RJNMSR
Review Journal of Neurological & Medical Sciences Review

Volume 4, Issue 5, 2026

PREDICTIVE ACCURACY OF PLASMA D-DIMER LEVELS IN PREDICTING POOR NEUROLOGICAL OUTCOMES IN PATIENTS WITH ACUTE ISCHAEMIC STROKE: A PROSPECTIVE STUDY FROM A TERTIARY CARE HOSPITAL IN LAHORE, PAKISTAN

Dr. Muhammad Saeed Akhtar[*1], Dr. Muhammad Haroon[2], Dr. Sayed Mahdi[3], Dr. Nasiruddin[4], Dr. Mohammad Omar Yousofzai[5], Dr. Fatima Zahara[6]

*[*1,2,4,5]Department of Medicine, Mayo Hospital / King Edward Medical University, Lahore, Pakistan*
[3]MS General surgery, Sir GangaRam hospital, Lahore, Pakistan
[6]MBBS UHS, Lahore, Pakistan

[*1]miansaeed62@gmail.com

Corresponding Author: *
Dr. Muhammad Saeed Akhtar
DOI: https://doi.org/10.5281/zenodo.20284269

Received	Accepted	Published
22 March 2026	01 May 2026	19 May 2026

ABSTRACT

Introduction: *Acute ischaemic stroke (AIS) is a leading cause of death and disability worldwide. Timely neurological stratification is critical but often limited by delayed radiological access. Plasma D-dimer, a fibrin degradation product reflective of coagulation activity, has emerged as a promising, inexpensive biomarker for stroke severity prediction.*

Objective: *To determine the predictive accuracy of plasma D-dimer levels in predicting poor neurological outcomes in AIS, using the National Institutes of Health Stroke Scale (NIHSS) as the gold standard.*

Study Design: *Prospective cross-sectional study.*

Setting: *Department of Medicine, Mayo Hospital (King Edward Medical University), Lahore, Pakistan.*

Duration: *December 2, 2023 to June 2, 2024.*

Methods: *Three hundred and twenty-one consecutive patients with first-episode AIS presenting within 24 hours were enrolled using non-probability consecutive sampling. Plasma D-dimer (threshold ≥310 ng/mL) was measured at admission. NIHSS was used to classify stroke severity. Sensitivity, specificity, PPV, NPV, and diagnostic accuracy were calculated. Stratified analyses were performed by age group and gender.*

Results: *The mean age was 52.63 ± 12.89 years. Males comprised 54.21% (n=174). Mean NIHSS was 8.74 ± 8.34. Against NIHSS-defined severe outcome (n=16), D-dimer achieved: sensitivity 87.50%, specificity 96.39%, PPV 56.00%, NPV 99.32%, and accuracy 95.95%. Stratified analyses demonstrated consistently high specificity (≥93%) across all age groups and genders, with highest sensitivity in the 61–70 age group (100%) and in females (90.0%).*

Conclusion: *Elevated plasma D-dimer (≥310 ng/mL) is a diagnostically accurate, low-cost biomarker for identifying poor neurological outcomes in AIS. Its exceptionally high NPV (99.32%) makes it a reliable rule-out tool in resource-limited settings.*

Keywords: *Acute ischaemic stroke; D-dimer; NIHSS; diagnostic accuracy; biomarker; Pakistan; tertiary care.*

INTRODUCTION

Stroke is defined as the sudden onset of a focal neurological deficit caused by disruption of cerebral blood flow. It is among the top causes of death and long-term disability globally. Approximately 15 million acute stroke events occur annually and an estimated 55 million people worldwide are living with its sequelae.[1] In Pakistan, the incidence of stroke has been reported at 250 per 100,000 population, placing a substantial burden on an already stretched healthcare infrastructure.[2]

Ischaemic stroke constitutes over 62% of all stroke events globally and is associated with significant morbidity, healthcare costs, and years of productive life lost.[3] Timely neurological stratification is critical for guiding therapeutic decisions, including eligibility for thrombolytic therapy. However, radiological confirmation is frequently delayed: computed tomography (CT) may appear normal in the early hours of infarction, and magnetic resonance imaging (MRI) is not universally available across tertiary centres in Pakistan. These delays can result in missed or deferred thrombolysis in otherwise eligible patients.[4]

The National Institutes of Health Stroke Scale (NIHSS) is a validated tool for objectively quantifying neurological deficit after stroke, widely adopted as the clinical gold standard for stroke severity assessment.[5] While reliable, its application depends on trained assessors and real-time clinical evaluation, limiting its use as a rapid biochemical triage parameter.

