



Incidence Of Vascular Events In Covid-19 Patients With Increased D-Dimer Levels At A Tertiary Care Institution In Chennai

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Abstract

Background: D-dimer is the degradation product of cross-linked fibrin; therefore, it reflects the ongoing activation of the hemostatic and thrombolytic system. It has been evaluated and found to be clinically useful in thrombus evaluation, predicting disseminated intravascular coagulation and excluding deep vein thrombosis. Arterial and venous thrombosis is one of the major complications of coronavirus disease 2019 (COVID-19) infection. Studies have not assessed the difference in D-dimer levels between patients who develop thrombosis and those who do not.

Aim of the study: The objective of the present study was to find out the incidence of vascular events that occurred in COVID-19 patients admitted to our hospital with elevated D-dimer values.

Methods: This is a retrospective study conducted in the Medical Records Department of Bhaarath Medical College and Hospital affiliated with Bharath Institute of Higher Education and Research (BIHER), Chennai after getting approval from the Bhaarath Institutional Ethics Committee. The data for this study were collected from the case records of 140 COVID-19 patients admitted to our hospital who fulfilled the eligibility criteria. The data of this study were analyzed using descriptive statistics (Frequency and Percentage).

Results: Most of the COVID-19 patients with comorbidities admitted to our hospital with elevated D-dimer values had developed various vascular events like cases related to thrombosis, acute kidney injury, etc. resulting in longer hospital stay, increased morbidity, and mortality.

Conclusion: D-dimer value was found to be the most important and reliable biomarker for COVID-19-related vascular complications in our study.

Keywords: COVID-19, Biomarker, D-dimer, Vascular event

Introduction

Coronavirus disease 2019 (COVID-19), a respiratory condition, is a universal pandemic. Endothelial dysfunction, thrombosis, coagulopathy, and multiple organ failure are the important pathogenesis of this disease.[1] After COVID-19 outbursts, the risk of thrombosis has drawn much attention.[2] Recent reports are showing an increased incidence of arterial and venous thrombotic events, and acute kidney

injury in COVID-19 patients.[3] D-dimer value of more than 0.5 µg/ml is linked with severe COVID-19 infection. [4]The abnormal D-dimer levels are reported to be associated with a poor prognosis. [5] D-dimers are fibrin degradation products, the elevated levels of it are found in conditions associated with thrombosis like Myocardial infarction, Stroke, Deep vein thrombosis, Pulmonary embolism, etc.[6] The thrombotic incidence and other

vascular events like acute kidney injury in COVID-19 patients have not been determined widely. [7] At the early stage of COVID-19, D-dimer may be one of the important biomarkers, which can detect the formation of thrombus and subsequent vascular events, which could help in preventing severe morbidity and mortality. However, the incidence of vascular events that occurred in COVID-19 patients with elevated D-dimer values has not been reported extensively. [8] So, in this study, we have checked the incidence of vascular events that occurred in COVID-19 patients admitted to our hospital with elevated D-dimer values and explored the importance of D-dimer.

Materials & Methods

This is a cross-sectional retrospective study conducted in the Medical Records Department of Bharath Medical College and Hospital affiliated with Bharath Institute of Higher Education and Research (BIHER), Chennai after getting approval from Bharath Institutional Ethics Committee (approval no: BIEC-020-21). The period of the study was 4 months from March 2021 to June 2021, when the COVID-19 second wave was at its peak. The data for this study were collected randomly from the case records of 140 COVID-19 patients admitted to our hospital who fulfilled the eligibility criteria. *Inclusion criteria:* Those COVID-19 patients with elevated D-dimer values admitted to our hospital fulfilling any one of the following criteria were included: COVID-19 positive patients with age greater than or equal to 12 years, RT-PCR positive patients, Rapid antigen test-positive patients, CT scan positive patients. *Exclusion criteria:* COVID-19 positive patients with an age lesser than 12 years. *Sample size:* Our sample size was determined by Daniel's sample size formula⁷ which came out to be 138. So, we have taken a total of 140 COVID-19 inpatient cases for our study. After fulfilling the eligibility criteria, from their case records, the details of general conditions of COVID-19 patients, age and sex details, the severity of COVID, blood investigations reports comprising D-dimer, WBC and Platelet parameters, CRP, LDH, and Ferritin, and the details of comorbidities and vascular events were taken for analysis. All the investigation parameters estimated at the time of admission were taken in this study. We have evaluated various vascular events in our COVID-19 patients classified based on different

