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Correlation Between Plasma D-Dimer Levels, Stroke Severity, and TOAST Classification in Patients with Acute Ischemic Stroke: A Cross-Sectional Analysis

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Abstract: ***Background**: Acute ischemic stroke (AIS) is a major cause of morbidity and mortality, especially in developing countries. D-dimer, a marker of fibrin degradation, reflects thrombotic activity and may correlate with stroke severity and etiology. **Objective**: To assess the association of plasma D-dimer levels with stroke severity and etiological subtypes (TOAST classification) in AIS. **Methods**: This hospital-based cross-sectional study included 80 adults with imaging-confirmed AIS (March 2023–February 2025). Patients with conditions affecting coagulation were excluded. Stroke severity was assessed using NIHSS. Plasma D-dimer levels were measured within 72 hours. Etiology was classified by TOAST criteria. Statistical analysis was performed using SPSS, with $p<0.05$ considered significant. **Results**: Mean age was 60.76±12.87 years. Large artery atherosclerosis was most common (72.5%), followed by cardioembolism (18.8%) and small vessel occlusion (8.8%). All patients had elevated D-dimer (mean 1.91±1.01 µg/mL). Levels were highest in cardioembolic stroke (3.64±0.72 µg/mL; $p<0.001$). A significant positive correlation existed between D-dimer and NIHSS ($r=0.448$, $p<0.001$). Elevated levels were also associated with poor outcomes ($p=0.034$). **Conclusion**: Plasma D-dimer correlates with stroke severity, etiology, and outcomes, supporting its role as a cost-effective biomarker for early risk stratification in AIS.***

Keywords: Acute ischemic stroke, D-dimer, NIHSS, TOAST classification, stroke severity

1. Introduction

Acute ischemic stroke (AIS) is a major global health concern and a leading cause of mortality and long-term disability, particularly in low- and middle-income countries. It is the second leading cause of death worldwide and a significant contributor to disability-adjusted life years (DALYs).[1,2] India contributes substantially to the global stroke burden, accounting for nearly 10% of cases, with an incidence of 105–172 per 100,000 population per year, and a tendency to occur at a younger age due to a high prevalence of vascular risk factors.[3]

The pathophysiology of AIS involves thrombus formation secondary to vascular injury, platelet activation, and activation of the coagulation cascade, followed by fibrinolysis. D-dimer, a degradation product of cross-linked fibrin, reflects ongoing thrombotic and fibrinolytic activity and has been associated with infarct size, stroke severity, and adverse clinical outcomes.[6, 7, 11]

Etiological classification using the TOAST system provides a standardized framework for identifying stroke subtypes, each with distinct mechanisms and prognostic implications.[4] Stroke severity is commonly assessed using the NIHSS, a validated clinical tool correlating with neurological deficit and outcome.[5] Elevated D-dimer levels have shown significant association with stroke subtype, severity, and prognosis.[8, 9, 14]

However, data from semi-urban Indian populations remain limited. Therefore, this study aims to evaluate the association of plasma D-dimer levels with stroke severity and TOAST classification in patients with AIS.

Aim:
To assess plasma D-dimer levels in relation to TOAST classification in patients with acute ischemic stroke

Objectives:
- To determine plasma D-dimer levels in patients with acute ischemic stroke.
- To analyse the variation of plasma D-dimer levels among different TOAST subtypes (large artery atherosclerosis, cardioembolic, small vessel occlusion, and others)

2. Literature Review

Acute ischemic stroke (AIS) remains a major global health burden and a leading cause of mortality and long-term disability worldwide.[1,2] Plasma D-dimer, a degradation product of cross-linked fibrin, reflects activation of coagulation and fibrinolysis and has been widely studied as a potential biomarker in AIS.[6]

Several studies have demonstrated that plasma D-dimer levels are elevated in patients with AIS and are associated with increased thrombotic activity and risk of stroke.[6,11] As a readily available and cost-effective laboratory parameter, D-dimer has gained importance in evaluating disease severity and prognosis.[7]

Multiple studies have reported a significant association between D-dimer levels and stroke severity. Elevated D-dimer levels have shown a positive correlation with NIHSS scores, indicating greater neurological impairment and larger infarct size.[9, 14, 15] Additionally, higher D-dimer levels have been linked to early neurological deterioration and disease progression.[9]

