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Original Article

Pathology Section

Evaluating Elevated D-Dimer Levels Associated Clinical Conditions in Hospitalised Patients: A Cross-sectional Study

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ABSTRACT

Introduction: D-dimer is widely used to exclude Venous Thromboembolism (VTE) and to support the diagnosis of Disseminated Intravascular Coagulation (DIC). However, Elevated plasma D-dimer levels are not specific to thromboembolic disorders and may be observed in several non-thrombotic conditions such as infections, malignancies, inflammatory disorders, trauma, and postoperative states. This broad range of associated conditions complicates the interpretation of D-dimer results, particularly in resource-limited rural settings where the burden of infectious and inflammatory diseases is relatively high.

Aim: To study the clinical conditions associated with elevated plasma D-dimer levels in hospitalised patients.

Materials and Methods: The present cross-sectional, retrospective, laboratory database-based study was conducted in the Department of Pathology at a rural tertiary-care medical college in Western Maharashtra, India, from 1st October 2023 to 30th September 2024. Patients were selected from the Laboratory Information System (LIS) database based on records of quantitative plasma D-dimer testing performed during the study period. All consecutive hospitalised patients with at least one D-dimer value greater than 250 µg/L D-dimer Units (DDU), which represents the upper reference limit in the study laboratory, were included in the study. Demographic details, final clinical diagnosis, and selected laboratory parameters including Haemoglobin (Hb), Total Leukocyte Count (TLC), platelet count, Prothrombin Time/International Normalised Ratio (PT/INR), Activated Partial Thromboplastin Time (APTT), C-Reactive Protein (CRP), and other available laboratory investigations were retrieved from hospital records. Data were analysed using descriptive statistics.

Results: Among 349 D-dimer tests, 247 were >250 µg/L DDU. After excluding duplicate tests (n=6) and cases with insufficient clinical information (n=6), 235 patients were analysed (139 males, 59.1%; 96 females, 40.9%). D-dimer values ranged from 255 to 75,860 µg/L DDU (mean 2,604.3 µg/L). The commonest cause was dengue (133/235, 56.6%), comprising 129 NS1 antigen-positive and 4 IgM-positive cases. Cardiovascular disorders {Myocardial infarction, Atrial Fibrillation, post Coronary artery bypass graft surgery (CABG)} constituted 28/235 (11.9%), followed by sepsis (16/235, 6.8%) and thromboembolic conditions (12/235, 5.1%). Other causes included Acute Respiratory Distress Syndrome (ARDS), fracture/osteomyelitis, pregnancy-related conditions, malignancy, snakebite and acute febrile illness. Overall mortality was 35/235 (14.9%) and was predominantly seen in patients with moderate-to-severe D-dimer elevation.

Conclusion: In the current rural hospital cohort, elevated D-dimer levels were most frequently associated with infectious conditions particularly dengue followed by cardiovascular disorders and sepsis, whereas confirmed thromboembolic events represented a small proportion of cases. Extremely high values were observed in severe systemic illnesses such as sepsis and snakebite and were associated with poorer outcomes. These findings suggest that, in tropical rural settings, elevated D-dimer often reflects infection-related coagulation activation rather than isolated thromboembolism. Clinical interpretation should therefore be guided by the underlying disease context.

Keywords: Cardiovascular disease, Dengue, Fracture, Malignancy, Pregnancy, Sepsis, Snakebite, Thromboembolism

INTRODUCTION

D-dimer is a fibrin degradation product generated when cross-linked fibrin is cleaved by plasmin, reflecting activation of coagulation and secondary fibrinolysis. Because of its high sensitivity and negative predictive value, D-dimer testing is routinely used to exclude deep vein thrombosis and Pulmonary Embolism (PE) when combined with clinical probability assessment [1]. Nevertheless, D-dimer lacks specificity: elevations occur with infection, systemic inflammation, trauma, surgery, pregnancy, malignancy and organ failure, among others. In rural Indian hospitals, where infectious diseases and envenomation contribute substantially to acute admissions, the diagnostic yield and clinical implications of an elevated D-dimer may differ from western populations. A range of D-dimer assays are available, differing in aspects like the specific epitope targeted, techniques for capture and detection, and instrumentation employed [1-3].