organ system involvement. For example, in the renal system involvement, we have checked for the presence of acute kidney injury which is diagnosed by an increase in serum creatinine. In the central nervous system, the acute cerebrovascular accident is diagnosed by non-contrast computed tomography (CT) of the head. In the cardiovascular system, NSTEMI is diagnosed in patients presenting with symptoms coherent with the acute coronary syndrome as well as increased troponin levels but without changes in ECG coherent with STEMI. The main difference between unstable angina and NSTEMI is the absence or presence of increased troponin levels respectively. For diagnosing angina, a physical exam, evaluation of symptoms and risk factors, including a family history of heart disease are checked, and also there are several tests to confirm angina like electrocardiogram (ECG or EKG), stress test, echocardiogram, nuclear stress test, Chest X-ray, blood tests, coronary angiography, cardiac computerized tomography (CT) scan, and cardiac MRI. Myocarditis is diagnosed by physical examination and a variety of tests which include electrocardiogram (ECG or EKG), chest X-ray, heart MRI (cardiac MRI), echocardiogram, blood test, and related tests to determine antibodies against viruses and other organisms that cause myocarditis-related infection, cardiac catheterization, and heart muscle biopsy. Coming to conduction abnormalities in the cardiovascular system, AV block signifies a delay in the impulse transmission from the atria to the ventricles. Atrioventricular (AV) conduction is assessed by evaluating the relationship between the P waves and QRS complexes in ECG. LBBB is often diagnosed by ECG. In arrhythmias, tachyarrhythmia supraventricular tachycardia, and bradyarrhythmia, sinus bradycardia can also be diagnosed through ECG. We have also checked other vascular events like an acute left ventricular failure which is diagnosed through echocardiography, and septic shock which is diagnosed by medical history, physical examination for signs and symptoms of infection, and focused ultrasonography to diagnose very complex physiologic manifestations of shock.

Statistical analysis: The data were analyzed using descriptive statistics (Frequency and Percentage) in this study.

Results

1. General conditions of COVID-19 patients admitted to our hospital: Out Of 140 COVID-19 patients (100%) admitted to our Bhaarith Medical College and Hospital (BMCH), 79 patients (56.4%) were improved and discharged, 56 patients (40%) were expired, 3 patients (2.1%) were discharged against medical advice, and 2 patients (1.4%) were referred. [Table 1]

2. Age and sex of COVID-19 patients admitted: 92 patients (65.71%) were aged more than 50 years and the remaining 48 patients (34.29%) were aged less than 50 years. The maximum age noted was 86 years and the minimum age observed was 26 years. 94 male patients (67.14%) and 46 female patients (32.86%) were included in this study. [Table 2]

3. The severity of COVID-19 in patients admitted: 69 patients (49.29%) had mild COVID, 8 patients (5.7%) had moderate COVID, and 63 patients (45%) had severe COVID. We have classified the severity of COVID-19 in our patients according to the “clinical guidelines for the management of adult COVID-19 patients” introduced by AIIMS/ ICMR-COVID-19 National Task Force/Joint Monitoring Group, Ministry of Health & Family Welfare, Government of India.²⁴[Table 3]

4. Blood investigations: D-dimer: Out of 140 COVID-19 patients (100%) admitted with increased D-dimer elevation above the normal value (0.5 µg/ml), 98 patients (70%) exhibited significant D-dimer elevation more than twice the normal value (>1 µg/ml), and the remaining 42 patients (30%) revealed D-dimer elevation above the normal value (>0.5 µg/ml) but less than twice the normal value (0.5-1 µg/ml). WBC and Platelet parameters: 88 patients (62.86%) presented with lymphocytopenia, 39(27.86%) with leukocytosis, 13(9.29%) with leukopenia, and 31(22.14%) with thrombocytopenia. Other blood investigation parameters: C-reactive protein (CRP) was elevated in 115 patients (82.14%), Lactate dehydrogenase (LDH) in 15 patients (10.71%), and Ferritin in 46 patients (32.86%). [Table 4]

