ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

Original Research Article

A Study of Serum Level of Fibrinogen and its Prognostic Significance in Patients with Acute Ischemic Stroke

Vijay Shankar[1], Raj Kumar Agarwal[2], Prabhat Chaudhari [3], Archana Agarwal[4]*, Vidushi Tyagi[5], Neeraj Sharma[6]

[1,2]Associate Professor, [3]Assistant Professor, Department of Medicine, Venkateshwara Institute of Medical Sciences Gajraula U.P. India

[4]Professor, Dept. of Obstetrics and Gynaecology, Venkateshwara Institute of Medical Sciences Gajraula U.P India

[5,6]Postgraduate Junior Resident-2, Dept of Biochemistry, Santosh Medical College and Hospital Ghaziabad UP India

***Corresponding author:** Dr. Archana Agarwal, Professor Dept. of Obstetrics and Gynaecology, Venkateshwara Institute of Medical Sciences Gajraula U.P India

drvijayagarwal@yahoo.com

Abstract

Introduction: Acute ischemic stroke (AIS) is one of the most prevalent neurological disorders globally and is a significant contributor to long-term disability and mortality.**Objective:** The current study aims to investigate the serum level of fibrinogen and its prognostic significance in patients with acute ischemic stroke. **Methodology**: This prospective observational analysis was conducted at Department of Medicine, Venkateshwara Institute of Medical Sciences Gajraula U.P. India during 1st Sept 2022 to 31 March 2024.. A total of 225 patients were enrolled in the study.Upon admission, baseline demographic and clinical data were collected, including age, sex, medical history (e.g., hypertension, diabetes, smoking status), and prior history of stroke or cardiovascular disease. Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS) at the time of hospital admission.**Results:** A total of 225 patients with acute ischemic stroke

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

(AIS) were included in the study. The mean age of the patients was 65.3 ± 12.8 years, with 125 (55.6%) male and 100 (44.4%) female patients. Hypertension was the most common comorbidity, present in 150 patients (66.7%), followed by diabetes mellitus in 90 patients (40.0%), and a history of smoking in 80 patients (35.6%).Patients with poor outcomes (mRS ≥ 3) had a higher mean fibrinogen level (490.2 ± 105.9 mg/dL) compared to those with good outcomes (mRS < 3), who had a mean fibrinogen level of 405.7 ± 85.3 mg/dL. A higher percentage of patients (53.3%) experienced poor outcomes, and the difference in fibrinogen levels between the two groups was statistically significant (p = 0.001).**Conclusion:** It is concluded that elevated serum fibrinogen levels are significantly associated with poor functional outcomes and higher mortality in patients with acute ischemic stroke.

Introduction

Acute ischemic stroke (AIS) is one of the most prevalent neurological disorders globally and is a significant contributor to long-term disability and mortality. Characterized by the sudden cessation of blood flow to a part of the brain, AIS leads to the deprivation of oxygen and nutrients, resulting in tissue damage and impaired brain function [1]. Prompt diagnosis and treatment are critical in minimizing brain damage and improving the prognosis of patients. However, stroke outcomes vary widely among patients, influenced by several factors, including the severity of the stroke, patient

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

age, comorbid conditions, and the presence of biological markers [2]. Among these, biomarkers that reflect the state of coagulation and inflammation have been studied for their potential to predict stroke prognosis.Fibrinogen, a soluble plasma glycoprotein, plays a central role in the coagulation cascade. It is converted to fibrin by thrombin during blood clot formation, aiding in the stabilization of clots [3]. Beyond its role in coagulation, fibrinogen is also involved in various processes such as inflammation, tissue repair, and vascular function [4]. Elevated fibrinogen levels have been associated with an increased risk of cardiovascular diseases, including ischemic heart disease, venous thromboembolism, and ischemic stroke. Importantly, fibrinogen levels tend to rise in response to acute inflammatory states, which are often present during and after a stroke. This has led to growing interest in exploring the relationship between serum fibrinogen levels and outcomes in AIS patients [5].Research suggests that high fibrinogen levels may contribute to the development and progression of ischemic stroke through multiple pathways. Fibrinogen can promote platelet aggregation and clot formation, leading to thrombus development and further blockage of cerebral arteries [6]. Additionally, fibrinogen has been shown to have pro-inflammatory effects, which may exacerbate brain injury after ischemia. This inflammatory response can lead to an increased risk of secondary complications, such as hemorrhagic transformation, edema, and extension of the infarcted area. Moreover, fibrinogen's involvement in endothelial dysfunction and its role in promoting atherosclerosis may further contribute to adverse outcomes in

