VOLUME - 12, ISSUE - 04, APRIL - 2023 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Neurology

A STUDY OF PLASMA FIBRINOGEN LEVELS IN STROKE

Dr. Heli Patel Resident, Department of Anaesthesia, Pacific Medical College and Hospital, Udaipur, Rajasthan.

Dr. Harsh Patel Resident, Department of Medicine, Pacific Medical College and Hospital, Udaipur, Rajasthan.

ABSTRACT

Introduction: Increased plasma fibrinogen is a risk factor for vascular diseases related to atherosclerosis. Its predictive value in stroke is not well established. We conducted this study to establish the significance of hyperfibrinogenemia with severity and functional outcome of acute stroke. **Methods:** We studied 100 patients who got admitted with stroke within 24 hours of symptom onset. We noted the history regarding risk factors and assessed the severity of stroke by Scandinavian stroke scale and functional outcome of stroke by modified Rankin scale at the time of admission and discharge. Plasma fibrinogen was measured in all patients. The values computed and analysed with Pearson correlation and chi-square tests. **Results:** The mean fibrinogen was 405.6 mg/dl. The mean value was increased in patients having ischemic stroke. Patients having hyperfibrinogenemia at the time of admission has increased severity of stroke ($p<0.01$) as assessed by Scandinavian stroke scale (mean-29.91) and similarly has poor functional outcome as evidenced by increased scores of modified Rankin scale ($p<0.01$) at the time of admission and discharge.12 patients were expired during the course of stay in hospital. The mean fibrinogen among the dead patients was significantly higher (439.58) as compared to overall mean fibrinogen value. Among the risk factors, although the mean value was increased in smokers, hypertension and diabetes, we could establish a significant relation only with diabetes. **Conclusion:** Increased plasma fibrinogen shortly after ischemic stroke predicts the severity and poor functional outcome of stroke.

KEYWORDS : fibrinogen, stroke severity, Scandinavian stroke scale, modified Rankin scale.

INTRODUCTION

Stroke is a common neurological illness causing significant morbidity and mortality among all hospital admissions in both developing and developed countries. The prevalence of stroke in India ranges from 84 to 262 per lakh in rural areas and 334 to 424 in urban areas .The case fatality rate is highest in Kolkata which corresponds to 42%. In urban India stroke accounts for 1% mortality of all hospital admissions, 4% in all medical cases and about 20% in all disorders of central nervous system [1]. Important Risk factor for stroke includes Diabetes, Hypertension, smoking and dyslipidemia. Fibrinogen is a soluble plasma glycoprotein that consists of three nonidentical pairs of polypeptide chains Aα, Bβ and γ chains [2]. In the first phase of thrombus formation, thrombin converts soluble fibrinogen into insoluble fibrin. Thrombin cleaves Aα and Bβ chains thereby releasing fibrinopeptides . These fibrinopeptides initiate a process in which fibrin monomers begin to gel. These fibrin monomers polymerise to form fibrin polymers. This process continues and elongation of polymers causes formation of protofibrils. Once a critical [1] mass of long protofibrils is established, the protofibrils form lateral contacts with other protofibrils thereby forming fibrin clot. Fibrin clot thereby potentiates formation of thrombosis. Epidemiological observations indicate that high plasma fibrinogen levels strongly correlate with two major thrombotic complications of atherosclerosis, stroke and myocardial infarction. Thrombosis is increasingly recognised as a central mechanism in stroke as well as in myocardial infarction. Fibrinogen is involved in events thought to play a major role in thrombosis [3]. At the beginning of stroke the elevated level of inflammatory markers such as C-reactive protein (CRP) or fibrinogen may reflect the underlying burden of atherosclerosis and/or the association of concomitant risk factors (e.g. Diabetes mellitus, Hypertension, Obesity)[4]. In addition, the blood level of these markers could rise during stroke as a part of the acute phase reaction [1] . There is a significant inter individual variability in inflammatory response after stroke. In Scottish heart health study it was found that plasma fibrinogen level was elevated in smokers, premature heart disease, known hypertensive patients, Diabetics and patients with intermittent claudication. In another study it was found that sustained increase in fibrinogen value during an acute stroke episode predicts the worse outcome irrespective of the baseline fibrinogen value. In this study, the fibrinogen was measured at day 1,7, and 14 and compared with stoke outcome scales NIHSS (National Institute of Health Stroke Scale) and Modified Rankin Scale. The relationship between fibrinogen and thrombosis may strengthen the predictive value of this protein and suggest new treatment in management of stroke. It remains uncertain whether this rise in inflammatory marker is an epiphenomenon to stroke severity or it contributes independently to functional stroke outcome. Many case control studies done previously proven that plasma fibrinogen levels was elevated in smokers, hypertensives and dyslipidemia patients. Hence this study is designed to investigate mainly the association between plasma fibrinogen levels and acute stroke outcome [5] . 3

METHODS

This study was conducted in our medical college hospital. Patients were recruited from medicals wards and IMCU. A total of about 110 patients were selected and 10 of them were excluded as per exclusion criteria used. The remaining 100 patients were included in the study. Informed consent was obtained from all patients. Plasma fibrinogen value was estimated in all 100 patients admitted with stroke who got admitted within 24 hours of stroke onset.

