

Original Research

Impact of plasma fibrinogen levels in patients with Acute Stroke

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ABSTRACT

Background: Stroke is described as sudden neurological deficit with a focused vascular origin. Atrial fibrillations, carotid stenosis, myocardial infarction, hypertension, diabetes, hyperlipidaemia, obesity, smoking and atrial myxomas are all risk factors for stroke and are closely related with high fibrinogen levels.

Stroke mortality in urban India accounts for 1% of all hospital admissions, 4% of all medical cases, and around 20% of all central nervous system illnesses. Higher plasma fibrinogen levels in stroke patients are associated with an increased risk of poor functional outcome, short-term death and new cardiovascular events. **Methodology:** The present case control study was conducted amongst 50 cases of acute stroke. Plasma fibrinogen levels of 50 consecutive patients with acute stroke presenting to the OPD/Casualty or getting admitted in Saraswathi Institute of Medical Sciences were compared with 50 controls who were not suffering from stroke with matched age, sex and risk factors. Unpaired t test was applied to compare mean fibrinogen level of two groups. For statistical significance p value less than 0.05 was taken with 95% confidence interval.

Results: Fibrinogen levels among control group (267.0 ± 98) were low compared to patients with overall stroke (428.8 ± 97.8), either ischemic (470 ± 80.5) or haemorrhagic stroke (387.6 ± 97.6). Patients with Ischemic Stroke consisting Mean Fibrinogen levels of ($508.8 \text{ mg/dL} \pm 74.6$) and haemorrhagic stroke with mean fibrinogen levels of 487.5 ± 66 had worst outcome.

Conclusion: There was significant difference of mean fibrinogen levels among survival and non-survival group of patients in ischemic and haemorrhagic stroke. Patients with poor outcome had higher mean fibrinogen levels compared to patients who survived.

Key words: Case-control study, Fibrinogen, Haemorrhagic stroke, Ischemic stroke

Received: 18 January, 2023

Accepted: 24 February, 2023

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This article may be cited as: Singhal P, Singh DP. Impact of plasma fibrinogen levels in patients with Acute Stroke. J Adv Med Dent Sci Res 2023;11(3):69-72.

INTRODUCTION

According to World Health Organization guidelines, a stroke is described as "rapidly developing clinical symptoms of focal or global impairment of brain function lasting longer than 24 hours (unless stopped by surgery or death) with no clear cause other than a vascular origin".¹

Stroke is described as a sudden neurological deficit with a focused vascular origin. Atrial fibrillation, carotid stenosis, myocardial infarction, hypertension, diabetes, hyperlipidaemia, obesity, smoking and atrial myxomas are all risk factors for stroke. Stroke mortality in urban India accounts for 1% of all hospital admissions, 4% of all medical cases, and around 20% of all central nervous system illnesses.

Stroke is the third most common cause of disability and the second most common cause of death globally.

Elevated fibrinogen levels are linked to carotid stenosis, peripheral vascular disease, atherosclerosis, and coronary heart disease.² Higher plasma fibrinogen levels in stroke patients are associated with an increased risk of poor functional outcome, short-term death, and new cardiovascular events.³

Increased plasma fibrinogen in high-risk patients with coronary heart disease predicts short-term death. Fibrinogen is used as a marker for both acute phase response and atherosclerosis. Fibrinogen (FIB) is a vital coagulation factor and an inactive precursor of fibrin. In addition to its role in coagulation, FIB plays an important part in systemic inflammation. Fibrinogen levels may be higher in stroke patients compared with nonstroke patients. High levels of fibrinogen can increase the risk of stroke and consequently induce a poorer outcome.^{4,5}

Therefore, clarifying the link between fibrinogen and thrombosis may increase the protein's predictive usefulness and provide a novel stroke care strategy. Consequently, the purpose of this investigation is to ascertain whether plasma fibrinogen levels are related to acute stroke.