With respect to etiological classification, significant variation in D-dimer levels has been observed across different stroke subtypes. Cardioembolic stroke is consistently associated with higher D-dimer levels compared to other subtypes, likely due to the presence of large fibrin-rich emboli and increased systemic thrombotic activity.[8, 12] The TOAST classification provides a standardized framework for categorizing these subtypes and understanding their pathophysiological differences.[4]

Furthermore, elevated D-dimer levels have been associated with poor clinical outcomes and increased mortality in patients with AIS.[7],[10] Higher levels at admission have been shown to predict unfavorable functional outcomes and worse prognosis.[10]

Despite these findings, D-dimer is a non-specific biomarker and may be influenced by various systemic conditions.[6] Therefore, it should be interpreted in conjunction with clinical assessment and neuroimaging findings.[5]

Overall, existing literature supports the role of plasma D-dimer as a useful adjunct biomarker in assessing stroke severity, etiological subtype, and prognosis. However, variability in findings and lack of standardized cutoff values highlight the need for further research, particularly in diverse and semi-urban populations.[1],[3]

3. Materials And Methods

This hospital-based observational cross-sectional study was conducted at Sri Siddhartha Medical College and Hospital, Tumakuru, a tertiary care teaching institution, between March 2023 and February 2025. All consecutive patients presenting with acute ischemic stroke (AIS) during the study period were included. Data were obtained from case records, laboratory investigations, and radiological findings.

Patients aged ≥18 years with a diagnosis of AIS confirmed by neuroimaging (computed tomography or magnetic resonance imaging) were eligible for inclusion. Patients with hemorrhagic stroke and those with conditions known to influence coagulation and fibrinolytic activity—including sepsis, malignancy, recent surgery, trauma, pregnancy, deep vein thrombosis, severe anemia, and chronic liver or renal disease—were excluded. Patients with incomplete clinical or laboratory data were also excluded. A total of 80 patients fulfilling the inclusion criteria were included in the final analysis.

Etiological classification was performed according to the TOAST criteria into large artery atherosclerosis, cardioembolic stroke, small vessel occlusion, and other subtypes, based on clinical evaluation, imaging findings, and relevant cardiac and vascular investigations.[4] Stroke severity was assessed at admission using the National Institutes of Health Stroke Scale (NIHSS) by trained clinicians.[5]

Plasma D-dimer levels were measured within 72 hours of stroke onset using a standardized immunoturbidimetric assay, reflecting ongoing coagulation and fibrinolytic activity.[6, 7] Demographic details, clinical characteristics, risk factors, stroke subtype, plasma D-dimer levels, and NIHSS scores were recorded using a structured case record format. All data were verified for accuracy and completeness prior to statistical analysis.

Statistical Analysis

Data analysis was performed after completion of data collection and verification. The collected data were entered into Microsoft Excel and analyzed using the Statistical Package for the Social Sciences (SPSS), version 22.0. Data cleaning and validation were carried out by cross-checking entries with case records, laboratory reports, and imaging findings to ensure accuracy and completeness.

Categorical variables such as gender and stroke subtypes based on the TOAST classification were summarized using frequencies and percentages[4] Continuous variables such as age, plasma D-dimer levels, and NIHSS scores were expressed as mean ± standard deviation.[5]

Comparison of plasma D-dimer levels across different TOAST subtypes was performed using appropriate statistical tests (analysis of variance [ANOVA] or equivalent non-parametric tests, as applicable). The correlation between plasma D-dimer levels and NIHSS score was assessed using Pearson's correlation coefficient, consistent with previously reported methodologies evaluating the association between D-dimer levels and stroke severity.[7],[14]

A p-value of <0.05 was considered statistically significant.

4. Results

Demographic Characteristics

A total of 80 patients with acute ischemic stroke were included in the study. The mean age of the study population was 60.76 ± 12.87 years. The majority of patients belonged to the middle-aged and elderly age groups. There was a nearly equal gender distribution among the study participants.

Stroke Subtype Distribution (TOAST Classification)

Based on the TOAST classification, large artery atherosclerosis was the most common subtype, observed in 58 patients (72.5%). Cardioembolic stroke was identified in 15 patients (18.8%), while small vessel occlusion was seen in 7 patients (8.8%). No cases of stroke of other determined or undetermined etiology were identified in the present study.

