Study of correlation of D-Dimer with covid-19 infection in diabetic patients

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ABSTRACT:
Introduction: Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) which is the cause of coronavirus disease 2019 (COVID-19), has rapidly spread around the world. D-dimer, a fibrin breakdown product, is frequently employed as a biomarker and prognostic marker of thromboembolism to predict the severity of the illness. COVID-19 is a procoagulant condition. Present study was aimed to study the levels of D-dimers in diabetic patients with COVID 19 infection. **Materials and Methods:** Present study is a cross sectional prospective study conducted from duration September 2022 to September 2023. 50 laboratory-confirmed (RTPCR or RAT) COVID-19 cases who were already diagnosed of diabetes were admitted. All enrolled patients were categorized into mild, moderate & severe on the basis of severity. D-dimer was evaluated in each patient by immunofluorescence. **Observations and Results:** Mild COVID-19 case was only 1 (2 %), moderate were 38 (76 %) & severe were 11 (22 %). Mild severity COVID-19 case was having D-dimer < 1.5 µg/ml. Amongst moderate **severity** COVID-19 case i.e 38 (76 %), 31 (62 %) had D-dimer < 1.5 µg/ml & 7 (14 %) had D-dimer ≥1.5 µg/ml. Amongst severe **severity** COVID-19 case i.e 11 (22 %), 2 (4 %) had D-dimer < 1.5 µg/ml & 9 (18 %) had D-dimer ≥1.5 µg/ml. D-dimer level & **severity** of COVID-19 showed statistically significant correlation (P=0.0002). **Conclusion:** To conclude, D-dimer levels can be correlated with severity of COVID-19 & these correlations can be used for risk assessment & choosing appropriate management

Keywords: COVID-19, D-dimers, diabetic patients

INTRODUCTION:

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) which is the cause of coronavirus disease 2019 (COVID-19)[1], has rapidly spread around the world, and on March 11, 2020, the World Health Organisation declared it to be a pandemic. Worldwide, there have been over 120 million confirmed cases of COVID-19[1]. One of the major comorbidities in COVID-19 patients has been diabetes. Diabetics are more susceptible to a number of infections. People with diabetes are particularly susceptible to the cytokine storm due to certain inherent variables. This syndrome may therefore be caused by an imbalance between fibrinolysis and coagulation factors, which may raise the risk of thrombotic events[2]. D-dimer, a fibrin breakdown product, is frequently employed as a biomarker and prognostic marker of thromboembolism to predict the severity of the illness. COVID-19 is a procoagulant condition. It is yet unknown how D-dimer readings affect the severity of the disease, given that COVID-19 has made diabetes a predictor of the disease's severity[2]. With this perspective present study was aimed to study the levels of D-dimers in diabetic patients with COVID 19 infection.

MATERIALS AND METHODS:

Present study is a cross sectional prospective study conducted from duration September 2022 to September 2023. Institutional ethics committee permission was taken prior to commencement of present study. 50 diabetic patients with COVID 19 infection fulfilling inclusion and exclusion criteria were enrolled. Study was explained to all participants and written informed consent was obtained from all.

Objectives:
1. To study clinical profile of diabetic patients with COVID 19 infection
2. To assess D-dimer in all participants
3. To assess prevalence of participants in various severity of COVID 19 infection
4. To correlate D-dimer with severity of patients

Inclusion Criteria:
50 laboratory-confirmed (Real Time Reverse Transcription Polymerse Chain Reaction, RTPCR or Rapid Antigen Test, RAT) COVID-19 cases who were already diagnosed of diabetes were admitted at this centre.

Exclusion Criteria:
5. < 18 years
6. History of venous thromboembolism
7. Cases on anticoagulants
8. Pregnant cases

PROCEDURE:
Detailed history taking with demographics like age, gender, laboratory data like random blood sugar (RBS), HbA1c done within 2 months of enrollment were noted in case record form. Respiratory rate & SpO2 was recorded in every enrolled patient. All enrolled patients were categorized on the basis of severity as[3].
A. Mild: Respiratory Rate <24/min & SpO2 > 94 % at room air
B. Moderate: Respiratory rate between 24-30/min & SpO2 90-94 % at room air
C. Severe: Respiratory rate > 30/min & SpO2 < 90 %) [7].

Each patient's D-dimer was assessed after these. Within 24 hours of admission, blood samples were taken for the D-dimer evaluation and transmitted to the appropriate hospital labs. Within two hours of the sample being collected, all measurements were completed in the labs. Using kits from several manufacturers in various locations, D-dimer was quantified by immunofluorescence. The biological reference range for each of the utilised kits was less than 0.5 µg/mlAll the data obtained was compiled & evaluated.