D-dimer is a fibrin degradation product released during fibrinolysis of cross-linked fibrin. Elevated D-dimer levels reflect heightened coagulation and thrombolytic activity, including intravascular clot formation and resolution. D-dimer is well established in the diagnosis of venous thromboembolism and disseminated intravascular coagulation.[6] Emerging evidence suggests it also correlates with stroke severity, infarct volume, and neurological progression in AIS.[7] Critically, D-dimer can be measured rapidly and inexpensively from a peripheral blood sample — properties that make it particularly attractive in resource-limited settings.

Despite these potential advantages, published data from Pakistan on the diagnostic accuracy of D-dimer against NIHSS-defined outcomes in AIS patients remains scarce. This prospective study was designed to determine the predictive accuracy of plasma D-dimer in identifying severe neurological outcomes in patients with AIS presenting to a large tertiary care centre in Lahore, using NIHSS as the gold standard.

PATIENTS AND METHODS

Study Design and Setting

This was a prospective, cross-sectional study conducted in the Department of Medicine, Mayo Hospital, Lahore — a major government tertiary care and teaching institution affiliated with King Edward Medical University. The study was carried out over six months, from 2 December 2023 to 2 June 2024.

Sample Size and Sampling

Sample size was calculated using reference sensitivity of 90.9% and specificity of 89.4% for D-dimer in predicting poor outcome in AIS, an expected poor-outcome prevalence of 20.3%, a margin of error of 7%, and 95% confidence level.[8] This yielded a minimum sample of 321 patients. Enrolment used non-probability consecutive sampling.

Inclusion and Exclusion Criteria

Adults aged 18–70 years of either sex presenting within 24 hours of first-episode ischaemic stroke were eligible. Ischaemic stroke was confirmed by new-onset focal motor deficit with a corresponding contralateral hypodense area on CT scan. Patients with recurrent stroke, haemorrhagic stroke confirmed on CT, or active anticoagulant therapy at presentation were excluded.

Data Collection and Measurements

Written informed consent was obtained from each participant or, where the patient lacked capacity, from an authorised family representative. Baseline demographic data (age, sex) and clinical assessment using the NIHSS were documented. Stroke severity was classified as minor (NIHSS 1–4), moderate (NIHSS 5–15), moderate-to-severe (NIHSS 16–20), or severe (NIHSS 21–42), in line with established NIHSS categories. For the primary binary diagnostic analysis, an NIHSS score indicating severe stroke (≥16) was designated the "poor outcome" threshold, consistent with prior literature.

Three millilitres of venous blood were drawn within the first 24 hours of admission and sent to the Central Laboratory, Mayo Hospital, for plasma D-dimer estimation. A level of ≥310 ng/mL was defined as elevated (positive), in accordance with the laboratory reference range. All routine baseline investigations — including renal function tests, fasting lipid profile, coagulation profile, serum electrolytes, and complete blood count — were performed concurrently.

Statistical Analysis

Data were entered and analysed using SPSS version 25.0. Quantitative variables were expressed as mean ± standard deviation (SD). Categorical variables were reported as frequencies and percentages. The diagnostic performance of D-dimer was assessed by computing sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy against NIHSS-defined severe outcome. A 2×2 contingency table was constructed. Post-stratification analyses were performed by age group and gender. All calculations were verified against the raw dataset.

RESULTS

Baseline Characteristics

A total of 321 patients with first-episode acute ischaemic stroke were enrolled. Demographic and clinical characteristics are summarised in Table 1. The mean age was 52.63 ± 12.89 years (range 18–70 years). Of the total, 174 patients (54.21%) were male and 147 (45.79%) were female. The mean serum creatinine was 1.02 ± 0.41 mg/dl and mean total cholesterol was 179.83 ± 48.26 mg/dl. The mean NIHSS score across the cohort was 8.74 ± 8.34.

Table 1: Baseline demographic and clinical characteristics (n = 321)

Variable	Value
Age – Mean ± SD (years)	52.63 ± 12.89
Age – Range (years)	18 – 70
Gender – Male	174 (54.21%)
Gender – Female	147 (45.79%)
Serum Creatinine – Mean ± SD (mg/dl)	1.02 ± 0.41
Total Cholesterol – Mean ± SD (mg/dl)	179.83 ± 48.26
NIHSS Score – Mean ± SD	8.74 ± 8.34

Stroke Severity Distribution

On NIHSS assessment, the majority of patients had moderate stroke: 185 patients (57.63%) scored 5–15, followed by 120 patients (37.38%) in the minor category (NIHSS 1–4). Fourteen patients (4.36%) had severe stroke (NIHSS 21–42) and 2 patients (0.62%) had moderate-to-severe stroke (NIHSS 16–20). The combined group with NIHSS ≥16 (n=16) formed the "poor outcome"

reference group for the primary diagnostic analysis (Table 2).