METHODOLOGY

The present case control study was conducted among 50 cases of acute stroke (25 cases of ischemic + 25 cases of Haemorrhagic stroke) and 50 controls without stroke history with matched age, sex and risk factors. Patients of acute cerebrovascular accident in whom CT scan showed cerebral infarct or haemorrhagic infarct were enrolled for the study. Patients with evidence of uraemia, infection, active hepatic disease, suffered from myocardial infarction in last three months, or have undergone surgery in last three months were excluded from the study. Data of 50 cases with acute stroke was collected within 24 hours of the onset of symptoms. Detailed history was taken to find out the risk factors such as hypertension, diabetes, smoking and alcohol consumption. Hypertension was diagnosed by JNC VII criteria. Diabetes was diagnosed by American Diabetes Association criteria. Patients were followed up till they were discharged from the hospital. Plasma fibrinogen levels of 50 consecutive patients with acute stroke presenting to the OPD/Casualty or getting admitted in Saraswathi Institute of Medical Sciences were compared with 50 controls who were not suffering from stroke. SPSS version 25 was used for statistical data analysis. Unpaired t test was applied to compare mean fibrinogen levels of two groups. For

statistical significance p value less than 0.05 was taken with 95% confidence interval.

RESULTS

The study included total 100 participants. Among them, 50 were controls and 50 were stroke patients. Among stroke patients, 25 were haemorrhagic stroke patients and 25 were ischemic stroke patients. The study ran through the age group of study-participants of 40 to 84 years, out of which 54% were females and 46% were males. Mean age of control group were 68 ± 7 which was higher as compared to stroke patients (62 ± 10.1) however the difference was statistically insignificant and both the groups were comparable. 11 stroke patients were alcoholics and 29 had tobacco consumption. 24% of control group study participants were overweight compared to 40% of stroke patients classified as BMI more than 25 as depicted in Table 1. As shown in table no. 2, fibrinogen levels among control group (267.0 ± 98) were low as compared to patients with overall stroke (428.8 ± 97.8), either ischemic (470 ± 80.5) or haemorrhagic stroke (387.6 ± 97.6). Difference of fibrinogen levels between the two groups was statistically significant.

As shown in Table no. 3, Patients with Ischemic Stroke consisting Mean Fibrinogen levels of $508.8 \text{ mg/dL} \pm 74.6$ and haemorrhagic stroke with mean fibrinogen levels of $487.5 \text{ mg/dl} \pm 66$ had the worst outcome. Haemorrhagic Stroke consisting Mean Fibrinogen levels of $356 \text{ mg/dL} \pm 84.3$ and ischemic stroke patients with mean fibrinogen levels of $428 \pm 66 \text{ mg/dl}$ survived well. There was significant difference of mean fibrinogen levels among survival and non-survival group of patients with ischemic and haemorrhagic stroke.

Table 1: Comparison of Socio-demographic profile of control group with stroke cases

Factors	Control group	Stroke cases			p value
		Haemorrhagic	Ischemic	Total case	
Age (years)	63 ± 7	61 ± 9.7	64 ± 10.4	62 ± 10.1	0.56
Male	23 (46%)	13 (52%)	10 (40%)	23 (46%)	>0.05
Female	27 (54%)	12 (48%)	15 (60%)	27 (54%)	>0.05
Alcoholics	10 (20%)	4 (16%)	7 (28%)	11 (22%)	0.80
Tobacco Consumers	8 (16%)	15 (60%)	14 (56%)	29 (58%)	<0.001*
BMI >25	12 (24%)	10 (40%)	10 (40%)	20 (40%)	0.021*

Table 2: Comparison of mean fibrinogen level of control group with stroke cases

Study group	Fibrinogen (mg/dL) Mean \pm sd	p value #
Control (n=50)	267.0 ± 98	-
Total Stroke Case (n=50)	428.8 ± 97.8	<0.001*
Ischemic (n=25)	470 ± 80.5	<0.001*
Haemorrhagic (n=25)	387.6 ± 97.6	<0.001*

Unpaired t test applied between control group mean fibrinogen level with stroke patients

Table 3: Comparison of mean fibrinogen level of stroke cases according to their survival status

Outcome	Fibrinogen (mg/dL) Mean±sd	value	p value #
Ischemic Stroke			
Alive	428±66	66.0	0.008*
Died	508.8±74.6	74.6	
Haemorrhagic Stroke			
Alive	356±84.3	84.3	0.002*
Died	487.5±66.4	66.4	

Unpaired t test was applied

DISCUSSION

Present case control study was done among 100 participants with randomly selected 50 stroke patients and 50 patients in control group without stroke. Out of total 100 patients, 46% were males and 54% were female. Mean age of patient among control were 63±7 years and among stroke group was 62±10.1 years. A similar study was done by Rizwan et al. included 118 patients, 79 of whom (66.9%) were men and 39 (33.1%) were women. Patients' ages ranged from 28 to 78, with a mean age of 49.46 + 9.35 years which was lower compared to our study findings.⁶Males had significantly greater fibrinogen levels than females that might be due to more use of tobacco consumption by male compared to females, and these levels increase with age.⁷