Plasma D-dimer Levels

All patients demonstrated elevated plasma D-dimer levels (>0.5 µg/mL). The overall mean plasma D-dimer level was 1.91 ± 1.01 µg/mL. Plasma D-dimer levels showed a statistically significant variation across different TOAST subtypes ($p < 0.001$). The highest mean D-dimer levels were observed in cardioembolic stroke (3.64 ± 0.72 µg/mL),

followed by large artery atherosclerosis, whereas the lowest levels were seen in small vessel occlusion.

Stroke Severity (NIHSS)

Stroke severity was assessed using the NIHSS score at the time of admission. A progressive increase in plasma D-dimer levels was observed with increasing stroke severity categories. Patients with higher NIHSS scores demonstrated significantly elevated D-dimer levels compared to those with mild stroke ($p < 0.001$).

Correlation Analysis

A statistically significant moderate positive correlation was observed between plasma D-dimer levels and NIHSS score ($r = 0.448$, $p < 0.001$). This indicates that higher plasma D-dimer levels are associated with greater neurological impairment and increased severity of stroke.

Clinical Outcome

Clinical outcomes were assessed during the hospital course. Elevated plasma D-dimer levels were significantly associated with poor clinical outcomes and mortality ($p = 0.034$). Patients with higher D-dimer levels were more likely to have unfavorable outcomes compared to those with lower levels.

Statistical Analysis and Inferences

A statistically significant association was observed between plasma D-dimer levels and stroke subtypes based on TOAST classification ($p < 0.001$). Patients with cardioembolic stroke demonstrated significantly higher D-dimer levels compared to other subtypes.

Furthermore, plasma D-dimer levels showed a significant positive correlation with stroke severity as measured by NIHSS score ($p < 0.001$), indicating that increased thrombotic activity is associated with more severe neurological deficits.

Additionally, elevated plasma D-dimer levels were significantly associated with poorer clinical outcomes ($p = 0.034$), suggesting its potential role as a prognostic biomarker in acute ischemic stroke

Table 1: Demographic characteristics of patients

Variable	Frequency	Percentage
Total Patients	80	100%
Sex: Male	42	52.5%
Sex: Female	38	47.5%
Age ≤40	16	20.0%
Age 41–60	36	45.0%
Age >60	28	35.0%
Mean Age (years)	60.76 ± 12.87	—

Table 2: Stroke subtype distribution (TOAST classification)

Stroke Subtype	Frequency	Percentage
Large artery atherosclerosis	58	72.5%
Cardioembolic	15	18.8%
Small vessel occlusion	7	8.8%
Other/Undetermined	0	0.0%

Table 3: Plasma D-dimer levels across TOAST subtypes

Stroke Subtype	Mean D-dimer (µg/mL)	SD	p-value
Large artery atherosclerosis	1.62	0.74	
Cardioembolic	3.64	0.72	
Small vessel occlusion	0.92	0.41	
Overall Comparison	—	—	**<0.001**

Table 4: Stroke severity based on NIHSS

Severity Category	Frequency	Percentage
Mild (0–4)	18	22.5%
Moderate (5–15)	42	52.5%
Severe (>15)	20	25.0%

Table 5: Comparison of D-dimer levels across NIHSS categories

NIHSS Category	Mean D-dimer (µg/mL)	SD	p-value
Mild	1.02	0.45	
Moderate	1.88	0.79	
Severe	2.96	0.88	
Overall Comparison	—	—	**<0.001**

Table 6: Association between D-dimer levels and clinical outcome

Outcome	Mean D-dimer (µg/mL)	SD	p-value
Favorable outcome	1.52	0.68	
Poor outcome	2.74	0.91	
Overall Comparison	—	—	**0.034**

Table 7: Association between TOAST subtype and D-dimer levels

Stroke Subtype	Elevated D-dimer (%)	p-value
Large artery atherosclerosis	72.4%	
Cardioembolic	100%	
Small vessel occlusion	57.1%	
Overall Comparison	—	**<0.001**

5. Discussion

The present study provides valuable insights into the relationship between plasma D-dimer levels, stroke severity, and etiological subtypes in patients with acute ischemic stroke. The findings highlight a significant association of elevated D-dimer levels with both stroke severity and TOAST classification, along with its potential role as a prognostic biomarker.[7,8]

In the present study, the mean age of the patients was 60.76 ± 12.87 years, with a nearly equal gender distribution. The majority of patients belonged to the middle-aged and elderly population, consistent with the known epidemiology of acute ischemic stroke.[1,3] This reflects the increasing burden of vascular risk factors such as hypertension, diabetes mellitus, and dyslipidemia in this age group.