Published literature has predominantly focused on VTE [1-5], while there is limited Indian rural data describing the broad diagnostic spectrum associated with elevated D-dimer and its relationship with outcomes. Understanding local epidemiology is essential to avoid misinterpretation of D-dimer, unnecessary imaging and delayed prioritisation of the true underlying illness.

The current research discussed D-dimer testing basics and explored causes of increased D-dimer levels in patients admitted to a tertiary hospital. It also analysed clinical outcomes of patients presenting with increased D-dimer concentrations. The aim of the present study was to assess D-dimer level distribution across major diagnostic categories and to document in-hospital outcome (survival vs mortality) in relation to D-dimer elevation.

MATERIALS AND METHODS

The Present cross-sectional, retrospective, laboratory database-based study conducted at the Department of Pathology, Rural

Medical College in Western Maharashtra, India from 1 October 2023 to 30 September 2024. Approved by the Institutional Ethics Committee (IEC No: BKLWRMC/IEC/127/2024).

Sample size calculation: All hospitalised patients for whom a quantitative plasma D-dimer test was performed and the reported value was >250 µg/L DDU during the study period.

Inclusion criteria:

- Inpatients with at least one D-dimer result >250 µg/L DDU;
- Availability of a final clinical diagnosis and outcome in the medical record.

Exclusion criteria:

- Duplicate repeat tests for the same admission (only the first eligible test retained);
- Incomplete clinical information preventing assignment to a diagnostic category.

Study Procedure

D-dimer assay: Quantitative D-dimer was measured on a fully automated coagulometer using a latex-enhanced turbidimetric immunoassay (wavelength 405 nm). Results were expressed as µg/L DDU. The D-Dimer Latex Reagent contains polystyrene latex particles coated with a monoclonal antibody specific to the D-Dimer domain in soluble fibrin derivatives. When plasma with D-dimer is combined with the latex reagent and reaction buffer, coated latex particles aggregate. The aggregation extent is proportional to the D-dimer concentration, measured by detecting decreased transmitted light at 405 nm (turbidimetric immunoassay). Sample collection used 3.2% trisodium citrate anticoagulant in a 9:1 blood-to-anticoagulant ratio. The results were expressed in µg/l DDU (D-dimer Units).

Variables recorded: Age, sex, D-dimer value, final clinical diagnosis, comorbidities (where documented) and selected laboratory tests (Hb, TLC, platelet count, PT/INR, APTT, CRP and others where available). Imaging performed following D-dimer testing (e.g., Doppler/CT angiography) was recorded and documented.

STATISTICAL ANALYSIS

Data were entered in Microsoft Excel and analysed descriptively. Continuous variables are summarised as mean and range; categorical variables as frequency and percentage.

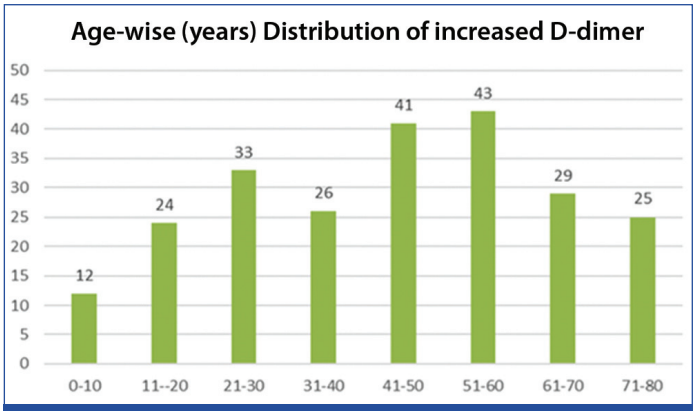
RESULTS

During the study period, 349 D-dimer tests were performed. Elevated D-dimer (>250 µg/L DDU) was observed in 247 tests. After excluding duplicate tests (n=6) and cases with insufficient clinical information (n=6), 235 unique patients were included for analysis. Sex distribution was 139 males (59.1%) and 96 females (40.9%).