24% participants from the control group were seen to have BMI more than 25. Whereas among stroke patients, Overweight were 28% and pre-Obese were 32%. It was seen to have significant association between BMI classification and Stroke. According to the Bingi S., B Balaji. et al. study, the mean body mass index (BMI) in Group B was not statistically different from Group A (P < 0.001). When compared to Group B, where 68 percent of the participants had a BMI between 21 to 25, 24% had a BMI between 26 to 30, and 8% had a BMI between 15 to 20, subjects in Group A had a BMI of between 21 to 25, 24% between 15 to 20, and 18% had a BMI of between 26 % 30.⁸

There was no significant association linked to past alcohol use with Stroke as 84% of Haemorrhagic Stroke and 72% of Ischemic Stroke had no history of Alcohol use. This conclusion goes parallel with Control group as well, having only 20% of participants having use of alcohol out of 50 subjects. According to Bingi S., B Balaji. et al. study, It was noted that the non-alcoholic study group's plasma fibrinogen levels were substantially higher than those of the other groups (F = 31.27, P < 0.001). Between alcoholic controls and non-alcoholic controls, alcoholic cases and alcoholic controls, and alcoholic cases and non-alcoholic controls, there was no statistically significant difference in plasma fibrinogen levels, P > 0.05.⁸

Tobacco consumption was seen to be significantly associated with Stroke cases. 60% of patients with Haemorrhagic Stroke and 56% of, the patients with

Ischemic Stroke were seen to have previous/current Tobacco use. For instance, a study by Lu et al. found that current tobacco use only increases the risk of ischemic stroke, whereas former smokers have an increased risk of both ischemic and hemorrhagic stroke of between 50 and 60 percent.⁹The percentage of hemorrhagic stroke attributed to smoking was 4-12% in men and 1-9% in women, according to a study by Woodward et al. The equivalent percentages for ischemic stroke were 11-27 and 1-22%.¹⁰

In present study it is average fibrinogen level (428.8±97.8 mg/dL) of total stroke patients was higher than control group. Where, ischemic stroke patients mean fibrinogen level was 470±80.5 mg/dL and haemorrhagic stroke was 387.6±97.6 mg/dL. Difference of fibrinogen level of cases and control was statistically significant. Similar to our finding Samir et al¹¹ study found a statistically significant increase in serum fibrinogen levels in stroke groups compared with a non-stroke group (P .001).

There was no a significant difference in fibrinogen levels based on gender, Alcohol use or smoking, corroborating the findings of Bruno et al.¹², who evaluated fibrinogen levels once in 1525 individuals with noninsulin-dependent diabetes. In contrast, Giansante et al.¹³discovered that male smokers had higher fibrinogen readings in 516 normal participants, whereas this was the opposite in non-smokers.

According to Samir et al. cut-off value of fibrinogen ≥ 557 mg/dL seems to be a guide for prediction of mortality in the ischemic stroke patients.¹¹Similarly our study revealed that a cut-off value of serum fibrinogen ≥508.8 mg/dL could be considered as a predictable value in determining the development of ischemic stroke supporting the results of similar studies.^{14,15}

One of the major limitations of our study was the measurement of fibrinogen after the occurrence of acute stroke, making it difficult to distinguish hyperfibrinogenaemia as a cause or a result (as one of the acute phase reactants), as well as the lack of serial daily measurement of fibrinogen with its impact on prognosis and outcome, necessitating a long-term prospective cohort study that followed high-risk individuals for the development of acute stroke with routine monitoring. The measurement of fibrinogen 48 hours after intensive care unit admission without a precise correlation to the stroke's start was another

limitation.. Lastly, this research did not take into account the correlation between imaging results and the Glasgow Coma Scale and fibrinogen levels.

CONCLUSION

There was significant difference of mean fibrinogen levels among survival and non-survival group of patients in ischemic and haemorrhagic stroke. Mean fibrinogen levels were higher in acute stroke patients compared to control group. Patients with poor outcome had higher mean fibrinogen levels compared to patients who survived at the end of the study.

CONFLICTS OF INTEREST

Nil

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