

A Clinical Study of Plasma Fibrinogen Level in Ischemic Stroke

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Abstract

Introduction: 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. Most cerebrovascular accidents are manifest by the abrupt onset of focal neurologic deficit as if the patient is “struck by the hand of the God.”

Aims and Objectives of the Study: This study aims to detect the plasma fibrinogen levels in patients with acute ischemic stroke.

Materials and Methods: Fasting plasma fibrinogen level of 50 consecutive patients presenting with acute ischemic stroke admitted in Mahatma Gandhi Memorial Hospital, Warangal, from August 2012 to August 2014 and compared with 50 controls not suffering from stroke with matched age, sex, and risk factors.

Observations and Results: The present study was undertaken in the Department of General Medicine. A total of 100 patients age, sex, and matched were recruited from Mahatma Gandhi Memorial Hospital, Warangal, for the present study, of which 50 subjects constituted the control group called as Group A and remaining 50 subjects constituted the study group called as Group B.

Conclusion: Fasting plasma fibrinogen levels of cases were compared to fasting plasma fibrinogen levels of age, sex, and risk factor-matched controls selected randomly at Mahatma Gandhi Memorial Hospital, Warangal.

Key words: Cardiovascular diseases, Ischemic stroke, Fibrinogen

INTRODUCTION

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] Most cerebrovascular accidents are manifest by the abrupt onset of focal neurologic deficit as if the patient is “struck by the hand of the God.”^[2] Stroke is defined as an abrupt neurologic deficit that is attributable to focal vascular cause. Risk factors for stroke are hypertension, atrial fibrillation, carotid stenosis, hyperlipidemia, diabetes, myocardial infarction, atrial myxomas, and smoking.^[2]

Epidemiological observations indicate that high plasma fibrinogen levels strongly correlate with the frequency of two major thrombotic complications of atherosclerosis, stroke, as well as myocardial infarction. Thrombosis is increasingly recognized as a central mechanism in stroke and myocardial infarction, and fibrinogen is believed to be involved in events thought to play a major role in thrombosis. Therefore, elucidation of the relationship between fibrinogen and thrombosis may strengthen the predictive value of this protein and suggest new treatment in the management of stroke.^[3]

In Warangal district, there are no studies published to show the correlation between the plasma fibrinogen levels and ischemic stroke. Hence, this study is designed to investigate the association between plasma fibrinogen levels and acute ischemic stroke.

Aims and Objectives of the Study

The objectives of this study were as follows:

1. To detect plasma fibrinogen levels in patients with

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- acute ischemic stroke
2. To compare and correlate the significance of plasma fibrinogen levels in patients with acute ischemic stroke with that of age-, sex-, and risk factor-matched controls.

MATERIALS AND METHODS

Source of Data

Fasting plasma fibrinogen level of 50 consecutive patients presenting with acute ischemic stroke admitted in Mahatma Gandhi Memorial Hospital, Warangal, from August 2012 to August 2014 and compared with 50 controls not suffering from stroke with matched age, sex, and risk factors.

Method of Collection of Data

The study will be carried out on 50 consecutive patients admitted to Mahatma Gandhi Memorial Hospital, Warangal, with acute ischemic stroke within 24 h of the onset of symptoms. Detailed history will be taken to find out the risk factors such as hypertension, diabetes, smoking, and alcohol consumption.

- Hypertension will be diagnosed by the Joint National Committee (JNC) VIII criteria.
- Diabetes will be diagnosed by the American Diabetes Association criteria.
- Smoking will be recorded in terms of number of cigarette pack-years smoked.
- Ischemic nature of stroke confirmed with computed tomography (CT) brain (plain).
- Through general and systemic examination will be carried out as per the pro forma.

In addition to routine investigations as per the standard protocol in the evaluation of stroke patient, fasting plasma fibrinogen level is estimated and compared to age-, sex-, and risk factor-matched controls.

Patient will be followed up until they are discharged from the hospital. Controls will be taken who are not suffering from stroke and are age, sex, and risk factor matched.

Inclusion Criteria

The following criteria were included in the study:

1. Patients presenting with acute stroke within 24 h of onset of symptoms
2. Patients of acute cerebrovascular accident in whom CT scan shows infarct
3. Age group between 20 and 60 years.