Elevated d-dimer levels were observed less frequently in younger age groups than in older populations, as noted in [Table/Fig-1].

All recorded diagnoses were incorporated into the database, including instances of pregnancy and known cancer. Results of imaging procedures conducted after D-dimer testing were also documented. Diagnoses were organised into predetermined major disease categories [Table/Fig-2] along with their corresponding elevated D-dimer values.

D-dimer values ranged from 255 to 75,860 µg/L DDU (mean 2,604.3 µg/L). The distribution of major diagnostic categories associated with elevated D-dimer is summarised in [Table/Fig-1].



[Table/Fig-1]: Age-wise distribution of increased d-dimer levels.

Diagnosis category	n (%)	Predominant D-dimer range*	Notable high values	Deaths (n)
Dengue	133 (56.6)	255-2,500	Up to 37,900	8
Cardiovascular disorders (MI/AF/CABG/others)	28 (11.9)	255-2,500	AF up to 18,120	-
Sepsis/septic shock/DIC	16 (6.8)	255-5,000	Up to 22,075	-
ARDS	15 (6.4)	255-2,500	-	-
Thromboembolic conditions (DVT/PE/ stroke/CVST)	12 (5.1)	255-6,000	One case 11,750	-
Fracture / osteomyelitis	11 (4.7)	402-4,716	Up to 8,405	0
Pregnancy-related conditions	6 (2.6)	455-2,302	Postpartum infarct 11, 750	2
Malignancy	8 (3.4)	255-3,727	-	0
Snakebite	2 (0.9)	24,920-75,860	Extremely high	2
Acute febrile illness (non-dengue)	7 (3.0)	255-500	-	0

[Table/Fig-2]: D-dimer distribution across major diagnostic categories (µg/L DDU) and outcomes.
*Ranges are based on the available dataset and may overlap between categories.
DDU: D- Dimer unit; MI: Myocardial infarction; AF: Atrial fibrillation; CABG: Coronary artery bypass graft surgery; DIC: Disseminated intravascular coagulation; ARDS: Acute respiratory distress syndrome; DVT: Deep vein thrombosis; PE: Pulmonary embolism; CVST: Cerebral venous sinus thrombosis; Death counts are presented only for categories with available outcome data

Category-wise observations

Thromboembolic conditions: Twelve patients (5.1%) had documented thromboembolism (DVT, PE, cerebral infarction, superior sagittal sinus thrombosis). [Table/Fig-3] summarises D-dimer and available coagulation parameters in these cases.

Cardiovascular disorders: Elevated D-dimer was observed in 28 patients (11.9%) [Table/Fig-4]. Post-CABG patients showed mild elevations (<2,500 µg/L) consistent with postoperative inflammation. Atrial fibrillation cases had higher D-dimer values than myocardial infarction fatalities, suggesting increased fibrin turnover in AF.

Sepsis: This study encountered 16 patients (6.8%) with sepsis. Clinical and laboratory characteristics are summarised in [Table/Fig-5]. Deceased patients exhibited significantly elevated d-dimer levels compared to survivors.

Snakebite: Two cases of snakebite showed exceptionally high d-dimer values, as shown in [Table/Fig-6]. While plasma PT remained normal, APTT was elevated in both instances. One patient developed myotoxicity, evidenced by increased Creatine Kinase (CK) levels. Both patients experienced complications and did not survive.

Cancer: The study period revealed elevated D-dimer levels in various malignancies, as illustrated in [Table/Fig-7].

