in effective patient management, quick and early diagnosis and policy making. However, this study has shown a clear guidance that women and older individuals are at a higher risk of developing thrombotic disorders during COVID-19 infection.

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