Inclusion Criteria

Patients who got admitted in our hospital within 24 hours of the onset of stroke.

Exclusion Criteria

1. Patients admitted with stroke more than 24 hours from onset.
2. Patients refused to give consent for the study,
3. Patients having renal failure,
4. Inflammatory disease,
5. Active viral hepatitis,
6. Infection,
7. Severe dehydration
8. History of myocardial infarction or
9. Surgery in 3 months.
10. Patients having space occupying lesions,

11. Subdural hematoma.

METHODOLOGY

For all the 100 cases admitted, detailed clinical examination done and history was taken regarding smoking, alcohol, diabetes, hypertension, coronary heart disease, renal disease, any infection, surgery, trauma. Blood sugar, ECG and routine investigation was done. CT BRAIN was done in all patients to classify ischemic or haemorrhagic stroke. And for all the patients in our study Scandinavian stoke scale was calculated at the time of admission. Also modified Rankin score was calculated in all the patients during the time of admission and discharge. Plasma fibrinogen was measured in all these 100 patients who are included in the study and the values interpreted.

DISCUSSION

This study was conducted among the Indian population involving 100 patients who got admitted in our hospital with clinical features and investigations suggestive of cerebrovascular accident. We evaluated history regarding smoking, alcoholism known hypertension and diabetes. And also we measured blood pressure random blood sugar and other parameters. We calculated the severity of stroke at the time of admission by Scandinavian stroke scale and measured the functional outcome of patients by modified Rankin scale at the time of admission and discharge. We measured plasma fibrinogen in all the patients in our study group. In our study no patients were treated with thrombolysis for stroke. Many studies demonstrated that increased level of inflammatory markers like IL-6, CRP, fibrinogen following an acute stroke predicts an unfavourable outcome among stroke patients. Fibrinogen is one such acute phase protein. Cerebral ischemia triggers the acute phase reaction and thereby increasing the concentration of fibrinogen value following an acute stroke. We evaluated the fibrinogen value with Scandinavian stroke scale(ranges from 0-58) and found that the fibrinogen value was inversely related with stroke severity and it was found to be statistically significant ($p<0.01$). The mean SSS scoring was 29.91.Hence patients having high fibrinogen value associated with increased severity of stroke. Swarowskaet all [80] conducted a study of about 266 patients admitted with stroke. They measured the fibrinogen value at admission 7th and 14th day and correlated with the severity and outcome of the patients with NIHSS and MRS measured at day 1 and 30th day and found a significant correlation between fibrinogen and stroke severity and outcome. Modified Rankin scale ranges from 0-6. The value of 6 indicates the patient is dead. Higher value of MRS score indicate poor functional outcome. In our study the modified Rankin scale measured at the time of admission and discharge correlated well with the fibrinogen value and was statistically significant. The mean MRS at the time of admission was 3.96. Hence higher the fibrinogen value at the time of admission poorer the functional outcome of stroke patients. We proceeded with computing correlation coefficient for these parameters and found a higher value for MRS-at the time of admission(correlation coefficient0.594) and least value with diastolic blood pressure(correlation coefficient 0.054) We also tried to correlate between the fibrinogen value with important risk factors like smoking, alcohol, systemic hypertension and diabetes. The mean fibrinogen value was increased with smoking systemic hypertension and diabetes. The mean fibrinogen was normal in patients who are alcoholic. And we could establish a statistically significant relationship only with patients having diabetes. In the Scottish heart health study, plasma fibrinogen was measured in 8824 patients and found a significant fibrinogen elevation in patients with premature heart disease, diabetes, hypertension and intermittent claudication. In Framingham study they found a significant correlation between smokers and fibrinogen value. The fibrinogen value was elevated in smokers as compared to non-smokers and found to be statistically significant. Also we found there was a significant correlation between the random blood sugar and diabetes with fibrinogen value depicting the importance of underlying atherosclerotic process in diabetes. In our study 12 patients were expired during the course of stay in hospital and we found that the mean fibrinogen was elevated among the dead patients indicating higher values of fibrinogen with worst outcome. The limitation of our study is that we did not measure other inflammatory markers associated with acute stroke like IL-6 C-Reactive protein.