Pregnancy: As indicated in [Table/Fig-8], every pregnant case exhibited D-dimer levels exceeding 250 µg/L. Two patients did not survive, one with dengue who had D-dimer levels of 970 µg/L, and another with postpartum stroke whose D-dimer level reached 11750 µg/L.

Fracture: Of 235 cases where d-dimer levels surpassed 250 µg/L, Fracture was present in 11 cases (4.7%). Case 11 had femur fracture with associated osteomyelitis (D-dimer=904

S. No.	Age (in years)	Sex	Diagnosis	D-dimer (µg/L)	Homocysteine (µmol/L)	PT (sec)	INR	APTT (sec)
1	18	M	Infarct left thalamus	925	12.9	NA	NA	NA
2	22	F	DVT - lower limb	3752	0.2	15.1	1.22	NA
3	25	F	Brain infarct due to peripartum vasculitis	11750	11.63	14.9	1.1	39.6
4	34	M	Cerebral infarct	504	32.0	11.9	1.0	32.7
5	37	M	PE	427	0.7	20.6*	1.72	NA
6	52	M	PE	885	NA	14.7	1.26	NA
7	53	F	DVT	1011	NA	NA	NA	NA
8	56	F	DVT	5770	NA	15.0	1.29	NA
9	67	M	Superior sagittal sinus thrombosis	611	2.2	NA	NA	NA
10	68	F	Left lower limb DVT	800	NA	12.5	1.06	NA
11	75	M	Right lower limb DVT	794	24.93	12.9	1.02	NA
12	75	F	DVT	5235	NA	11.8	1.0	NA

[Table/Fig-3]: Thromboembolic conditions and laboratory parameters (corrected values marked with *).
DVT: Deep vein thrombosis

S. No.	Diagnosis	D-dimer (µg/L)	No	Diagnosis	D-dimer (µg/L)
1	Myocardial infarction	290	1	Atrial Fibrillation	6460
2	Myocardial infarction	5250	2	Atrial Fibrillation	18120
3	Myocardial infarction	1180	3	Atrial Fibrillation	9945
4	Myocardial infarction	3690			
5	Myocardial infarction	449			

[Table/Fig-4]: D-dimer levels in cardiac fatalities.

developed complications and did not survive. [Table/Fig-11] shows D-dimer levels and concurrent infections in non-survivors. Of the eight fatalities, one patient also had *P. Vivax*, another tested positive for H1N1, and a third was a pregnant woman in her trimester, with d-dimer levels of 37900, 726, and 970 µg/l, respectively. Amongst survivors, the youngest patient was three-month-old, the oldest 82-year-old. Both exhibited slightly elevated d-dimer levels of 513 and 449 µg/l. The comparative spectrum of elevated D-dimer across studies have been demonstrated in [Table/Fig-12] [2-6].

S. No.	Age (in years)	Sex	Outcome	Clinical diagnosis sepsis	D-dimer	FDP	Plt count	PT
1	25	M	Improved	Pneumonia	1869	Positive	153000	NA
2	74	F	DAMA	COPD	1159	NA	12000	12.5
3	24	M	Expired	Septic shock	8990	NA	206000	17.7
4	54	M	Improved	Pancreatitis	1880	NA	90000	16
5	18	M	Improved	Sepsis	808	NA	253000	13.5
6	78	M	Expired	sepsis	6565	NA	80000	NA
7	53	F	Expired	Sepsis, DIC	3466	NA	83000	NA
8	79	M	Expired	Pneumonia	2928	NA	271000	12.6
9	74	M	Expired	Sepsis	13495	NA	163000	NA
10	52	M	DAR	Sepsis	2190	NA	84000	15.5
11	46	F	DAR	Septic shock	2684	NA	193000	NA
12	53	F	Expired	AKI	22075	NA	420000	NA
13	61	F	Improved	Multiple ischiorectal abscesses	4630	NA	277000	NA