5. Comorbidities: COVID-19 patients admitted presented with 16 comorbidities. Among these comorbidities, Type 2 Diabetes Mellitus (T2DM) was seen in 71 patients (50.71%). 31 patients (22.14%) presented T2DM as a single entity while it was seen as a combined presentation with other comorbidities

in the remaining 40 patients (28.57%). Hypertension (HT) was seen in 49 patients (35%). 8 patients (5.7%) presented HT as a single entity while it was seen as a combined presentation with other comorbidities in the remaining 41 patients (29.29%). Remaining 14 comorbidities shown by the patients were 1 patient (0.71%) presented with post-mastectomy status, 2 patients (1.4%) with old inferior wall myocardial infarction, 2 patients (1.4%) with ischemic cardiomyopathy, 1 patient (0.7%) with pregnancy-induced hypertension (PIH), 1 patient (0.7%) with gestational diabetes mellitus (GDM), 1 patient (0.7%) with chronic obstructive pulmonary disease (COPD), 1 patient (0.7%) with atrial fibrillation (AF), 1 patient (0.7%) with congestive heart failure (CHF), 1 patient (0.7%) with Myasthenia gravis, 10 patients (7.14%) with coronary artery disease, 7 patients (5%) with post coronary artery bypass graft surgery (post-CABG), 6 patients (4.3%) with hypothyroidism, 1 patient (0.7%) with old cerebrovascular disease (old CVA) and 2 patients (1.4%) with hypercholesterolemia. 49 patients (35%) presented with more than one comorbidity. 50 patients (35.7%) were free from any comorbidities. [Table 5]

6. COVID-19 patients admitted presented with various vascular events: 50 COVID-19 patients (35.7%) admitted to BMCH presented with various vascular events. *A. Renal system:* 11 patients (7.86%) presented with acute kidney injury (AKI). *B. Central nervous system:* Acute Cerebrovascular accident (acute CVA) detected in 2 patients (1.4%). *C. Cardiovascular system. coronary artery disease:* In acute coronary syndrome, 5 patients (3.57%) presented with ST-segment elevation myocardial infarction (STEMI), and 2 patients (1.4%) with non-ST segment elevation myocardial infarction (NSTEMI). Angina was seen in 10 patients (7.14%). *b. Myocarditis:* Myocarditis was observed in 4 patients (2.86%). *c. Conduction abnormalities:* Atrioventricular block (AV block) was seen in 6 patients (4.3%) and left anterior fascicular block (LAFB) was observed in 5 patients (3.6%). *d. Arrhythmias:* In Tachyarrhythmias, supraventricular tachycardia (SVT) was seen in 2 patients (1.43%), and in Bradyarrhythmia, Sinus bradycardia was observed in 1 patient (0.7%). *D. Other vascular events:* COVID-19 patients admitted to BMCH also presented with 2 other vascular events. Acute Left Ventricular failure was seen in 1 patient (0.7%) and

septic shock was observed in 1 patient (0.7%). [Table 6 & 11]

7. COVID-19 patients admitted presented with other clinical events: 5 patients presented with other clinical events. 2 patients with COPD (1.4%), 1 with Pneumothorax (0.7%), 1 with Diabetic Ketoacidosis (0.7%), and another one with Ramsay Hunt syndrome (0.7%). [Table 7]

8. Deaths due to vascular events occurred in COVID-19 patients: 28 COVID-19 patients (20%) with vascular events admitted to BMCH were expired. Among the COVID-19 patients affected with renal system involvement, 7 patients (5%) died due to AKI, among the COVID-19 patients affected with cardiovascular system involvement, 3 patients (2.14%) died due to AV block, 1 patient (0.71%) with SVT, 5 patients (3.57%) with STEMI, 2 patients (1.43%) with NSTEMI, 3 patients (2.14%) with myocarditis, 5 patients (3.57%) with angina, and among the COVID-19 patients affected by other vascular events, 1 patient (0.71%) died due to acute LV failure, and 1 patient (0.71%) with septic shock. [Table 8]

9. Significantly elevated/elevated D-dimer values in vascular events occurred in COVID-19 patients: 50 COVID-19 patients (35.71%) admitted to BMCH presented with various vascular events. Out of these 50, 38 patients had comorbidities (27.14%), and the remaining 12 patients had no comorbidities

