



## ORIGINAL- ARTICLE



# Prognostic value of d dimer in ischemic stroke

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### Abstract

**Background:** Stroke is a major contributor to both disability and death worldwide. Meanwhile, the D-dimer blood test has become an increasingly valuable tool in diagnostic protocols for ruling out venous thromboembolism. This test detects the presence of D-dimer, a substance that forms during the breakdown of blood clots containing fibrin, making it a straightforward and effective means of screening for this condition. Numerous research studies have explored the relationship between plasma hemostatic markers and the outcomes of acute ischemic stroke (AIS). Within this area of investigation, one particular marker that has received a great deal of attention is D-dimer. This substance has emerged as a focal point of research into its potential role in AIS, with multiple studies examining its impact on this condition. **Aim of stud:** To evaluate the prognostic value of D-dimer in patients with ischemic stroke **Patients and methods:** Prospective control study of 67 patients admitted to hospital with ischemic stroke envaulted by D-dimer assay at admission and evaluate for prognostic value of D- dimer in Versus with 69 healthy control individuals **Results and discussion:** In this study There is significant difference between D-dimer level between patients with ischemic stroke and control group with P value 0.0001 Our findings were consistent with results of previous prospective studies showing that D-dimer levels were elevated in the acute phase of AIS compared with the healthy control population The results of this study suggest that there is no significant correlation between levels of D-dimer and the presence of complications, venous thrombosis, or mortality. Additionally, the study found a weak correlation between D-dimer levels and the occluded artery or the volume of infarction, with non-significant P values in both ANOVA and ETA analyses. However, D-dimer levels were found to be higher in cases of middle cerebral artery occlusion compared to occlusion of smaller vessels. Another study conducted by Anna Ramos et al found that higher levels of D-dimer were independently associated with large vessel occlusion (LVO), even after adjusting for other biomarkers and clinical covariates. This association may be due to the composition and quantity of the thrombus, as larger and fibrin-rich thrombi tend to result in a greater increase in D-dimer levels. Higher D-dimer levels have also been observed in patients with larger pulmonary or deep vein thrombosis in previous studies. **Conclusion** Is this study we conclude close relationship between the ischemic stroke and D-dimer but no clear association with complications during hospitalization and volume and type of blood vessel involved of stroke and we need large sample and 30 days follow to assess their correlation

**Key words:** Stroke, D-dimer ,prognostic ,complications, venous thrombosis

## 1 | BACKGROUND

Stroke is a major contributor to both mortality and physical disability worldwide, with ischemic stroke accounting for nearly 80% of all strokes. This type of stroke occurs as a result of cerebral blood

vessel occlusion. Several factors have been identified as being associated with acute ischemic stroke (AIS) outcomes, such as age, gender, stroke severity, atrial fibrillation, congestive heart failure, and diabetes. However, even experienced neurologists find it challenging to predict outcomes in AIS patients. Therefore, it is essential to identify

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new predictors to assist with managing this condition. In recent years, numerous studies have investigated the relationship between plasma hemostatic markers and AIS outcomes. One marker that has received considerable attention in this regard is D-dimer, which has emerged as a focus of research in the field of AIS. (1),(2).

The D-dimer blood test has become an increasingly valuable tool in diagnostic algorithms for ruling out venous thromboembolism in low-risk groups. This test detects the presence of D-dimer, a substance that forms during the breakdown of blood clots containing fibrin, making it a straightforward and effective means of screening for this condition. D-dimer levels have several advantages over other measures of thrombin generation, including resistance to *ex vivo* activation, relative stability, and a long half-life(3).

The concentration of D-dimer in the bloodstream provides valuable information about the extent of fibrin turnover in the body. D-dimer is a degradation product resulting from the cleavage of cross-linked fibrin by plasmin, and its presence indicates the breakdown of blood clots. Research has shown that even modest increases in circulating D-dimer values may reflect minor increases in blood coagulation, thrombin formation, and turnover of cross-linked intravascular fibrin, which may be associated with coronary heart disease. Studies have also found that elevated D-dimer concentrations are positively associated with coronary heart disease incidence and recurrence, regardless of traditional risk factors.