[Table/Fig-5]: Diagnostic tests in sepsis cases.
FDP: Fibrin degradation products; Plt count: Platelet count; PT: Prothrombin time; DAMA: Discharged against medical advice; COPD: Chronic obstructive pulmonary disease; DIC: Disseminated intravascular coagulation; NA: Not available; DAR: Discharged at request; AKI: Acute kidney injury

S. No.	Age (in years)	Sex	Clinical outcome	D-dimer (µg/L)	PT(Sec)	INR	APTT (Sec)
1	5	M	Expired	24920	13.7	1.17	33.1
2	64	M	Expired	75860	13.5	1.17	72.47

[Table/Fig-6]: Raised D-dimer levels in snakebite.
DDU: D-dimer Units, PT: prothrombin time; INR: International normalised ratio
APTT: Activated partial thromboplastin time

microgram/L) and is included under fracture/osteomyelitis; therefore [Table/Fig-9] and [Table/Fig-10] contain 11 cases. [Table/Fig-9] provides details about the affected bones, as well as patient age and gender, which may explain the observed differences in d-dimer levels.

As illustrated in [Table/Fig-10] the diverse d-dimer measurements for identical bone fractures. D-dimer levels in both cases of fractured femur are different.

Dengue: Dengue infections constitute many diagnosed cases. Dengue was diagnosed in 133/235 cases (56.6%): 129 were NS1 antigen-positive and 4 were IgM-positive. Among these, eight

DISCUSSION

The present hospital-based study highlights that elevated D-dimer primarily reflects activation of coagulation and secondary fibrinolysis rather than a disease-specific diagnosis. Although widely used in VTE exclusion algorithms, D-dimer is a global biomarker of fibrin turnover and is influenced by inflammatory, malignant, infectious, traumatic and physiological states [1].

Western literature, particularly emergency department cohorts enriched for suspected PE, frequently identifies VTE as a leading cause of markedly elevated D-dimer. Schutte T et al., demonstrated that extremely elevated levels were often associated with VTE, malignancy and severe infection, with many patients having multiple concurrent diagnoses [2]. Similarly, Choi J et al., evaluating ultra-high D-dimer values (>5000 µg/L), reported a substantial prevalence of VTE and cancer but emphasised that such elevations are not VTE-specific [3]. These studies largely represent selected populations with high pretest probability.

S. No.	Age (in years)	Sex	Clinical diagnosis	D-dimer (µg/L)	PT Sec	INR	APTT Sec	Doppler
1	37	F	Leukaemia	806	10.8	0.98	42	Not available
2	47	F	Lymphoma (vasculitis)	3727	11.4	0.89	36	Not available
3	65	F	Ovarian cancer Convulsions	255	-	-	-	Normal
4	68	M	Mid-oesophagus Squamous cell carcinoma	413	15.3	1.34	37	Normal
5	73	F	Cervixca Right lower limb cellulitis	2435	11.7	0.9	42.1	suggestive of Peripheral artery diseases
6	74	f	Buccalmucosa Squamous cell carcinoma	693	11.9	0.92	36	Normal
7	78	M	Nasopharyngeal carcinoma	996	12.2	1.02	37	Normal
8	78	M	Buccalmucosa Squamous cell carcinoma	2690	12.3	1.0	36.4	Normal

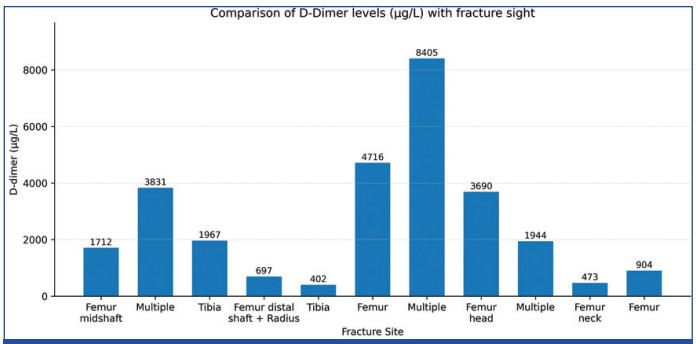
[Table/Fig-7]: D-dimer levels in various malignancies.
PT: Prothrombin time; INR: International normalised ratio; APTT: Activated partial thromboplastin time