(8.57%). In patients with vascular events, significant D-dimer elevation more than twice the normal value was seen in 36 patients (25.71%), and the remaining 14 patients (10%) revealed D-dimer elevation above the normal value but less than twice the normal value. D-dimer significantly elevated more than twice the normal value was observed in 26 patients with vascular events having comorbidities (18.57%) and in 10 patients without comorbidities (7.14%). D-dimer elevated above the normal value but less than twice the normal value was seen in 12 patients with vascular events having comorbidities (8.57%) and in 2 patients without comorbidities (1.43%). [Table 9]

10. Significantly elevated/elevated D-dimer values in vascular events occurred in dead COVID-19 patients 28 COVID-19 patients (20%) with vascular events admitted to BMCH were expired. Out of these 28, significant D-dimer elevation of more than twice the normal value was seen in 22 patients (15.71%), and the remaining 6 patients (4.29%) revealed D-dimer elevation above the normal value but less than twice the normal value. D-dimer significantly elevated more than twice the normal value was observed in 17 dead patients with vascular events having comorbidities (12.14%) and in 5 patients without comorbidities (3.57%). D-dimer elevated above the normal value but less than twice the normal value was seen in 4 dead patients with vascular events having comorbidities (2.86%) and in 2 patients without comorbidities (1.43%). [Table 10].

Table 1. General Conditions Of Covid-19 Patients Admitted To Our Hospital

Conditions of the COVID-19 patients admitted	Total/140	Percentage %
Total No of patients admitted	140	100
Total No of patients dead	56	40
Total No of patients improved	79	56.43
Patients discharged Against medical advice	3	2.14
Referred	2	1.43

Table 2. Age And Sex Of Covid-19 Patients Admitted

Age of COVID-19 patients admitted	Total/140	Percentage %
COVID-19 patients aged more than 50 years	92	65.71%
COVID-19 patients aged less than 50 years	48	34.29%

Total male and female COVID patients admitted		
Male	94	67.14
Female	46	32.86

Table 3. Severity of COVID-19 in patients admitted

Severity of COVID-19 in patients admitted	Total/140	Percentage %
Mild COVID	69	49.29
Moderate COVID	8	5.71
Severe COVID	63	45

Table 4. Blood Investigation Parameters Of Covid-19 Patients Admitted

Blood investigation parameters of COVID-19 patients admitted	Total/140	Percentage %
D-dimer		
D dimer significantly elevated (elevated more than twice the normal value)	98	70
D dimer elevated (elevated but less than twice the normal value)	42	30
WBC and Platelet parameters		
Lymphocytopenia	88	62.86
Leukocytosis	39	27.86
Leukopenia	13	9.29
Thrombocytopenia	31	22.14
Other blood investigation parameters		
CRP	115	82.14
LDH	15	10.71
Ferritin	46	32.86

Table 5. COVID-19 patients admitted presented with various comorbidities

S.NO	COVID-19 patients admitted presented with various comorbidities	Total/140	Percentage %
1.	T2DM	71	50.71
2.	HT	49	35
3.	Post-mastectomy status	1	0.71
4.	Old IWMI	2	1.43

5.	Ischemic cardiomyopathy	2	1.43
6.	PIH	1	0.71
7.	GDM	1	0.71
8.	COPD	1	0.71
9.	AF	1	0.71
10.	CHF	1	0.71
11.	Myasthenia gravis	1	0.71
12.	CAD	10	7.14
13.	Post CABG	7	5
14.	Hypothyroidism	6	4.29
15.	Old CVA	1	0.71
16.	Hypercholesterolemia	2	1.43
COVID-19 patients admitted presented with more than one comorbidity			
More than one comorbidity		49	35
COVID-19 patients admitted presented with no comorbidity			
No comorbidity		50	35.71

Table 6. Covid-19 Patients Admitted Presented With Various Vascular Events

COVID-19 patients admitted presented with various vascular events	Total/140	Percentage %
A. Renal system:		
1. Acute kidney injury	11	7.86
B. Central nervous system:		
1. Acute CVA	2	1.43
C. Cardiovascular system:		
a. coronary artery disease:		
Acute coronary syndrome:		
1. STEMI	5	3.57
2. NSTEMI / Unstable angina	2	1.43
Angina:		
1. Angina	10	7.14

b. Myocarditis:		
1. Myocarditis	4	2.86
c. Conduction abnormalities:		
1. AV block	6	4.29
2. LBBB/LAFB	5	3.57
d. Arrhythmias:		
Tachyarrhythmia:		
1. SVT	2	1.43
Bradyarrhythmia:		
1. Sinus bradycardia	1	0.71
D. Other vascular events:		
1. Acute LV failure	1	0.71
2. Septic shock	1	0.71