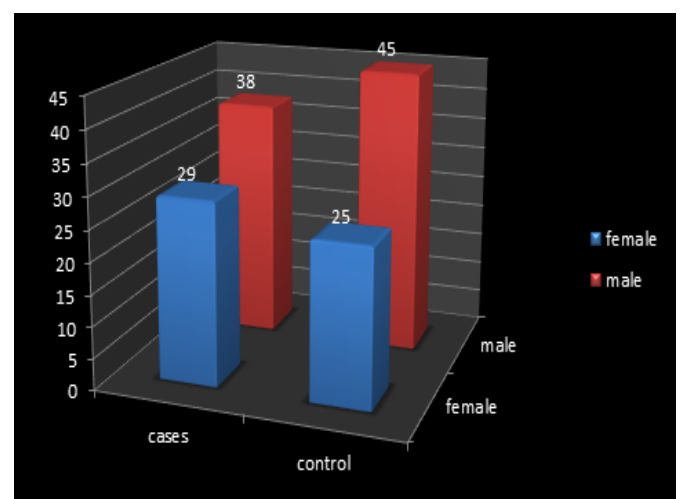
Furthermore, high levels of D-dimer have been linked to cerebral venous sinus thrombosis. (4),(5),(6) (7) In medical research, various studies have explored the association between D-dimer levels and different health conditions. For instance, D-dimer levels have been linked to acute pulmonary embolism and spontaneous intracerebral hemorrhage, as well as long-term neurologic outcomes in Childhood-Onset Arterial Ischemic Stroke. Additionally, prior research has suggested that D-dimer levels could be associated with specific subtypes of health conditions, and may be useful in assessing prognosis and predicting bad outcomes for patients with ischemic stroke or traumatic brain injury. Therefore, D-dimer may serve as an important indicator of disease severity and prognosis in various clinical settings. (8),(9),(10),(11),(12),(13), (14),(15).

In clinical practice Abnormal elevation of D-dimer levels is a crucial clinical indicator of thrombosis, while low levels can effectively rule out critical thromboembolic events such as deep venous thrombosis (DVT) and pulmonary embolism (PE). Although studies have demonstrated the association between D-dimer levels and long-term mortality in the general population, only a limited number of studies have investigated the correlations between D-dimer levels and stroke risk, as well as adverse clinical outcomes in patients who have already experienced a stroke. (16),(17),(18),(19),(20),(21)

## 2 | PATIENTS AND METHODS

A prospective study was conducted on 67 patients who were admitted to the hospital due to ischemic stroke. The study aimed to evaluate the prognostic value of D-dimer, which was measured using an assay at the time of admission. The results were compared with those of 69 healthy individuals who served as control subjects in the study.

## 3 | RESULTS AND DISCUSSION



**Figure 1:** Distribution of studied population according to their gender

$\chi^2 = 0.821$ ,  $p = 0.387$ ,  $OR = 1.374$

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In this study there is no significant difference sex difference between stroke group and control group [P value 9.387] but in stroke group male is more effected than female [38:29] as seen in figure 1 which goes with most epidemiological studies

**Table 1:** Distribution of cases and control according D-Dimer

Case. Control	D-Dimer		Total	X <sup>2</sup> , P value, Odd's ratio
	Normal	High		
<b>Cases</b>	36	31	67	32.339
	53.7%	46.3%	48.9%	0.0001
<b>Control</b>	67	3	70	0.561
	95.7%	4.3%	51.1%	
<b>Total</b>	103	34	137	
	75.2%	24.8%	100.0%	

The results of this study indicate a significant difference in D-dimer levels between patients with ischemic stroke and the control group, with a P value of 0.0001. These findings align with previous prospective studies that have demonstrated elevated D-dimer levels in the acute phase of AIS when compared to the healthy control population. (22),(23) Smith et al (24) reported that D-dimer could predict incident stroke in the general population, even though no significant association was seen in the Three-City French cohort study (25)

**Table 2:** D-Dimer according Sex

Sex		D-Dimer		Total	
		Normal	High		
Female		37	17	54	2.121
		68.5%	31.5%	100.0%	0.145
Male		66	17	83	0.862
		79.5%	20.5%	100.0%	
<b>Total</b>	<b>Count</b>	103	34	137	
	<b>% within Sex</b>	75.2%	24.8%	100.0%	

In our study there is no significant difference in d-dimer between male and female in normal and high levels [ P values 0.145 and 0.862]

**Table 3:** Distribution of studied population according to their age

	N	Mean	S. D	Minimum	Maximum	ANOVA, P
<b>Age Case</b>	67	65.63	10.863	36	86	87.227
<b>Control</b>	70	51.60	6.182	40	67	.0001
<b>Total</b>	137	58.46	11.233	36	86	