S. No.	Age (in years)	Clinical outcome	Associated Condition	D-dimer (µg/L)	FDP	plt	PT	INR	DIC Score
1	37	Improved	Pregnancy	455	Neg	247000	11	0.9	NA
2	42	Improved	Abruptio	587	neg	150000	15.5	1.37	NA
3	23	Improved	Dengue IUD	726	NEG	48000	10.4	0.86	NA
4	27	Expired	Dengue IUD	970	NEG	27000	NA	NA	NA
5	28	Improved	Abruptio	2302	411	108000	11.8	0.9	<5
6	25	Expired	Postpartum Brain infarct	11750	409	100000	14.9	1.1	>5

[Table/Fig-8]: D-dimer levels in pregnancy.
FDP: Fibrin degradation products; Plt: Platelet count; PT: Prothrombin time; INR: International normalised ratio; DIC: Disseminated intravascular coagulation; IUD: Intrauterine death. NA: Not available

S. No.	Age (in years)	Sex	Diagnosis	Site of Fracture	D-dimer ((µg/L))
1	17	M	Fracture	Femur midshaft	1712
2	20	M	Fracture	Multiple	3831
3	34	M	Fracture	Tibia	1967
4	36	M	Fracture	Femur-distal shaft Radius	697
5	37	M	Fracture	Tibia	402
6	45	F	Fracture	Femur	4716
7	47	M	Fracture	Multiple	8405
8	75	M	Fracture	Femurhead	3690
9	75	F	Fracture	Multiple	1944
10	79	F	Fracture	Femurneck	473
11	59	F	Fracture	Osteomyelitis Femur	904

[Table/Fig-9]: D-dimer levels in fractures, including one femur fracture with associated osteomyelitis.



[Table/Fig-10]: D-Dimer levels in different fracture sites.

Age-adjusted D-dimer thresholds have been validated to safely reduce unnecessary imaging in suspected PE populations [4], reinforcing the principle that interpretation must always be contextual and probability-driven rather than threshold-driven alone. In contrast, unselected hospitalised medical cohorts demonstrate a broader etiological spectrum. Review literature emphasises infection, malignancy and systemic inflammatory states as predominant contributors to elevated D-dimer, often exceeding isolated thromboembolic events [1].

S. No.	Age	Sex	Clinical details	D-dimer (µg/L)
1	14	F	Dengue	512
2	65	M	Dengue+H1N1	726
3	27	F	Dengue+30 week pregnancy	970
4	65	M	Dengue	2193
5	65	F	Dengue+Leptospira	2314
6	48	M	Dengue	11900
7	43	F	Dengue	21585
8	57	F	Dengue+*Plasmodium vivax* Malaria	37900

[Table/Fig-11]: Clinical details and D-Dimer levels in dengue-related deaths.

In the present rural tertiary-care cohort, infectious aetiologies-particularly dengue and sepsis accounted for the majority of elevated D-dimer cases, while confirmed VTE constituted only 5.1%. This pattern aligns more closely with Indian Intensive Care Unit (ICU) and tropical inpatient data than Western PE-enriched emergency cohorts.

To contextualise the findings of the present study, a structured comparison with representative Indian and Western cohorts is presented below.

The contrast between Western and Indian data is striking. Western emergency-based studies enriched for suspected PE naturally demonstrate higher VTE prevalence because of selection bias and referral patterns [2-4]. In contrast, Indian ICU and medical inpatient cohorts, similar to present study, show predominance of infection and systemic inflammation [5]. This epidemiological difference is critical when applying diagnostic algorithms developed in high-income countries to rural tropical settings. A reflex imaging strategy based solely on elevated D-dimer may lead to over-investigation in low-prevalence populations. These findings therefore reinforce that D-dimer interpretation must be population-specific and integrated with validated clinical prediction rules.