Exclusion Criteria

The following criteria were excluded from the study:

1. Patients with evidence of uremia.
2. Patients with evidence of infection.

3. Patients with evidence of active hepatic disease.
4. Patients who have suffered from myocardial infarction in past 3 months.
5. Patients who have undergone surgery in the past 3 months.
6. Patients with acute cerebrovascular accident whose plain CT scan brain showing hemorrhage.

OBSERVATIONS AND RESULTS

The present study was undertaken in the Department of General Medicine, Mahatma Gandhi Memorial Hospital, Warangal. A total of 100 patients age, sex, and matched were recruited from SVS Medical College and Hospital, for the present study, of which 50 subjects constituted the control group called as Group A and remaining 50 subjects constituted the study group called as Group B.

The above cases were recruited irrespective of the presence of any risk factors such as hypertension, diabetes, smoking, and alcohol. Hypertension was diagnosed by JNC VIII criteria and diabetes will be diagnosed by the American Diabetes Association criteria.

Group A comprised controls that were selected randomly from subjects attending the outpatient department of the hospital for minor ailments, subjects accompanying patients, or among office working staff from various departments. Controls were selected irrespective of the presence of any risk factors such as hypertension, diabetes, smoking, and alcohol but without having ischemic stroke in the present or past or any evidence of CVA.

All the Controls were Screened by Clinical Examination and Normal Electrocardiogram

Group B comprised cases of acute ischemic stroke presenting within 24 h of onset of symptoms CT scan brain was done to confirm the ischemic origin of stroke by the presence of infarct. The presence of any risk factors was also recorded in patients.

Through general and systemic examination will be carried out as per pro forma. In addition to routine investigations as per the standard protocol in the evaluation of stroke patient, fasting plasma fibrinogen level is estimated and compared to age, sex, and risk factor-matched controls.

Risk Factor Matching

The age of the patients varied from a minimum age of 20 years to a maximum of 60 years. The mean age of the patients in Group A was 49.22 and the mean age in Group B was 49.12, the mean age in two groups was not significantly different from each other $t = 0.66$, $P = 0.94$. 54% of patients in Group A and Group B were in the age

Table 1: Distribution of subjects by age group

Age group in years	Group A	Group B
	n (%)	n (%)
20–30	1 (2)	1 (2)
31–40	4 (8)	5 (10)
41–50	18 (36)	17 (34)
51–60	27 (54)	27 (54)
Total	50 (100)	50 (100)
Mean±SD	49.22±7.08	49.12±8.13

T: 0.66, P: 0.94

Table 2: Sex-wise distribution of subjects among two groups

Sex	Group A	Group B
	n (%)	n (%)
Male	26 (52)	26 (52)
Female	24 (48)	24 (48)
Total	50 (100)	50 (100)

χ²: 0.0, P: 1.0

Table 3: Distribution of subjects according to BMI in different groups

BMI	Group A	Group B
	n (%)	n (%)
15–20	12 (24)	4 (8)
21–25	29 (58)	34 (68)
26–30	9 (18)	12 (24)
Total	50 (100)	50 (100)
Mean±SD	22.82±2.4	23.4±2.3

T: 1.36, P: 0.175, BMI: Body mass index

Table 4: Mean±SD values of studied parameters in controls and patients with acute ischemic stroke

Parameter	Group A	Group B	t-value	P value
	Mean±SD	Mean±SD		
Plasma fibrinogen	292.22±73.7	523.1±175.9	8.55	<0.001

SD: Standard device

Table 5: Smoking

Smoking	Group A	Group B	Chi-square value	P value
	Number of patients (%)	Number of patients (%)		
Present	11 (22)	10 (20)	0.6	0.8
Absent	39 (78)	40 (80)		

group of 51–60 years, 36% of patients in Group A were in the age group of 41–50 years compared to Group B where 34% of patients were in the age group of 41–50 years.

Among the total 50 patients in Group A, 26 were male (52%) and 24 were female (48%) compared to Group B where 26 were male (52%) and 24 were female (48%).

Table 6: Alcoholism

Alcohol	Group A	Group B	Chi-square value	P value
	Number of patients (%)	Number of patients (%)		
Present	8 (16)	8 (16)	0	1.0
Absent	42 (84)	42 (84)		

Table 7: Hypertension

HTN	Group A	Group B	Chi-square value	P value
	Number of patients (%)	Number of patients (%)		
Present	16 (32)	20 (40)	0.69	0.4
Absent	34 (68)	30 (60)		

Table 8: Diabetes

Diabetes	Group A	Group B	Chi-square value	P value
	Number of patients (%)	Number of patients (%)		
Present	14 (28)	12 (24)	0.2	0.6
Absent	36 (72)	38 (76)		

There was no significant difference observed in the sex distribution of subjects among two groups, Chi-square value was 0.0 and statistical significance $P > 0.05$.