There is significant difference regarding mean age between ischemic group and control group p value 0.001

**Table 4:** Distribution of studied population according to their and D-dimer

D. Dimer	Case	67	559.39	672.144	126	5680	15.841
<b>Control</b>	70	231.64	148.507	29	528	.0001	
<b>Total</b>	137	391.93	507.418	29	5680		

This table showed that D0dimer is significantly elevated in ischemic group versus control group as table 1

**Table5:** Relationship of D. Dimer with Sex, complication venous thrombo-embolism and death

	Sex	N	Mean	S. D.	ANOVA, P, ETA
Sex	Female	29	538.0357	250.11812	0.120
	Male	38	582.4737	870.18438	.887
Complication	No	62	548.3710	693.72937	.221
	Yes	5	696.0000	299.83996	.640
Venous thrombo-embolism	No	61	567.1311	702.37854	.089
	Yes	6	480.6667	187.81125	.766
Death	No	59	575.6780	712.93370	.287
	Yes	8	439.2500	171.67307	.594
<b>Total</b>		67	559.3881	672.14426	.066

In this study there is no correlation between d-dimer level and presence of complications, venous thrombosis and even death

Sienkiewicz-Jarosz et al conducted a study to assess the levels of D-dimer in patients with acute ischemic stroke at different time points, including admission, and at 24 and 72 hours after stroke onset. They found that patients with poor outcomes (mRS ≥3) had significantly higher D-dimer levels compared to those with good outcomes at all three

time points. The increase in D-dimer levels in patients with poor outcomes was more prominent at 48 hours. Furthermore, elevated D-dimer levels on admission and at 24 hours were significantly associated with poor outcome. However, the association between D-dimer levels and outcome was not significant at 48 hours. Therefore, more studies are needed to investigate the relationship between D-dimer levels on admission, which is not influenced by therapy, and outcomes in patients with acute ischemic stroke. (26)

Alessandro Squizzato and colleagues found that although there was no significant difference in mean D-dimer levels between patients who died and those who survived after an acute cerebrovascular event, there was a higher mortality risk associated with D-dimer levels of at least 0.50 µg/ml. However, after adjusting for age and stroke subtype, this association was not significant. Furthermore, the mean D-dimer levels were similar between patients who did and did not experience a new vascular event, and D-dimer levels of at least 0.50 µg/ml did not predict an increased risk of subsequent events. Based on these findings, it seems that D-dimer levels measured in the acute phase after an acute cerebrovascular event do not predict the long-term clinical outcome. (27)

**Table 6:** Distribution of D-Dimer mean according to brain imaging among stroked patients:

Brain imaging	Mean	N	S. D	ANOVA, P, ETA
ACA	602.7500	4	380.78811	.202
Brain stem	505.8333	6	280.08743	.984
Cerebellar	504.4000	10	252.06489	.153
Lacunar	435.5000	6	117.62610	
MCA	647.5152	33	926.11774	
PCA	368.0000	6	201.71564	
Thalamic	290.0000	1	.	
Total	559.3881	67	672.14426	

This study did not find a significant correlation between D-dimer levels and the specific artery occluded or the volume of infarction (non-significant ANOVA and ETA values). However, there was a higher occurrence of elevated D-dimer levels in patients with middle cerebral artery

occlusion compared to occlusion of smaller vessels. In contrast, Anna Ramos and colleagues found a significant association between D-dimer levels and large vessel occlusion (LVO) even after adjusting for other biomarkers and clinical factors. This relationship between D-dimer and LVO may be attributed to the composition and quantity of thrombus, with larger and fibrin-rich thrombi leading to greater increases in D-dimer levels. Higher D-dimer levels have also been observed in patients with larger pulmonary or deep vein thrombosis. (28)

#### 4 | CONCLUSION

The findings of this study suggest a strong correlation between D-dimer levels and ischemic stroke. However, there was no clear association between D-dimer levels and the occurrence of complications during hospitalization, or the volume and type of blood vessel involved in the stroke. To further investigate these correlations, larger sample sizes and longer follow-up periods of at least 30 days may be necessary.