Table 2: Distribution of stroke severity by NIHSS category (n = 321)

Stroke Severity (NIHSS Category)	n	%	Cumulative %
Minor (NIHSS 1–4)	120	37.38	37.38
Moderate (NIHSS 5–15)	185	57.63	95.01
Moderate-to-Severe (NIHSS 16–20)	2	0.62	95.63
Severe (NIHSS 21–42)	14	4.36	100.00
Total	**321**	**100.00**	–

Overall Diagnostic Performance of D-Dimer

Table 3 presents the 2×2 contingency table comparing D-dimer positivity (≥310 ng/mL) against NIHSS-defined severe outcome (NIHSS ≥16). Of the 16 patients with severe outcome, D-dimer correctly identified 14 (true positives). Of the 305 patients without severe outcome, 294 were correctly classified as D-dimer negative (true negatives). Eleven patients without severe NIHSS had elevated D-dimer (false positives), and 2 patients with severe NIHSS had a negative D-dimer (false negatives).

Overall, D-dimer achieved a sensitivity of 87.50%, specificity of 96.39%, PPV of 56.00%, NPV of 99.32%, and a diagnostic accuracy of 95.95%. The high NPV indicates that a negative D-dimer effectively excludes severe neurological deficit in this population.

Table 3: Diagnostic performance of D-dimer vs. NIHSS-defined poor outcome (n = 321)

D-Dimer Result	NIHSS Poor Outcome (Yes; n=16)	NIHSS No Poor Outcome (No; n=305)	Diagnostic Statistics
Positive (≥310 ng/mL; n=25)	14 (TP)	11 (FP)	**Sensitivity = 87.50% Specificity = 96.39%**
Negative (<310 ng/mL; n=296)	2 (FN)	294 (TN)	**PPV = 56.00% NPV = 99.32% Accuracy = 95.95%**

TP = True Positive; FP = False Positive; FN = False Negative; TN = True Negative; PPV = Positive Predictive Value; NPV = Negative Predictive Value.

Stratification by Age Group

Age-stratified diagnostic performance is presented in Table 4. No severe-outcome events occurred in the 18–30 (n=30) or 31–40 (n=19) age groups; sensitivity and PPV are therefore not calculable for these strata. Specificity remained high across all age groups (≥93.5%). The 41–50 age group (n=51) demonstrated a sensitivity of 80.0% with perfect specificity (100%) and PPV (100%). The 51–60 group (n=116), which contained the largest number of patients, showed a sensitivity of 87.5% and specificity of 93.5%. The 61–70 group (n=105) achieved the highest sensitivity of 100% with a specificity of 97.1%. Diagnostic accuracy across groups ranged from 93.10% to 100.00%. Grand totals across all age groups verify to the primary table: TP=14, FP=11, FN=2, TN=294.

Table 4: Age-stratified diagnostic performance of D-dimer vs. NIHSS (n = 321)

Age Group	n	TP	FP	FN	TN	Sensitivity	Specificity	PPV	NPV	Accuracy
18–30	30	0	1	0	29	—†	96.7%	—†	100.0%	96.67%
31–40	19	0	0	0	19	—†	100.0%	—†	100.0%	100.00%
41–50	51	4	0	1	46	80.0%	100.0%	100.0%	97.9%	98.04%
51–60	116	7	7	1	101	87.5%	93.5%	50.0%	99.0%	93.10%
61–70	105	3	3	0	99	100.0%	97.1%	50.0%	100.0%	97.14%
Total	**321**	**14**	**11**	**2**	**294**	–	–	–	–	**95.95%**

† Sensitivity and PPV not calculable — no patients with NIHSS-defined poor outcome in this age stratum.

Stratification by Gender

Gender-stratified results are presented in Table 5. In male patients (n=174), D-dimer achieved a sensitivity of 83.3%, specificity of 98.8%, PPV of 71.4%, and NPV of 99.4%, with a diagnostic accuracy of 98.28%. In female patients (n=147), sensitivity was slightly higher at 90.0%, with specificity of 93.4%, PPV of 50.0%, NPV of 99.2%, and accuracy of 93.20%. The NPV was consistently high in both sexes (>99%), indicating reliable rule-out performance regardless of gender. Grand totals verify to the primary table.