Statistical analysis:
Statistical analysis was performed using SPSS software, version 20. Data were expressed as mean ± SD and frequency with percentages N (%). χ2-test was used to evaluate qualitative data and to study association between two variables. Statistical significance was assumed if P value less than 0.05.

OBSERVATION AND RESULT:

Table 1: Clinical history

Sr No	Parameter	Number of cases (n)/ Mean	Percentage (%) SD
1	Age (Mean ± SD)	59.06	5.97
2	Gender		
	a. Male	39	78 %
	b. Female	11	22 %
3	RBS (Mean ± SD)	147.63	48.90
4	HbA1c (Mean ± SD)	6.96	1.27

As per result shown in **Table 1,** Mean ± SD of age (years) of all participants was 59.06 ± 5.97. Male cases were about 39 (78 %) whereas females were 11 (22 %). Mean ± SD of RBS (mg/dl) of all participants was 147.63 ± 48.90 & Mean ± SD of HbA1c (%) of all participants was 6.96 ± 1.27.

Table 2: Correlation of D-dimer with COVID-19 severity

Sr No	D-dimer (µg/ml)	Number of cases (n)	Percentage (%)
1	< 1.5	34	68 %
3	≥1.5	16	32 %
Total		50	100 %

D-dimer < 1.5 µg/ml was observed in 34 (68 %) cases & ≥1.5 was observed in 16 (32 %) cases.

Table 3: COVID-19 severity

| Sr No	Parameter	Number of cases (n)	Percentage (%)
1	Mild	1	2 %
2	Moderate	38	76 %
3	Severe	11	22 %
Total		50	100 %

Mild COVID-19 case was only 1 (2 %), moderate were 38 (76 %) & severe were 11 (22 %)

Table 4: Correlation of D-dimer with COVID-19 severity

Sr No	D-dimer (mg/L)	COVID-19 severity			Total n (%)	Chi square	P value
		Mild n (%)	Moderate n (%)	Severe n (%)			
1	< 1.5	1 (2 %)	31 (62 %)	2 (4 %)	34 (68 %)	16.23	0.0002 (S)
2	≥1.5	0 (0 %)	7 (14 %)	9 (18 %)	16 (32 %)		
Total n (%)		1 (2 %)	38 (76 %)	11 (22 %)	50 (100 %)		

Mild severity COVID-19 case was having D-dimer < 1.5 µg/ml. Amongst moderate severity COVID-19 case i.e 38 (76 %), 31 (62 %) had D-dimer < 1.5 µg/ml & 7 (14 %) had D-dimer ≥1.5 µg/ml. Amongst severe severity COVID-19 case i.e 11 (22 %), 2 (4 %) had D-dimer < 1.5 µg/ml & 9 (18 %) had D-dimer ≥1.5 µg/ml. D-dimer level & severity of COVID-19 showed statistically significant correlation (P=0.0002) (Graph 1)