#### REFERENCES

1. prognostic role of early D-dimer level in patients with acute ischemic stroke Jing Zhang, Lin Liu, Jie Tao, Yanlin Song, Yimeng Fan, Maling Gou, Jianguo Xu Published: February 1, 2019 <https://doi.org/10.1371/journal.pone.0211458>
2. Wang J, Ning R, Wang Y. Plasma D-dimer Level, the Promising Prognostic Biomarker for the Acute Cerebral Infarction Patients. *J Stroke Cerebrovascular Dis.* 2016;25(8):2011–5. Epub 2016/05/29. pmid:27234921. • View Article PubMed/NCBI Google Scholar
3. Lowe G (2005) Fibrin D-dimer and cardiovascular risk. *Semin Vasc Med* 5: 387–398. [PubMed] [Google Scholar]

4. Lowe GD, Rumley A (1999) Use of fibrinogen and fibrin D-dimer in prediction of arterial thrombotic events. *Thromb Haemost* 82: 667–672. [PubMed] [Google Scholar]
5. Lippi G, Filippozzi L, Montagnana M, Salvagno GL, Guidi GC (2008) Diagnostic value of D-dimer measurement in patients referred to the emergency department with suspected myocardial ischemia. *J Thromb Thrombolysis* 25: 247–250. [PubMed] [Google Scholar]
6. Barber M, Langhorne P, Rumley A, Lowe GD, Stott DJ (2006) D-dimer predicts early clinical progression in ischemic stroke: confirmation using routine clinical assays. *Stroke* 37: 1113–1115. [PubMed] [Google Scholar]
7. Meng R, Wang X, Hussain M, Dornbos D 3rd, Meng L, et al. (2013) Evaluation of plasma d-dimer plus fibrinogen in predicting acute CVST. *Int J Stroke*; doi: 10.1111/ij.s.12034. [Epub ahead of print] [PMC free article] [PubMed]
8. Gutte H, Mortensen J, Jensen C V, Von der Recke P, Petersen CL, et al. (2010) ANP, BNP and D-dimer predict right ventricular dysfunction in patients with acute pulmonary embolism. *Clin Physiol Funct Imaging* 30: 466–472. [PubMed] [Google Scholar]
9. Chiu CC, Li YN, Lin LJ, Hsiao CT, Hsiao KY, et al. (2012) Serum D-dimer as a predictor of mortality in patients with acute spontaneous intracerebral hemorrhage. *J Clin Neurosci* 19: 810–813. [PubMed] [Google Scholar]
10. Goldenberg NA, Jenkins S, Jack J, Armstrong-Wells J, Fenton LZ, et al. (2013) Arteriopathy, D-Dimer, and Risk of Poor Neurologic Outcome in Childhood-Onset Arterial Ischemic Stroke. *J Pediatr* 162: 1041–1046. [PMC free article] [PubMed] [Google Scholar]
11. Montaner J, Perea-Gainza M, Delgado P, Ribó M, Chacón P, et al. (2008) Etiologic diagnosis of ischemic stroke subtypes with plasma biomarkers. *Stroke* 39: 2280–2287. [PubMed] [Google Scholar]
12. Hiltunen S, Putaala J, Haapaniemi E, Salonen O, Tatlisumak T (2013) D-dimer and clinic radiologic features in cerebral venous thrombosis. *J Neurol Sci* 327: 12–13. [PubMed] [Google Scholar]
13. Brouns R, Van Den Bossche J, De Surgeloose D, Sheorajpanday R, De Deyn PP (2009) Clinical and biochemical diagnosis of small-vessel disease in acute ischemic stroke. *J Neurol Sci* 285: 185–190. [PubMed] [Google Scholar]
14. Hudak AM, Caesar RR, Frol AB, Krueger K, Harper CR, et al. (2005) Functional outcome scales in traumatic brain injury: a comparison of the Glasgow Outcome Scale (Extended) and the Functional Status Examination. *J Neurotrauma* 22: 1319–1326. [PubMed] [Google Scholar]
15. Ungerstedt JS, Grenander A, Bredbacka S, Blombäck M (2003) Clotting onset time may be a predictor of outcome in human brain injury: a pilot study. *J Neurosurg Anesthesiol* 15: 13–18. [PubMed] [Google Scholar]
16. Taylor HA Jr., Wilson JG, Jones DW, Sarpong DF, Srinivasan A, Garrison RJ, et al. Toward resolution of cardiovascular health disparities in African Americans: design and methods of the Jackson Heart Study. *Ethn Dis.* (2005) 15(Suppl. 6):S6-4-17. doi:10.1097/00001648-200509000-00256 PubMed Abstract | CrossRef Full Text | Google Scholar
17. Duprez DA, Otvos J, Sanchez OA, Mackey RH, Tracy R, Jacobs DR Jr. Comparison of the predictive value of Glyc A and other biomarkers of inflammation for total death, incident cardiovascular events, no cardiovascular and noncancer inflammatory-related events, and total cancer events. *Clin Chem.* (2016) 62:1020–31. doi:10.1373/clinchem.2016.255828 PubMed Abstract | CrossRef Full Text | Google Scholar
18. Di Castelnuovo A, Agnoli C, de Curtis A, Giurdanella MC, Sieri S, Mattiello A, et al. Elevated levels of D-dimers increase the risk of ischemic and hemorrhagic stroke. Findings from the EPICOR Study. *Thromb Haemost.* (2014) 112:941–6. doi: 10.1160/th14-04-0297 PubMed Abstract | CrossRef Full Text | Google Scholar