CONCLUSION

Following conclusion was made from our study. 1. Plasma fibrinogen level at the time of admission correlated with the severity of stroke. This is evidenced by as the plasma fibrinogen value increases the Scandinavian stroke scale decreases. 2. Although the mean fibrinogen value was increased among smokers, hypertensive, and diabetes we could not establish a statistically significant correlation between fibrinogen and smokers and hypertension patients, whereas in diabetics a significant correlation was observed. 3. Plasma fibrinogen acts as a prognostic marker to predict functional outcome of stroke. This is evidenced by higher plasma fibrinogen values correlated with modified Rankin scale at the time of admission and discharge.

Future Directions

Although the fibrinogen as an inflammatory marker, predicts the severity and functional outcome in acute stroke, it was still unclear whether the elevation is an epiphenomenon to stroke. Hence it is important to recognise the mechanisms leading to elevation of this inflammatory marker in stroke so that fibrinogen could be a potential therapeutic target.

REFERENCES

1. Mistry P, Chawla KP, Rai HP, Jaiswal P. Plasma fibrinogen levels in stroke. J Postgrad Med 1990; 36:1-4
2. Rand ML, Murray RK. Hemostasis and thrombosis. In: Murray K, Granner DK, Mayes PA, Rodwell VW, editors. Harper's Illustrated Biochemistry. Vol 1.26th Edn. New Delhi: McGraw Hill; 2003.p.598608.
3. Diminno G, Mancini M. Measuring plasma fibrinogen to predict stroke and myocardial infarction. Arteriosclerosis 1990; 10:1-7.
4. Beutler E, Patrick M, Copan A. In: Fuster V, Alexander RW, O'Rourke RA, Williams GA editors.Text book of hematology.5th Edn. California: Mcgraw Hill publications.p.87-88.
5. Smith WS, Johnston SC, Easton JD. Cerebrovascular diseases. In: Kasper DL, Fauci AS, Longo DL, Braunwald E, Hauser SL, Jameson LJ, editors. Harrison's Principles of Internal Medicine. Vol 2.16th Edn. New York: McGraw Hill;2005.p.2372-2393
6. Jain S, Maheshwari MC. Cerebrovascular Diseases: A Review of the Indian Experience in the Last 35 years.Neuroepidemiology 1986;5 116.
7. Markus HS. Cerebral perfusion and stroke. J NeurolNeurosurg Psychiatry 2004; 75:353.
8. Atkins ER, Brodie FG, Rafelt SE, et al. Dynamic cerebral autoregulation is compromised acutely following mild ischaemic stroke but not transient ischaemic attack. Cerebrovasc Dis 2010; 29:228.
9. Aries MJ, Elting JW, De Keyser J, et al. Cerebral autoregulation in stroke: a review of transcranial Doppler studies. Stroke 2010; 41:2697.
10. Deb P, Sharma S, Hassan KM. Pathophysiologic mechanisms of acute ischemic stroke: An overview with emphasis on therapeutic significance beyond thrombolysis. Pathophysiology 2010; 17:197.
11. Doyle KP, Simon RP, Stenzel-Poore MP. Mechanisms of ischemic brain damage. Neuropharmacology 2008; 55:310.
12. Caplan LR. Basic pathology, anatomy, and pathophysiology of stroke. In: Caplan's Stroke: A Clinical Approach, 4th ed, Saunders Elsevier, Philadelphia 2009. p.22.
13. Douen AG, Akiyama K, Hogan MJ, et al. Preconditioning with cortical spreading depression decreases intraischemic cerebral glutamate levels and down-regulates excitatory amino acid
14. Szatkowski M, Barbour B, Attwell D. Non-vesicular release of glutamate from glial cells by reversed electrogenic glutamate uptake. Nature 1990; 348:443.
15. Rossi DJ, Oshima T, Attwell D. Glutamate release in severe brain ischaemia is mainly by reversed uptake. Nature 2000; 403:316.
16. Grewer C, Gameiro A, Zhang Z, et al. Glutamate forward and reverse transport: from molecular mechanism to transporter-mediated release after ischemia. IUBMB Life 2008; 60:609.
17. Nandagopal K, Dawson TM, Dawson VL. Critical role for nitric oxide signaling in cardiac and neuronal ischemic preconditioning and tolerance. J PharmacolExpTher 2001; 297:474.