Table 5: Gender-stratified diagnostic performance of D-dimer vs. NIHSS (n = 321)

Gender	n	TP	FP	FN	TN	Sensitivity	Specificity	PPV	NPV	Accuracy
Male	174	5	2	1	166	83.3%	98.8%	71.4%	99.4%	98.28%
Female	147	9	9	1	128	90.0%	93.4%	50.0%	99.2%	93.20%
Total	**321**	**14**	**11**	**2**	**294**	**87.5%**	**96.4%**	**56.0%**	**99.3%**	**95.95%**

DISCUSSION

This prospective study evaluated the accuracy of plasma D-dimer (threshold ≥310 ng/mL) in predicting NIHSS-defined poor neurological outcomes in 321 patients with first-episode AIS at a tertiary care centre in Lahore, Pakistan. The primary finding is that D-dimer achieved an overall diagnostic accuracy of 95.95%, with a sensitivity of 87.50%, a specificity of 96.39%, and a clinically outstanding NPV of 99.32%. These results, derived from verified raw data, support D-dimer as a reliable triage biomarker in settings where advanced neuroimaging may not be immediately available.

The mean age of 52.63 ± 12.89 years in our cohort is substantially younger than the mean of 78 years reported by Nam et al. (2023) in South Korean patients.[9] This is consistent with broader epidemiological evidence showing an earlier age of stroke onset in South Asian populations, likely attributable to higher prevalence of uncontrolled hypertension, type 2 diabetes, and tobacco use at younger ages in Pakistan. The male predominance (54.21%) aligns with the 56.5% reported by Nam et al., reflecting the well-established higher stroke incidence in males.[9] Mean total cholesterol in our cohort (179.83 mg/dl) was modestly higher than the 162 mg/dl observed in the Nam et al. series, suggesting differing cardiovascular risk profiles.

The overall sensitivity (87.50%) and specificity (96.39%) of D-dimer in this study are comparable to previously published data. Dhar et al. reported sensitivity of 90.9% and specificity of 89.4% for D-dimer in predicting poor short-term outcomes in AIS patients in Bangladesh.[8] A prospective study

by Yao et al. found that plasma D-dimer ≥0.315 mg/L was associated with poor functional outcome with sensitivity 83.8% and specificity 41.4%, noting that the lower specificity was partly attributable to confounding comorbidities.[10] Our specificity of 96.39% using a similar threshold compares favourably, potentially reflecting stricter enrolment criteria excluding anticoagulated patients.

The NPV of 99.32% is the most clinically impactful result of this study. In practical terms, fewer than 1% of patients with a negative D-dimer will have a severe neurological deficit as defined by NIHSS ≥16. This near-perfect rule-out performance means D-dimer can be confidently used to rapidly de-prioritise patients from intensive neurological intervention pathways in busy emergency settings — a particularly valuable characteristic in resource-constrained centres across Pakistan where NIHSS assessment by a trained physician may not always be immediately available.

The relatively modest PPV of 56.00% is an expected statistical consequence of the low prevalence of the severe-outcome group (4.99% of the cohort with NIHSS ≥16). D-dimer elevations are not specific to severe stroke and can occur across the coagulation-inflammatory cascade in moderate and even minor strokes. The PPV should therefore be interpreted in the context of clinical pre-test probability: in patients with an already moderate-to-severe clinical presentation, a positive D-dimer provides additional prognostic weight.

Age-stratified analysis revealed important nuances. The two youngest age groups (18–30 and 31–40) had no patients with severe NIHSS, rendering sensitivity incalculable for these strata — this likely reflects the lower biological likelihood of catastrophic stroke in younger adults rather than a limitation of D-dimer per se. Specificity was ≥93.5% across all age groups, confirming D-dimer's consistent rule-out capability regardless of patient age. The highest sensitivity was observed in the 61–70-year group (100%), consistent with the greater severity and extent of infarction expected in older patients with longer vascular risk factor exposure.

Gender-stratified analysis showed comparable performance in males (sensitivity 83.3%, specificity 98.8%) and females (sensitivity 90.0%, specificity 93.4%). The slight difference in PPV between genders (male 71.4% vs. female 50.0%) likely reflects the higher number of female patients with false-positive D-dimer elevations (n=9 vs. n=2 in males), possibly related to hormonal or coagulation differences. Importantly, NPV was ≥99% in both groups, confirming consistent rule-out performance across sexes.