Table 7. Covid-19 Patients Admitted Presented With Other Clinical Events

COVID-19 patients admitted presented with other clinical events	Total/140	Percentage %
COPD	2	1.43
Pneumothorax	1	0.71
Diabetic Ketoacidosis	1	0.71
Ramsay Hunt syndrome	1	0.71

Table 8. Deaths Due To Vascular Events Occurred In Covid-19 Patients

Vascular events	Total No of deaths due to vascular events	Percentage %
A. Renal system:		
1. Acute kidney injury	7	5
B. Central nervous system:		
1. Acute CVA	0	0

C. Cardiovascular system:		
a. coronary artery disease:		
Acute coronary syndrome:		
1. STEMI	5	3.57
2. NSTEMI / Unstable angina	2	1.43
Angina:		
1. Angina	5	3.57
b. Myocarditis:		
1. Myocarditis	3	2.14
c. Conduction abnormalities:		
1. AV block	3	2.14
2. LBBB/LAFB	0	0
d. Arrhythmias:		
Tachyarrhythmia:		
1. SVT	1	0.71
Bradyarrhythmia:		
1. Sinus bradycardia	0	0
D. Other vascular events:		
1. Acute LV failure	1	0.71
2. Septic shock	1	0.71

Table 9. Significantly Elevated/Elevated D-Dimer Values In Vascular Events Occurred In Covid-19 Patients

Significantly elevated/elevated D-dimer values in vascular events occurred in COVID-19 patients	Total/140	Percentage %
Total No of patients with vascular events	50	35.71
Total No of patients with vascular events having comorbidities	38	27.14
Total No of patients with vascular events having no comorbidities	12	8.57
D dimer was significantly elevated (elevated more than twice the normal value) in patients with vascular events	36	25.71
D dimer was significantly elevated (elevated more than twice the normal value) in patients with vascular events having comorbidities	26	18.57

D dimer was significantly elevated (elevated more than twice the normal value) in patients with vascular events having no comorbidities	10	7.14
D dimer elevated (elevated but less than twice the normal value) in patients with vascular events.	14	10
D dimer elevated (elevated but less than twice the normal value) in patients with vascular events having comorbidities	12	8.57
D dimer elevated (elevated but less than twice the normal value) in patients with vascular events having no comorbidities	2	1.43

Table 10. Significantly Elevated/Elevated D-Dimer Values In Vascular Events Occurred In Dead Covid-19 Patients

Significantly elevated/elevated D-dimer values in vascular events occurred in dead COVID-19 patients	Total/140	Percentage %
Total No of deaths due to vascular events	28	20
D dimer significantly elevated (elevated more than twice the normal value) in dead patients with vascular events	22	15.71
D dimer was significantly elevated (elevated more than twice the normal value) in dead patients with vascular events having comorbidities	17	12.14
D dimer was significantly elevated (elevated more than twice the normal value) in dead patients with vascular events having no comorbidities	5	3.57
D dimer elevated (elevated but less than twice the normal value) in dead patients with vascular events	6	4.29
D dimer elevated (elevated but less than twice the normal value) in dead patients with vascular events having comorbidities	4	2.86
D dimer elevated (elevated but less than twice the normal value) in dead patients with vascular events having no comorbidities	2	1.43

Table 11. Important vascular events occurred in COVID-19 patients

Patient No.	Age	Sex	Severity of COVID	Comorbidity	D-dimer Value	D-dimer Status	Vascular event	The outcome of the patient
1.	50	Male	Mild	T2DM	6.72	Significantly elevated	SVT	Dead
2.	60	Male	Mild	T2DM and HT	0.76	Elevated	Acute LV failure	Dead
3.	65	Male	Severe	T2DM	3	Significantly elevated	AV Block	Dead