There was no statistical difference in mean body mass index (BMI) in Group B compared to Group A ($P < 0.001$). 58% of subjects in Group A had a BMI between 21 and 25, 24% had a BMI between 15 and 20, and 18% had BMI between 26 and 30 compared to Group B where 68% of subjects had a BMI between 21 and 25, 24% had BMI between 26 and 30, and 8% had a BMI between 15 and 20.

The mean values for plasma fibrinogen were significantly higher in Group B compared to Group A ($P < 0.001$).

Group A comprised 22% of cases who gave a positive history of smoking compared to 20% in Group B. There was no significant difference in number of smokers in between groups ($\chi^2 = 0.6$) ($P > 0.05$).

Group A comprised 16% of cases who gave a positive history of chronic alcoholism compared to same 16% in Group B [Table 1]. There was no statistical significance in the distribution of alcoholic patients in either group ($\chi^2 = 0$) ($P > 0.05$).

Group A comprised 32% of cases who had a positive history of hypertension compared to 40% in Group B. There was no statistical difference observed in the distribution of hypertensive patients in both groups ($\chi^2 = 0.69$) ($P > 0.05$) [Table 2].

Table 9: Mean±SD of plasma fibrinogen in diabetic and non-diabetic subjects within groups

Parameter	Group A		Group B		F value	P value
	Non-diabetic	diabetic	Non-diabetic	diabetic		
Plasma fibrinogen	291.11±73.3	295.07±77.38	568.87±170.3	378.17±100.8	36.64	< 0.001

SD: Standard deviation

Group A comprised 28% of cases who had a positive history of diabetes compared to 24% in Group B. There was no statistical difference observed in the distribution of hypertensive patients in both groups ($\chi^2 = 0.2$) ($P > 0.05$).

In the present study, it was observed that plasma fibrinogen was significantly more in the non-diabetic study group compared to others ($F = 36.64$, $P < 0.001$).

Hypertension and Fibrinogen

In the present study, it was observed that plasma fibrinogen was significantly more in the hypertensive study group compared to others ($F = 66.08$, $P < 0.001$).

It was observed that fibrinogen levels significantly more in hypertensive cases compared to non-hypertensive cases, hypertensive controls, and non-hypertensive controls, $P < 0.001$ [Table 3].

Plasma fibrinogen levels significantly more in hypertensive cases compared to non-hypertensive controls ($P < 0.001$). In the present study, there was no statistical significance in plasma fibrinogen levels between hypertensive controls and non-hypertensive controls.

Lee *et al.*^[4] have demonstrated that plasma fibrinogen was higher among hypertensive [Table 4].

Showed that fibrinogen levels are more in hypertensive patients when compared to controls which are statistically significant < 0.01 [Table 5].

Alcohol and Fibrinogen

In the present study, it was observed that plasma fibrinogen was significantly more in the non-alcoholic study group compared to others ($F = 31.27$, $P < 0.001$) [Table 6].

It was observed that fibrinogen levels significantly more in nonalcoholic cases compared to alcoholic cases, alcoholic controls, and non-alcoholic controls, $P < 0.001$ [Table 7].

There was no statistical significance in plasma fibrinogen levels between alcoholic controls and non-alcoholic controls, alcoholic cases and alcoholic controls, and alcoholic cases and non-alcoholic controls, $P > 0.05$.

Meade *et al.*^[5] study showed that plasma fibrinogen levels are low in alcoholics than non-alcoholics.

Fibrinogen is an intermediate factor in the association between alcohol consumption and cardiovascular disease.^[6]

Alcohol intake is associated with lower fibrinogen levels.^[7] Several cross-sectional studies showed an inverse association between fibrinogen and alcohol consumption.^[6]

Alcohol seems to be related to cardiovascular disease in a U-shaped fashion and fibrinogen may be one of the mediators for its effect on cardiovascular disease.^[6]

Smoking and Fibrinogen

In the present study, it was observed that there was no statistical significance in plasma fibrinogen levels between smoker controls and non-smoker control, $P > 0.05$.

In the present study, it was observed that plasma fibrinogen was significantly more in the non-smoker study group compared to others ($F = 24.38$, $P < 0.001$).