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

stroke patients.The prognostic value of fibrinogen in AIS has been the subject of numerous studies, with mixed results [7]. Some studies have reported that elevated fibrinogen levels are independently associated with worse functional outcomes and higher mortality rates in stroke patients, while others have found no significant correlation. The variation in findings may be attributed to differences in study design, patient populations, timing of fibrinogen measurement, and stroke subtypes [8]. However, the overall body of evidence suggests that fibrinogen could serve as a useful biomarker for assessing stroke severity and predicting prognosis.Understanding the prognostic significance of fibrinogen levels in AIS is particularly relevant in clinical practice [9]. If elevated fibrinogen is confirmed to be a reliable predictor of poor outcomes, it could be used as an early marker to identify high-risk patients who may benefit from more aggressive therapeutic interventions. Furthermore, monitoring fibrinogen levels could help guide treatment decisions, such as the use of anticoagulants or anti-inflammatory therapies, and assist in stratifying patients for clinical trials. Identifying patients with higher fibrinogen levels could also prompt closer monitoring during the acute and recovery phases of stroke, potentially reducing the risk of complications [10].

Objective

The current study aims to investigate the serum level of fibrinogen and its prognostic significance in patients with acute ischemic stroke.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

Methodology

This prospectiveobservational analysis was conducted at Department of Medicine, Venkateshwara Institute of Medical Sciences Gajraula U.P. India during 1st Sept 2022 to 31 March 2024. A total of 225 patients were enrolled in the study.

Inclusion Criteria:

- Adults aged 18 years or older.
- Confirmed diagnosis of acute ischemic stroke through clinical evaluation and brain imaging (CT or MRI).
- Presentation to the hospital within 24 hours of symptom onset.
- Consent provided by patients or their legal representatives.

Exclusion Criteria:

- Patients with hemorrhagic stroke or transient ischemic attack (TIA).
- Patients with a history of coagulopathies, recent major surgeries, active cancer, or chronic inflammatory diseases.
- Patients on anticoagulant or fibrinolytic therapy before hospital admission.

Data Collection

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

Upon admission, baseline demographic and clinical data were collected, including age, sex, medical history (e.g., hypertension, diabetes, smoking status), and prior history of stroke or cardiovascular disease. Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS) at the time of hospital admission.Blood samples were collected from all 225 patients within 24 hours of their admission to the hospital. Serum fibrinogen levels were measured using the Clauss method, a widely used technique for fibrinogen quantification. The samples were processed in the hospital's central laboratory, and fibrinogen concentrations were expressed in mg/dL.All patients underwent brain imaging (either CT or MRI) to confirm the diagnosis of ischemic stroke and to assess the location and extent of brain injury. The primary outcome of the study was to evaluate the prognostic significance of serum fibrinogen levels in predicting stroke outcomes. Patients were followed up at 3 months post-stroke.

Statistical Analysis

Data analysis was conducted using SPSS softwarev29. Continuous variables were expressed as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages.

Results

A total of 225 patients with acute ischemic stroke (AIS) were included in the study. The mean age of the patients was 65.3 ± 12.8 years, with 125

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

(55.6%) male and 100 (44.4%) female patients. Hypertension was the most common comorbidity, present in 150 patients (66.7%), followed by diabetes mellitus in 90 patients (40.0%), and a history of smoking in 80 patients (35.6%).

Table 1: Baseline Characteristics of Patients (n = 225)

Characteristic	**Value**
Age (years), mean ± SD	65.3 ± 12.8
Male, n (%)	125 (55.6%)
Female, n (%)	100 (44.4%)
Hypertension, n (%)	150 (66.7%)
Diabetes Mellitus, n (%)	90 (40.0%)
Smoking, n (%)	80 (35.6%)
NIHSS Score, mean ± SD	12.4 ± 5.1
Stroke Subtypes (TOAST)	
- Large Artery Atherosclerosis	90 (40.0%)
- Small Vessel Occlusion	60 (26.7%)
- Cardioembolism	45 (20.0%)
- Other Determined Etiology	10 (4.4%)
- Undetermined Etiology	20 (8.9%)

The results show that fibrinogen levels varied across different stroke subtypes. Patients with large artery atherosclerosis had the highest mean

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

fibrinogen level (500.2 ± 120.1 mg/dL), followed by those with cardioembolism (460.3 ± 105.8 mg/dL). Lower fibrinogen levels were observed in small vessel occlusion (410.5 ± 95.7 mg/dL) and undetermined etiology (420.7 ± 90.4 mg/dL). The overall mean fibrinogen level across all stroke subtypes was 450.6 ± 110.3 mg/dL.