4.	79	Female	Severe	No	1.20	Significantly elevated	NSTEMI	Dead
5.	73	Female	Severe	T2DM	1.82	Significantly elevated	STEMI	Dead
6.	57	Male	Severe	T2DM/HT	10.22	Significantly elevated	Myocarditis	Dead
7.	55	Male	Severe	HT/old CVA	8.87	Significantly elevated	AKI	Dead
8.	80	Male	Severe	No	4.27	Significantly elevated	SEMI	Dead
9.	50	Female	Severe	T2DM	9.19	Significantly elevated	Angina	Dead
10.	47	Female	Mild	Post-mastectomy status	0.64	Elevated	Bradycardia	Improved
11.	72	Male	Mild	Ischemic cardiomyopathy/CAD/Old IWMI	8.68	Significantly elevated	Acute CVA	Improved
12.	41	Female	Severe	T2DM	2.78	Significantly elevated	Septic shock	Dead
13.	37	Female	Severe	No	4.36	Significantly elevated	SVT	Discharged against Medical Advice

Discussion

Out Of 140 COVID-19 patients (100%) admitted to BMCH, most of the patients presented with fever and cough followed by breathlessness. Other important symptoms noted in the patients are loss of smell in 21 patients (15%) and Diarrhoeain 10 patients (7.14%). 2 patients (1.4%) demonstrated complaints of upper and lower limb weakness diagnosed to have the acute cerebrovascular disease and 1 patient (0.71%) revealed with the inability to feel sensation in the right side of the face and inability to close right side eye diagnosed to have Ramsay Hunt syndrome[9,10] COVID-19 patients aged greater than 50 years (65.71%) were more than the patients aged less than 50 years (34.29%). In total male and female COVID patients admitted, male patients (67.14%) were more than female patients (32.86%). [11] According to the “clinical guidelines for the management of adult COVID-19 patients” introduced by AIIMS/ ICMR-

COVID-19, patients categorized as a mild disease should have upper respiratory tract symptoms (&/or fever) without shortness of breath or hypoxia, patients with moderate disease should have any one of the two events i.e., 1. Respiratory rate more than or equal to 24/min with breathlessness and 2. SpO2 level should be less than or equal to 93% on room air but should be more than 90% and the patients classified under severe disease should have any of the two outcomes i.e., 1. Respiratory rate more than 30/min and 2. SpO2 level should be less than 90% on room air.[12] Based on this classification, we have checked the severity of COVID-19 in patients admitted. Mild COVID patients (49.3%) were more than the moderate (5.7%) and severe COVID patients (45%).[13] The association between hypercoagulation and COVID-19 has been well established. We evaluated the blood investigation parameters in these admitted patients in our study. Since we have taken 140 COVID-19 patients

admitted with elevated D-dimer values above the normal value, to bring out better comparison, results, and conclusions in vascular events that occurred in COVID-19 patients admitted in BMCH, we have separated the D-dimer values into significantly elevated /elevated values. [14] Patients with a significant D-dimer elevation of more than twice the normal value (70%) were found to be more compared to the patients with D-dimer elevated above the normal value but less than twice the normal value (30%). [15] On evaluating WBC and Platelet parameters in COVID-19 patients, we found lymphocytopenia (62.86%) was more than leukocytosis (27.86%), leukopenia (9.29%), and thrombocytopenia (22.14%). These results were comparable to the findings from another similar study. [16] We have also checked other blood investigation parameters, where we found CRP (82.14%) was found to be more compared to LDH (10.71%), and Ferritin (32.86%). These findings were also similar to the results shown by another study. [17,18] Type 2 Diabetes Mellitus (T2DM) was the most common comorbidity presented in these patients (50.71%). [19] Now coming to vascular events that occurred in COVID-19 patients in our study, the most important system involved was the cardiovascular system followed by the renal system. But by comparing the individual presentation of vascular events in all systems, Acute kidney injury (7.86%) was the dominant presentation followed by angina (7.14%), AV block (4.29%), STEMI (3.57%), LAFB (3.57%), Myocarditis (2.86%), acute CVA (1.43%), etc. [20]