With regard to etiological classification, large artery atherosclerosis was the most common subtype (72.5%), followed by cardioembolic stroke (18.8%) and small vessel occlusion (8.8%). These findings are consistent with previous studies, where large artery atherosclerosis remains the predominant subtype.[3,4]

A key finding of the present study was the significant variation in plasma D-dimer levels across different stroke subtypes ($p < 0.001$). The highest levels were observed in cardioembolic stroke, followed by large artery atherosclerosis, and the lowest in small vessel occlusion. This is biologically plausible and consistent with previous studies demonstrating higher D-dimer levels in cardioembolic stroke due to increased thrombotic burden.[8],[12]

Plasma D-dimer levels also showed a significant positive correlation with stroke severity as assessed by NIHSS score ($r = 0.448$, $p < 0.001$). Patients with higher NIHSS scores had markedly elevated D-dimer levels, indicating greater thrombotic activity and neurological impairment. This finding is consistent with earlier studies reporting a correlation between D-dimer levels, infarct size, and stroke severity.[9],[14],[15]

Furthermore, elevated plasma D-dimer levels were significantly associated with poor clinical outcomes and mortality ($p = 0.034$). Patients with higher levels were more likely to have unfavorable outcomes, supporting previous evidence that D-dimer serves as a useful prognostic biomarker in acute ischemic stroke.[7],[10],[11]

The findings of the present study are in agreement with earlier studies demonstrating higher D-dimer levels in severe stroke and cardioembolic subtypes, reinforcing its role as an adjunct biomarker in early stroke evaluation.[8],[11],[14]

The clinical implications of this study are significant. Measurement of plasma D-dimer is simple, rapid, and widely available, making it a practical tool in routine clinical settings. When used alongside clinical assessment and neuroimaging, it may aid in early risk stratification, identification of high-risk patients, and differentiation of stroke subtypes.[6],[7]

However, certain limitations should be considered. The study was conducted at a single tertiary care center with a relatively small sample size, which may limit generalizability. Additionally, as a cross-sectional study, causal relationships cannot be established.

Overall, the present study underscores the importance of plasma D-dimer as a potential biomarker in acute ischemic stroke. Further large-scale, multicentric studies are required to validate these findings and establish standardized cutoff values for clinical application.

6. Conclusion

Elevated plasma D-dimer levels were significantly associated with different etiological subtypes of acute ischemic stroke based on TOAST classification. Higher D-dimer levels were predominantly observed in cardioembolic stroke and were also associated with increased stroke severity and poorer clinical outcomes.[7],[8],[12]

Although plasma D-dimer is a non-specific biomarker, its significant correlation with stroke severity and etiological subtypes highlights its potential role as an adjunct tool in the early evaluation of acute ischemic stroke.[6],[7],[14] These findings emphasize the importance of incorporating D-dimer assessment alongside clinical and radiological evaluation for improved risk stratification.

Early identification of patients with elevated D-dimer levels may aid in prompt etiological differentiation, particularly in identifying cardioembolic stroke, and in anticipating adverse clinical outcomes.[8],[11] Strengthening the use of simple and accessible biomarkers such as D-dimer may help optimize early management strategies and improve overall prognosis in patients with acute ischemic stroke.

7. Future Scope

Further large-scale, multicentric prospective studies are needed to validate the role of plasma D-dimer in acute ischemic stroke and improve generalizability.[1],[2] Establishing standardized cutoff values and evaluating serial D-dimer measurements may enhance its utility in predicting stroke severity, subtype, and outcomes.[6],[7],[14] Integration of D-dimer with other biomarkers and neuroimaging modalities could improve early risk stratification and guide therapeutic decisions, particularly in cardioembolic stroke.[8],[10]

8. Limitations

This study was conducted at a single tertiary care center with a relatively small sample size, limiting generalizability.[1],[3] Its cross-sectional design precludes assessment of causal relationships and long-term outcomes. Plasma D-dimer levels may also be influenced by unrecognized confounding factors despite exclusion criteria, and serial measurements were not performed.[6],[7]

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Conflict of Interest
The authors declare that there is no conflict of interest.

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