Graph 1: Correlation of D-dimer with COVID-19 severity
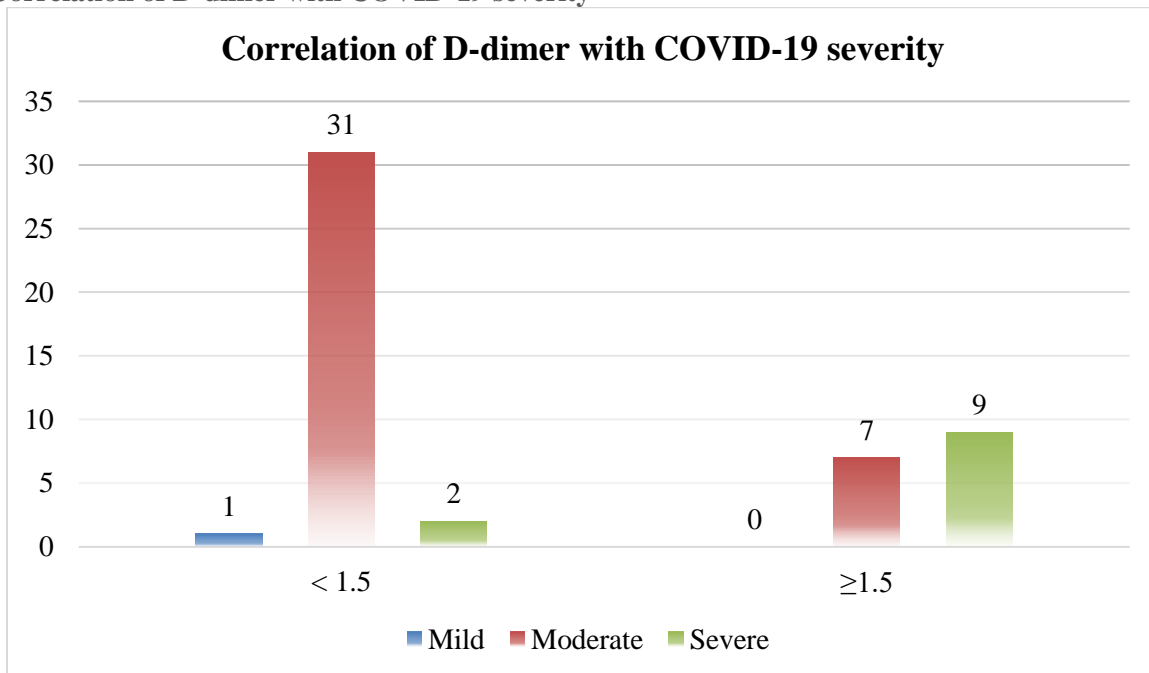
DISCUSSION:
Diabetes is one of the most common associated comorbidities with severe acute respiratory syndrome coronavirus (SARS-CoV-2) patients. Coagulation disorders with D-dimer levels are increased in both diseases. In present 50 diabetic patients infected with COVID-19 were enrolled. They were categorised into mild, moderate & severe on the basis of severity. D-dimer levels were evaluated in all. Mean ± SD of age was 59.06 ± 5.97. Male were 39 (78 %) & females were

11 (22 %). Mean ± SD of RBS (mg/dl) was 147.63 ± 48.90 & of HbA1c (%) was 6.96 ± 1.27. In similar study by Chaymae Miri et al (2021)[4] the median age of participants was 64 years & interquartile range was 56-73. 113 (56%) were male cases. Yogendra Mishra et al (2020)[5] in their study found Among the 98 enrolled patients, 71% were males and 28.6% were females. In present study D-dimer < 1.5 µg/ml was observed in 34 (68 %) cases & ≥1.5 was observed in 16 (32 %) cases. Chaymae Miri et al (2021)[4] found optimal cut-off value at admission for D-dimer in all patients as 1220 ng/mL. Yogendra Mishra et al (2020)[5] in their study found Mean ± SD of D-dimer as 1509 ± 2420 ng/ml. Poudel A et al (2021)[6] in their study found D-dimer < 1.5 µg/ml in 126 cases & ≥1.5 in 56 cases. In present study mild COVID-19 case was only 1 (2 %), moderate were 38 (76 %) & severe were 11 (22 %). Yogendra Mishra et al (2020)[5] in their study found amongst 98 enrolled cases 52 were moderate & 46 were severe. In present study mild severity COVID-19 case was having D-dimer < 1.5 µg/ml. Amongst moderate severity COVID-19 case i.e 38 (76 %), 31 (62 %) had D-dimer < 1.5 µg/ml & 7 (14 %) had D-dimer ≥1.5 µg/ml. Amongst severe severity COVID-19 case i.e 11 (22 %), 2 (4 %) had D-dimer < 1.5 µg/ml & 9 (18 %) had D-dimer ≥1.5 µg/ml. D-dimer level & severity of COVID-19 showed statistically significant correlation (P=0.0002). Yogendra Mishra et al (2020)[5] in their study also found that Severity of disease & D-dimer level showed statistically significant correlation (P=0.041).

Patients with diabetes had more severe disease with higher D dimer levels. Persistent hyperglycemia can lead to endothelial dysfunction and inflammation which can lead to thrombus formation[7]. Therefore, it is likely that severe SARS-CoV-2 infection with diabetes is more likely to cause coagulopathy and resultant poor outcome. However clinical implications of these findings are yet to be seen.

Limitations:
Some limitation of our study includes evaluating D-dimer on admission as time from illness onset to hospital presentation may affect the D-dimer values. D-dimer evaluation by different kits can create possible bias due to the use of different equipment. We have not evaluated any outcome variable.

CONCLUSION:
To conclude, D-dimer levels can be correlated with severity of COVID-19 & these correlations can be used for risk assessment & choosing appropriate management. Also, D-dimer is a widely available, relatively inexpensive, and easy to perform laboratory test so incorporating it in routine investigation can prove useful in tackling this global health challenge.

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