Sepsis-induced coagulopathy results from cytokine-mediated endothelial injury, thrombin generation and secondary fibrinolysis. Elevated D-dimer correlates strongly with organ dysfunction and mortality [6]. Meta-analytic evidence supports its prognostic value

Study	Setting	Population	Predominant causes	VTE proportion	Interpretation
Present study (Rural India)	Tertiary rural hospital	Unselected medical inpatients	Dengue, Sepsis, Cardiac disorders	5.1%	Infection-driven fibrinolysis predominates
Schutte T et al., 2016 [2]	Netherlands	Extremely elevated D-dimer	VTE, Cancer, Sepsis	High	Extreme values indicate severe systemic illness
Choi J et al., 2021 [3]	USA	Ultra-high D-dimer	VTE, Malignancy	Moderate–High	Not specific for thrombosis
Righini M et al., 2014 [4]	Europe	Suspected PE cohort	VTE-focused	High (selected)	Age-adjusted cut-offs reduce imaging
Sahu KK et al., 2020 [5]	India ICU	Critically ill patients	Sepsis, ARDS	Lower than Western	Correlates with severity
Berger JS et al., 2020 [6]	USA	Viral infection cohort	Severe viral illness	Variable	Inflammation-driven elevation

[Table/Fig-12]: Comparative spectrum of elevated D-dimer across studies [2-6].
VTE: Venous thromboembolism; USA: United States of America; ICU: Intensive care unit; ARDS: Acute respiratory distress syndrome

but not its specificity for thromboembolism [7]. The study cohort demonstrated similar patterns, where D-dimer elevation paralleled sepsis severity rather than confirmed VTE.

Dengue is a major driver of coagulation activation in tropical regions. Endothelial dysfunction, plasma leakage and secondary fibrinolysis contribute to significant D-dimer elevation, particularly in severe dengue [8]. Viral systemic illnesses have also been associated with elevated D-dimer independent of thrombosis [9]. The predominance of dengue in the present study explains the infection-driven fibrinolytic pattern observed.

D-dimer elevation in cardiovascular disease reflects chronic endothelial dysfunction and thrombin generation. Atrial fibrillation is associated with significantly higher D-dimer levels, reflecting embolic risk rather than acute thrombosis [10]. The study cohort demonstrated similar elevations in cardiovascular disorders without proportional VTE confirmation.

Cancer-associated hypercoagulability arises from tumor-derived procoagulants and inflammatory cytokines. Elevated D-dimer correlates with advanced stage and adverse outcomes [11]. Persistent unexplained elevation warrants evaluation for occult malignancy. Venom-Induced Consumption Coagulopathy (VICC) is underrepresented in Western literature but clinically relevant in rural India. Early extreme D-dimer elevation may precede conventional coagulation abnormalities [12], making it a useful early biomarker in tropical toxicology settings. Trauma-related elevation reflects tissue injury, inflammation and immobilisation-associated fibrin turnover. Wide inter-individual variability limits specificity for thromboembolism [13].

Across diverse clinical conditions, D-dimer functions as a biomarker of systemic activation of coagulation and fibrinolysis rather than a disease-specific indicator. While Western studies on D-dimer predominantly focus on thromboembolic disorders such as VTE, data from Indian and other tropical settings, including the findings of the present study, demonstrate a predominance of infectious and inflammatory etiologies associated with elevated levels. Therefore, D-dimer results should always be interpreted in the context of clinical pretest probability when considering further imaging for suspected thrombosis. Additionally, regional epidemiological factors play an important role in determining the aetiological spectrum of elevated D-dimer levels. In many clinical scenarios, increased D-dimer reflects the overall severity of the underlying illness and systemic inflammatory response rather than the presence of isolated thrombotic disease.