In the present study, it was observed that fibrinogen levels significantly more in non-smoker cases compared to smoker controls and non-smoker controls, $P < 0.001$.

However, there was no statistical significance in plasma fibrinogen levels between non-smoker cases and smoker cases, $P > 0.05$.

Plasma fibrinogen levels significantly more in smoker cases compared to non-smoker controls and smoker controls ($P < 0.001$). There was no statistical significance in plasma fibrinogen levels between smoker controls and non-smoker control.

Vannien *et al.* study showed higher plasma fibrinogen levels in smokers than non-smokers.^[8]

In the study of Eliasson *et al.*, male smokers had 3.58 g/L and non-smokers had 3.29 g/L fibrinogen value.^[9]

In the study of Mennen *et al.*, the male current smokers had 3.84 ± 0.02 g/L fibrinogen value compared to non-

smokers who had 2.87 ± 0.02 g/L fibrinogen value, respectively.

The other studies, which found higher fibrinogen levels in smokers than non-smokers, were Rankinen *et al.* study and Balleisen *et al.* study in this study, current male smokers had 263.0 mg/dL fibrinogen value and non-smokers had 232.0 mg/dL [Table 8].

In the study of Bruno *et al.* and Raynaud *et al.*, they found that fibrinogen level increases with smoking and Folsom in his study found a correlation between fibrinogen and smoking.

In the study of Kannel *et al.*, the current male smokers had 296mg/dL compared to non-smokers who had 275 mg/dL [Table 9].

Cross-sectional studies indicate that cigarette smokers have higher mean fibrinogen values than non-smokers, and it increases in proportion to the amount smoked. 25–50% of the relation of cigarette smoking to occurrence of atherosclerotic cardiovascular disease is attributable to the effect of smoking on fibrinogen levels which, in turn, enhances thrombotic tenderness, leading to occlusive clinical events.

DISCUSSION

Fibrinogen and Ischemic Stroke

The present study involved 50 ischemic stroke patients and 50 age-, sex-, gender-, and risk factor-matched controls. The mean fibrinogen level among cases is 523.1 mg% in ischemic group; in controls, the mean fibrinogen is 291.22 mg% which is statistically significant.

Mistry *et al.*^[1] in their study involving 56 patients admitted in the hospital within 24 h of onset of symptoms. The levels were found to be raised significantly (531.73 ± 74 mg%) compared to those of the age- and sex-matched control group (445.78 ± 92.28 mg%).

When the levels of plasma fibrinogen in stroke group with one risk factor were compared to those of individuals with comparable control group with same risk factor, a significant difference was observed in hypertensive, smokers, alcoholics, and atherosclerotic stroke groups.

Hazra *et al.*, 48 in their study involving 33 patients of cerebral thrombosis and 30 patients with cerebral hemorrhage admitted within 24 h of onset of stroke concluded that the mean plasma fibrinogen concentration in patients of cerebral thrombosis (378.67 mg/dL) is significantly higher when compared to patients with

cerebral hemorrhage (224.4 mg/dL) and in the control group (216.67).

CONCLUSION AND SUMMARY

1. This is a case–control study conducted on 50 acute ischemic stroke patients presented to SVS Medical College Hospital between 2012 and 2014 (who were selected according to inclusion and exclusion criteria mentioned earlier) in them through history, physical examination, and routine laboratory tests were sent along with fasting plasma fibrinogen levels.
2. Fasting plasma fibrinogen levels of cases were compared to fasting plasma fibrinogen levels of age-, sex-, and risk factor-matched controls selected randomly at SVS Medical College Hospital.
3. Mean plasma fibrinogen levels were significantly higher in cases compared to age-, sex-, and risk factor-matched controls.
4. In cases, the relationship between risk factors and mean plasma fibrinogen was studied.
5. Diabetic cases had significantly lower mean plasma fibrinogen than non-diabetic cases.
6. Hypertensive cases had significantly high mean plasma fibrinogen levels than non-hypertensive cases.
7. Non-alcoholic cases had significantly higher mean plasma fibrinogen levels than alcoholic cases.
8. No significant difference found in mean plasma fibrinogen levels between smoker and non-smoker cases.
9. No significant difference found in mean plasma fibrinogen levels between obese and non-obese cases.
10. As it is a small case–control study done on small number of cases, further large prospective studies are needed to further support this association.

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