Similarly, we also evaluated deaths due to vascular events that occurred in COVID-19 patients admitted where we found the maximum death was seen in the COVID-19 patients affected with renal system involvement comprising AKI (5%) followed by the COVID-19 patients affected with the cardiovascular system involving STEMI (3.57%), angina (3.57%), myocarditis (2.14%), AV block (2.14%), NSTEMI (1.43%), etc. we have also noted that most of the patients died due to these vascular events were aged more than 50 years with comorbidities showing significantly elevated D-dimer value two times more than the normal value. [21,22] On analyzing COVID-19 patients with vascular events with elevated D-dimer values, we found the patients with vascular events having comorbidities (27.14%), were more

than the patients having no comorbidities (8.57%). Even in patients with vascular events, significant D-dimer elevation of more than twice the normal value (25.71%) was found to be more compared to the patients with D-dimer elevated above the normal value but less than twice the normal value (10%). [23] Also, among patients with vascular events, significant D-dimer elevation more than twice the normal value was found to be more in patients with comorbidities (18.57%) than the patients without comorbidities (7.14%). [24] D-dimer elevated above the normal value but less than twice the normal value was also more in patients with vascular events having comorbidities (8.57%) than the patients without comorbidities (1.43%). [25] In evaluating dead COVID-19 patients with vascular events with elevated D-dimer values, we have found similar results. Dead patients with significantly elevated D-dimer values more than twice the normal value (15.71%) were found to be more compared to the dead patients with D-dimer elevated above the normal value but less than twice the normal value (4.29%). [26] Also, in dead patients with vascular events, D-dimer significantly elevated more than twice the normal value and was found to be more in patients with comorbidities (12.14%) than the patients without comorbidities (3.57%). [27] D-dimer elevated above the normal value but less than twice the normal value was also more in dead patients with vascular events having comorbidities (2.86%) than the dead patients without comorbidities (1.43%). [28] Our study is also comparable to another study, where they have demonstrated similar results that in COVID-19 patients, elevated D-dimer value was linked with a greater risk of life-threatening ailments like thrombosis, acute kidney injury, and mortality. [29] The novelty of our study compared with other studies is that this was the first study in India that checked the incidence of vascular events in COVID-19 patients with increased D-dimer values. In this study, the incidence of vascular events that occurred in COVID-19 has been determined. D-dimer value could be useful to clinicians in giving correct treatment and may also aid them effectively in preventing and managing vascular events. It could help the clinicians in tailoring guidelines to the individual patient treatment and admission to ICU. [29] It could also help in reducing morbidity and mortality. It could improve the prognosis and

minimize mortality by improving patient care. It could have a stronger implication for the community, physicians & institutions by helping in early recognition of the problem and earlier starting of anticoagulants before admission into the hospital.[30] This study may aid in segregating the patients for advanced care during the early phase of the disease, could help in evaluating the patient's prognosis, reducing the hospital stay and burden, initiating early correct treatment of the patient, providing early recovery and early discharge by curing the disease, reducing the progression of complications, preventing the late complication, halting the disease, and mainly by preventing the community spread of disease.[31] Most importantly, from this study, it may be inferred that even the smallest elevation in D-dimer value above the normal value in COVID-19 patients with comorbidities was at higher risk of getting vascular events like acute kidney injury, myocardial infarction, and stroke resulting in longer hospital stay, morbidity, and mortality. So, the COVID-19 patients with comorbidities having elevated D-dimer values should start early oral anticoagulants like rivaroxaban, and the patients with mild COVID having comorbidities should check D-dimer values, which can help in preventing the progression of the disease, hospital admission, and burden, and most importantly, it can prevent the development of vascular events leading to high morbidity and mortality.[32]

Conclusion

In this study, we were able to verify the incidence of vascular events that occurred in COVID-19 patients admitted to our hospital. We have found various vascular events like acute kidney injury, myocardial infarction, acute cerebrovascular accident, etc resulting in longer hospital stay, higher morbidity, and mortality, particularly in those with comorbidities having significantly elevated D-dimer value two times above the normal value. The incidence of COVID-19 patients with vascular events having comorbidities is 27.1%. The incidence of D-dimer significantly elevated in such patients with comorbidities is 18.57%. This proves the D-dimer to be the most important and reliable biomarker for COVID-19-related vascular complications in our study. D-dimer value can help clinicians in giving correct treatment and can aid them effectively in preventing and managing vascular events by earlier

starting of oral anticoagulants at-home isolation for COVID-19 patients with comorbidities showing elevated D-dimer value.

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