Limitation(s)

The present study has certain limitations. The retrospective laboratory database–based design involved physician-directed D-dimer testing, which may have introduced selection bias. In addition, complete coagulation parameters such as fibrinogen, serial PT/APTT, and FDP were not available for all patients, limiting the application of formal DIC scoring systems. Imaging confirmation for VTE was also not uniformly available in all suspected cases. Furthermore, as this was a single-centre study from a rural tertiary-care setting, the findings may not be fully generalisable to other regions or healthcare settings.

CONCLUSION(S)

In the present cross-sectional rural hospital cohort, elevated D-dimer was predominantly attributable to non-thrombotic causes- especially dengue, cardiovascular disorders, sepsis and snakebite- while confirmed thromboembolism constituted a small fraction. Markedly raised values were associated with severe systemic illness and mortality. D-dimer should be interpreted in conjunction with clinical context and pre-test probability, rather than as a stand-alone indicator of VTE.

REFERENCES

[1] Linkins LA, Takach Lapner S. Review of D-dimer testing: Good, bad, and ugly. Int J Lab Hematol.2017;39(Suppl 1):98-103.
[2] Schutte T, Thijs A, Smulders YM. Never ignore extremely elevated D-dimer levels: They are specific for serious illness. Neth J Med. 2016;74(10):443-48.
[3] Schafer K, Goldschmidt E, Oostra D, Fish J, Russell T, Lurie F. The clinical significance of ultra-high D-dimer levels. J Vasc Surg Venous Lymphat Disord. 2022;10(1):08-13.
[4] Righini M, Van Es J, Den Exter PL, Roy PM, Verschuren F, Ghuysen A, et al. Age-adjusted D-dimer cutoff levels to rule out pulmonary embolism: The ADJUST-PE study. JAMA. 2014;311(11):1117-24.
[5] Lian H, Cai H, Zhang H, Ding X, Wang X, Zhang S. The Prediction Value of D-Dimer on Prognosis in Intensive Care Unit among Old Patients (≥65 Years): A 9-Year Single-Center Retrospective Study of 9261 Cases. Oxid Med Cell Longev. 2022 Sep 22;2022:2238985.
[6] Levi M, van der Poll T. Coagulation and sepsis. Thromb Res. 2017;149:38-44.
[7] Ramya KN, Katta NS, Kumar AV, Aditya C. An Assessment Of D-Dimer Levels as A Prognostic Marker in Patients with Sepsis in A Tertiary Care Hospital. International Journal of Medical and Pharmaceutical Research. 2026;7:3410-16.
[8] Setrkraising K, Bongsebandhu-phubhakdi C, Voraphani N, Pancharoen C, Thisyakorn U, Thisyakorn C et al. D-dimer as an indicator of dengue severity. Asian Biomed. 2007;1(1):53-57.
[9] Berger JS, Kunichoff D, Adhikari S, Ahuja T, Amoroso N, Aphinyanaphongs Y, et al. Prevalence and outcomes of D-dimer elevation in patients with infections. Arterioscler Thromb Vasc Biol. 2020;40(10):2539-47.
[10] Danese E, Montagnana M, Cervellin G, Lippi G. Hypercoagulability, D-dimer and atrial fibrillation. Ann Med. 2014;46(6):364-71.
[11] Ay C, Dunkler D, Pirker R, Thaler J, Quehenberger P, Wagner O, et al. High D-dimer levels are associated with poor prognosis in cancer patients. Haematologica. 2012;97(8):1158-64.
[12] Isbister GK, Noutsos T, Jenkins S, Isoardi KZ, Soderstrom J, Buckley NA. D-dimer testing for early detection of venom-induced consumption coagulopathy after snakebite in Australia (ASP-29). Med J Aust. 2022;217(4):203-07.
[13] Cushman M, Folsom AR, Wang L, Aleksic N, Rosamond WD, Tracy RP et al. Fibrin fragment D-dimer and the risk of future venous thrombosis. Blood. 2003;101(4):1243-8.

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