Several limitations of this study should be acknowledged. The cross-sectional design provides a single-timepoint assessment and does not capture longitudinal functional outcomes such as 90-day modified Rankin Scale (mRS) scores. The single-centre setting may limit generalisability to community hospitals with different patient demographics. D-dimer was measured at one point on admission; serial measurements may improve predictive utility. Lastly, conditions that independently elevate D-dimer — such as atrial fibrillation, active malignancy, and recent surgery — were not systematically excluded beyond the stated criteria, and their contribution to the observed false-positive rate cannot be fully excluded.

CONCLUSION

Plasma D-dimer at a threshold of ≥310 ng/mL is a diagnostically accurate, cost-effective, and rapidly available biomarker for identifying severe neurological outcomes in patients with acute ischaemic stroke. Against NIHSS-defined poor outcome, it demonstrated an overall accuracy of 95.95%, sensitivity of 87.50%, and an outstanding NPV of 99.32%. Its consistently high specificity across all age groups and both sexes makes it a reliable rule-out tool in Pakistani tertiary care emergency departments where advanced neuroimaging may not be immediately accessible. Incorporation of D-dimer into routine AIS assessment protocols may facilitate early risk stratification and support timely, evidence-based therapeutic decisions.

ACKNOWLEDGEMENTS

The authors acknowledge the patients and their families who consented to participate in this study,

and the staff of the Department of Medicine and the Central Laboratory, Mayo Hospital, Lahore, for their cooperation in data collection.

Conflict of Interest: None declared.
Funding: No external funding was received for this study.
Ethical Approval: Obtained from the Institutional Review Board, King Edward Medical University / Mayo Hospital, Lahore.

REFERENCES

1. Grotta JC. Fifty years of acute ischemic stroke treatment: a personal history. Cerebrovasc Dis. 2021;50(6):666-80.
2. Farooq A, Venketasubramanian N, Wasay M. Stroke care in Pakistan. Cerebrovasc Dis Extra. 2021;11(3):118-21.
3. GBD 2019 Stroke Collaborators. Global, regional, and national burden of stroke 1990-2019. Lancet Neurol. 2021;20(10):795-820.
4. Abbas NI, Sayed O, Samir S, et al. D-dimer level is correlated with prognosis, infarct size, and NIHSS in acute ischemic stroke. Indian J Crit Care Med. 2021;25(2):193-8.
5. Kwah LK, Diong J. National Institutes of Health Stroke Scale (NIHSS). J Physiother. 2014;60(1):61.
6. Spronk E, Sykes G, Falcione S, et al. Hemorrhagic transformation in ischemic stroke and the role of inflammation. Front Neurol. 2021;12:661955.
7. Yang XY, Gao S, Ding J, et al. Plasma D-dimer predicts short-term poor outcome after acute ischemic stroke. PLoS One. 2014;9(2):e89756.
8. Dhar K, Habib M, Ghose SK, et al. Short-term outcome in patients with acute ischemic stroke on the basis of admission plasma D-dimer level. Bangladesh J Neurosci. 2018;34(2):72-8.
9. Nam KW, Kwon HM, Lee YS. Clinical significance of D-dimer levels during the acute period in ischemic stroke. Thromb J. 2023;21(1):1-8.
10. Yao T, Tian BL, Li G, et al. Elevated plasma D-dimer levels are associated with short-term poor outcome in patients with acute ischemic stroke: a prospective, observational study. BMC Neurol. 2019;19(1):1-8.
11. Park YW, Koh EJ, Choi HY. Correlation between serum D-dimer level and volume in acute ischemic stroke. J Korean Neurosurg Soc. 2011;50(2):89-94.
12. Khan MS, Ahmad S, Ghafoor B, et al. Inpatient assessment of neurological outcome in acute stroke patients based on NIHSS. Ann Med Surg. 2022;82.
13. Berge E, Friis P, Sandset PM. Hemostatic activation in acute ischemic stroke. Thromb Res. 2001;101(2):13-21.
14. Ferrari F, Moretti A, Villa RF. Hyperglycemia in acute ischemic stroke: physiopathological and therapeutic complexity. Neural Regen Res. 2022;17(2):292-9.
15. Hahne K, Mönnig G, Samol A. Atrial fibrillation and silent stroke: links, risks, and challenges. Vasc Health Risk Manag. 2016;12:65-74.