19. Folsom AR, Gottesman RF, Appiah D, Shahar E, Mosley TH. Plasma d-Dimer and incident ischemic stroke and coronary heart disease: the atherosclerosis risk in community's study. *Stroke*. (2016) 47:18–23. doi: 20.1161/STROKEAHA.115.011035 PubMed Abstract | Cross Ref Full Text | Google Scholar
20. Zhang J, Liu L, Tao J, Song Y, Fan Y, Gou M, et al. Prognostic role of early D-dimer level in patients with acute ischemic stroke. *PLoS ONE* . (2019) 14:e0211458. doi: 10.1371/journal.pone.0211458 PubMed Abstract | CrossRef Full Text | Google Scholar
21. Wang J, Ning R, Wang Y. Plasma D-dimer Level, the promising prognostic biomarker for the acute cerebral infarction patients. *J Stroke Cerebrovascular Dis.*(2016) 25:2011–5. doi:10.1016/j.jstrokecerebrovasdis.2015.12.031 Pub Med Abstract | CrossRef Full Text | Google Scholar
22. Kataoka S, Hirose G, Hori A, Shirakawa T, Saigan T (2000) Activation of thrombosis and fibrinolysis following brain infarction. *J Neurol Sci* 181: 82–88. [PubMed] [Google Scholar]
23. Tombul T, Atbas C, Anlar O (2005) Hemostatic markers and platelet aggregation factors as predictive markers for type of stroke and neurological disability following cerebral infarction. *J Clin Neurosci* 12: 429–434. [PubMed] [Google Scholar]
24. Smith A, Patterson C, Yarnell J, Rumley A, Ben-Shlomo Y, et al. (2005) Which hemostatic markers add to the predictive value of conventional risk factors for coronary heart disease and ischemic stroke? The Caerphilly Study. *Circulation* 112: 3080–3087. [PubMed] [Google Scholar]
25. Carcaillon L, Gaussem P, Ducimetiere P, Giroud M, Ritchie K, et al. (2009) Elevated plasma fibrin D-dimer as a risk factor for vascular dementia: the Three-City cohort Study. *J Thromb Haemost* 7: 1972–1978. [PubMed] [Google Scholar]
26. Sienkiewicz-Jarosz H, Galecka-Wolska M, Bidzinski A, Turzynska D, Sobolewska A, Lipska B, et al. Predictive value of selected biochemical markers of brain damage for functional outcome in ischemic stroke patients. *Neurol Neurochir Pol.* 2009;43(2):126–33.Epub 2009/06/02. pmid:19484689.View Article PubMed/NCBI Google Scholar
27. D-dimer is not a long-term prognostic marker following acute cerebral ischemia Squizzato, Alessandro; Ageno, Waltera; Finazzi, Sergiob; Mera, Valentina; Romualdi, Erica; Bossi, Annac; Venco, Achillea Author Information *Blood Coagulation & Fibrinolysis*: June 2006 - Volume 17 - Issue 4 - p 303-306doi:10.1097/01.mbc.0000224850.57872.d0
28. D-Dimer as Predictor of Large Vessel Occlusion in Acute Ischemic Stroke Anna Ramos-Pachón, Elena López-Cancio, Alejandro Bustamante, Natàlia Pérez de la Ossa, Mònica Millán, Maria Hernández-Pérez, Teresa Garcia-Berrocoso, Pere Cardona, Marta Rubiera, Joaquín Serena, Xavier Ustrell, Moisés Garcés, Mikel Terceño, Antoni Davalos and Montaner Originally published 10 Feb 2021 <https://doi.org/10.1161/STROKEAHA.120.031657>Stroke.2021;52:852–858

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