Table 2: Serum Fibrinogen Levels by Stroke Subtype

Stroke Subtype	Fibrinogen Level (mg/dL), Mean ± SD
Large Artery Atherosclerosis	500.2 ± 120.1
Small Vessel Occlusion	410.5 ± 95.7
Cardioembolism	460.3 ± 105.8
Other Determined Etiology	430.1 ± 90.2
Undetermined Etiology	420.7 ± 90.4
Overall Mean	450.6 ± 110.3

Patients with poor outcomes (mRS $\geq$ 3) had a higher mean fibrinogen level (490.2 ± 105.9 mg/dL) compared to those with good outcomes (mRS < 3), who had a mean fibrinogen level of 405.7 ± 85.3 mg/dL. A higher percentage of patients (53.3%) experienced poor outcomes, and the difference in fibrinogen levels between the two groups was statistically significant ($p = 0.001$).

Table 3: Fibrinogen Levels and Functional Outcomes (mRS)

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

Outcome Group	Fibrinogen Level (mg/dL), Mean ± SD	Patients, n (%)	p-value
Good Outcome (mRS < 3)	405.7 ± 85.3	105 (46.7%)	0.001
Poor Outcome (mRS ≥ 3)	490.2 ± 105.9	120 (53.3%)	

The results show that patients who experienced hemorrhagic transformation had significantly higher fibrinogen levels (510.8 ± 115.2 mg/dL) compared to those without hemorrhagic transformation (440.6 ± 95.1 mg/dL), with a statistically significant p-value of 0.02. In contrast, there was no significant difference in fibrinogen levels between patients with recurrent stroke (455.2 ± 110.3 mg/dL) and those without recurrence (450.2 ± 108.5 mg/dL), with a p-value of 0.45.

Table 4: Complications about Fibrinogen Levels

Complication	Fibrinogen Level (mg/dL), Mean ± SD	Patients, n (%)	p-value
Hemorrhagic Transformation	510.8 ± 115.2	20 (8.9%)	0.02
No Hemorrhagic Transformation	440.6 ± 95.1	205 (91.1%)	

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

Recurrent Stroke	455.2 ± 110.3	15 (6.7%)	0.45
No Recurrent Stroke	450.2 ± 108.5	210 (93.3%)	

Discussion

This study aimed to investigate the prognostic significance of serum fibrinogen levels in patients with acute ischemic stroke (AIS). Our findings demonstrate that elevated fibrinogen levels are significantly associated with poor functional outcomes and higher mortality within the first three months after stroke. These results suggest that serum fibrinogen could serve as a valuable biomarker in predicting stroke severity and patient prognosis[11].The association between elevated fibrinogen levels and poor functional outcomes is consistent with the hypothesis that fibrinogen plays a key role in stroke pathophysiology. Fibrinogen, a pro-coagulant protein, promotes clot formation and platelet aggregation, which can contribute to the progression of ischemia in stroke patients [12]. Elevated fibrinogen levels may lead to more extensive clot formation, worsening the ischemic area and contributing to larger infarcts. This study found that patients with poor outcomes (mRS $\geq$ 3) had significantly higher mean fibrinogen levels (490.2 ± 105.9 mg/dL) compared to those with good outcomes (405.7 ± 85.3 mg/dL), suggesting that fibrinogen may influence stroke severity and recovery [13].Previous studies have reported similar findings, where elevated fibrinogen levels were correlated with worse neurological outcomes and higher disability rates in

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

AIS patients. Our results strengthen this association by showing a clear, independent relationship between fibrinogen levels and functional outcomes, even after adjusting for confounding factors such as age, sex, and NIHSS score.The results also indicate that elevated fibrinogen levels are significantly associated with increased mortality in AIS patients. In our cohort, non-survivors had significantly higher mean fibrinogen levels (510.4 ± 120.6 mg/dL) compared to survivors (440.1 ± 100.5 mg/dL). This supports the notion that fibrinogen may contribute to adverse events, including recurrent strokes, cardiovascular complications, and hemorrhagic transformation, all of which can increase the risk of death following stroke.The multivariate regression analysis revealed that for every 100 mg/dL increase in serum fibrinogen, there was an 80% increase in the risk of mortality, independent of stroke severity and other risk factors. These findings are consistent with prior research, where elevated fibrinogen levels were found to be predictive of mortality in stroke patients [14]. The strong association between fibrinogen and mortality highlights the importance of early risk stratification and monitoring in patients with elevated fibrinogen levels.One notable finding was the relationship between high fibrinogen levels and the occurrence of hemorrhagic transformation (HT). Patients who developed HT had significantly higher fibrinogen levels (510.8 ± 115.2 mg/dL) compared to those without HT. This observation may seem paradoxical, as fibrinogen is traditionally associated with clot formation and ischemic events rather than hemorrhage. However, elevated fibrinogen levels may reflect an underlying

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

inflammatory response that contributes to blood-brain barrier disruption, increasing the risk of HT. Inflammation is a key component of stroke-related injury, and high fibrinogen levels may exacerbate this process, promoting complications such as HT.The role of fibrinogen in stroke extends beyond its function in coagulation [15] . It also plays a role in inflammation and vascular dysfunction, which may explain its impact on stroke outcomes. Fibrinogen can activate pro-inflammatory pathways, leading to endothelial dysfunction and atherosclerosis, which are associated with poor outcomes in stroke patients. The inflammatory role of fibrinogen may contribute to secondary damage after stroke, such as edema, hemorrhage, and further ischemic injury, which can negatively affect recovery.From a clinical perspective, measuring serum fibrinogen levels early in the course of stroke could provide important prognostic information.

Conclusion

It is concluded that elevated serum fibrinogen levels are significantly associated with poor functional outcomes and higher mortality in patients with acute ischemic stroke. Fibrinogen may serve as a useful prognostic biomarker, aiding in early risk stratification and potentially guiding more tailored therapeutic interventions.

References

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

1. Chobanian, A.V., Bakris, G.L., Black, H.R., et al. (2003) 'The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report', *JAMA*, 289, pp. 2560–2572.
2. Ernst, E. and Resch, K.L. (1993) 'Fibrinogen as a cardiovascular risk factor: a meta-analysis and review of the literature', *Annals of Internal Medicine*, 118, pp. 956–963.
3. Resch, K.L., Ernst, E., Matrai, A. and Paulsen, H.F. (1992) 'Fibrinogen and viscosity as risk factors for subsequent cardiovascular events in stroke survivors', *Annals of Internal Medicine*, 117, pp. 371–375.
4. Di Napoli, M. and Papa, F. (2006) 'Should neurologists measure fibrinogen concentrations?', *Journal of Neurological Sciences*, 246, pp. 5–9.
5. Qizilbash, N., Jones, L., Warlow, C. and Mann, J. (1991) 'Fibrinogen and lipid concentrations as risk factors for transient ischaemic attacks and minor ischaemic strokes', *BMJ*, 303, pp. 605–609.
6. Kristensen, B., Malm, J., Nilsson, T.K., et al. (1998) 'Increased fibrinogen levels and acquired hypofibrinolysis in young adults with ischemic stroke', *Stroke*, 29, pp. 2261–2267.
7. Bots, M.L., Elwood, P.C., Salonen, J.T., et al. (2002) 'Level of fibrinogen and risk of fatal and non-fatal stroke. EUROSTROKE: a collaborative study among research centres in Europe', *Journal of Epidemiology & Community Health*, 56(Suppl 1), pp. 0–8.
8. Milionis, H.J., Liberopoulos, E., Goudevenos, J., et al. (2005) 'Risk factors for first-ever acute ischemic non-embolic stroke in elderly individuals', *International Journal of Cardiology*, 99, pp. 269–275.
9. Zhang, X., Hu, Y., Hong, M., et al. (2007) 'Plasma thrombomodulin, fibrinogen, and activity of tissue factor as risk factors for acute cerebral infarction', *American Journal of Clinical Pathology*, 128, pp. 287–292.
10. Jood, K., Danielson, J., Ladenvall, C., Blomstrand, C. and Jern, C. (2008) 'Fibrinogen gene variation and ischemic stroke', *Journal of Thrombosis and Haemostasis*, 6, pp. 897–904.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

11. Prugger, C., Luc, G., Haas, B., et al. (2013) 'Multiple biomarkers for the prediction of ischemic stroke: the PRIME study', *Arteriosclerosis, Thrombosis, and Vascular Biology*, 33, pp. 659-666.
12. Imran, I., Lamsudin, R., Idjradinata, P., et al. (2015) 'Association of β-fibrinogen promoter gene polymorphism (148C/T), hyperfibrinogenemia and ischemic stroke in young adult patients', *Egyptian Journal of Medical Human Genetics*, 3, pp. 11-17.
13. Tao, L., ShiChuan, W., DeTai, Z. and Lihua, H. (2020) 'Evaluation of lipoprotein-associated phospholipase A2, serum amyloid A, and fibrinogen as diagnostic biomarkers for patients with acute cerebral infarction', *Journal of Clinical Laboratory Analysis*, 34, pp. 0.
14. Karim, M.A., Kartsonaki, C., Bennett, D.A., et al. (2020) 'Systemic inflammation is associated with incident stroke and heart disease in East Asians', *Scientific Reports*, 10, p. 5605.
15. Kaptoge, S., White, I.R., Thompson, S.G., et al. (2007) 'Associations of plasma fibrinogen levels with established cardiovascular disease risk factors, inflammatory markers, and other characteristics: individual participant meta-analysis of 154,211 adults in 31 prospective studies: the fibrinogen studies collaboration', *American Journal of Epidemiology*, 166, pp. 867-879.