



## RESEARCH ARTICLE

### SIGNIFICANCE OF PLASMA FIBRINOGEN LEVELS IN ISCHEMIC STROKE

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#### ABSTRACT

**Background:** The pathogenic factors in stroke like atherosclerosis and thrombosis are the same as for myocardial infarction in the latter disease, significant increase in plasma fibrinogen level has been detected, which has a correlation with severity of myocardial damage. It was therefore of interest to measure the plasma fibrinogen levels in patients with acute stroke and also to investigate whether these levels increase if the patient has additional risk factors like hypertension, diabetes, and smoking. The objective of the study is to measure plasma fibrinogen levels in patients with acute stroke and comparing with age, sex and risk factor matched controls.

**Materials and Methods:** 200 consecutive patients of acute ischemic stroke admitted within 24 hours of development of symptoms who were admitted to SVS Medical College were included in the study. CT Brain (plain) done to confirm ischemic stroke & Fasting plasma fibrinogen in mg/dl was estimated using Clauss method and compared to age, sex and risk factor matched controls.

**Results:** In this study Mean plasma fibrinogen level amongst cases was 523.1 mg/ dL. Mean fibrinogen controls was 292.22mg/ dL. Statistically 't' and 'p' values were 8.55 and < 0.001.

**Interpretation & Conclusion:** This study shows that the plasma fibrinogen levels are significantly elevated in patients with ischemic strokes when compared to age, sex and risk factor matched controls. Plasma fibrinogen levels rise as age advances. Diabetes, hypertension and smoking do not influence plasma fibrinogen levels.

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## INTRODUCTION

Stroke remains the third leading cause of death and the leading cause of severe disability in the United States, Europe and portions of Asia in young (Naess *et al.*, 2012) and elderly people (Perls *et al.*, 2002; Lo *et al.*, 2003; Donnan *et al.*, 2008). Actually, the successful therapy for acute stroke is thrombolysis and bleeding is often a complication that can also depend on the lesion size (del Zoppo, 2004). Recent report shows that inflammation in the setting of acute ischaemic stroke (AIS) is associated with infarct size, supporting the hypothesis that inflammation in acute stroke primarily reflects an acute phase response determined by the degree of cerebral injury. Acute inflammation that develops following the initial ischemic episode is a major mechanism by which cells in the penumbra degenerate and the participation of inflammatory factors could be associated to the presence of early neurological deterioration and infarct volume (Tuttolomondo *et al.*, 2012). The first prospective study to show an association

between fibrinogen levels and subsequent cardiovascular disease risk was the Gothenburg Heart Study from Sweden in 1984. It remains unclear, however, whether elevated fibrinogen levels are a cause or consequence of atherosclerosis (Hennekens, 1998). EUROSTROKE (Bots *et al.*, 2002) project indicates that fibrinogen is a powerful predictor of stroke. Results did not disclose a differential in this relation of fibrinogen and fatal or non-fatal stroke, or with type of stroke (ischaemic or haemorrhagic). Fibrinogen belongs to acute phase proteins. Hyperfibrinogenemia in acute cerebral ischemia is associated with increased risk of death within 1 year after stroke (Turaj *et al.*, 2006) and poor functional outcome (del Zoppo *et al.*, 2009). Elevated fibrinogen level predicts also unfavorable prognosis in stroke patients treated with intravenous thrombolysis (González-Conejero *et al.*, 2006; Tanne *et al.*, 2006). Cerebral ischemia triggers acute phase reaction, and the blood concentration of inflammatory parameters could rise during brain infarction (Dziedzic, 2008).

## MATERIALS AND METHODS

Plasma fibrinogen of 200 consecutive patients presenting with acute ischemic stroke admitted in S.V.S MEDICAL

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COLLEGE HOSPITAL, MAHABOOB NAGAR, from August 2012 to August 2015 and compared with 100 controls not suffering from stroke with matched age, sex and risk factors (controls). Detailed history, clinical examination and relevant laboratory investigations were done as per proforma both in cases and controls. Fasting plasma fibrinogen in mg/dl was estimated using Clauss method and compared to age, sex and risk factor matched controls.

## RESULTS AND OBSERVATIONS

The age of the patients varied from a minimum age of 29 years to a maximum of 69 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 were not significantly different from each other  $t = 0.66$ ,  $p = 0.94$ .

**Table 1. Distribution of subjects by Age group**

Age group in years	Group A [Stroke]		Group B [Control]	
	Number	%	Number	%
20 – 30	4	2	2	2
31 – 40	16	8	10	10
41 – 50	72	36	34	34
51 – 60	98	49	52	52
61 and above	10	5	2	2
Total	200	100	100	100
Mean ± SD	49.22 ± 7.08		49.12 ± 8.13	

$T = 0.66$ ,  $p = 0.94$

**Table 2. Gender wise distribution of subjects among three groups**

Sex	Group A [Stroke]		Group B [Control]	
	Number	%	Number	%
Male	104	52	52	52
Female	96	48	48	48
Total	200	100	100	100

$\chi^2 = 0.0$ ,  $p = 1.0$

**Table 3. Distribution of subjects according to BMI in different groups**

BMI	Group A [Stroke]		Group B [Control]	
	Number	%	Number	%
15 – 20	72	36	8	8
21 – 25	92	46	62	62
26 – 30	32	16	29	29
More than 31	4	2	1	1
Total	100	100	50	100
Mean ± SD	22 ± 2.7		24.2 ± 2.3	

't' value = 4.23, 'p' value = <0.001

**Table 4. Role of Smoking as a risk factor**

Smoking	Group A [Stroke]		Group B [Control]		Chi square value	p value
	No of Patients	%	No of Patients	%		
Present	44	22	20	20	0.6	0.8
Absent	156	78	80	80		

**Table 5. Role of Alcohol as a risk factor**

Alcohol	Group A [Stroke]		Group B [Control]		Chi square value	p value
	No of Patients	%	No of Patients	%		
Present	32	16	16	16	0	1.0
Absent	148	84	84	84		

**Table 6. Role of Hypertension as a risk factor**

HTN	Group A [Stroke]		Group B [Control]		Chi square value	p value
	No of Patients	%	No of Patients	%		
Present	80	40	40	32	0.69	0.4
Absent	120	60	60	68		

**Table 7. Role of Diabetes as a risk factor**

Diabetes	Group A [Stroke]		Group B [Control]		Chi square value	p value
	No of Patients	%	No of Patients	%		
Present	56	28	24	24	0.2	0.6
Absent	144	72	76	76		

**Table 8. Mean ± SD values of studied parameters in controls and patients with Acute ischemic stroke**

Parameter	Group A [Stroke]		Group B [Control]		t value	p value
	MEAN	SD	MEAN	SD		
Plasma fibrinogen	523.1	175.9	292.22	73.7	8.55	<0.001

**Table 9. Mean ± SD of plasma fibrinogen in diabetic and non-diabetic subjects with in groups**

Parameter	Group A [Stroke]		Group B [Control]		F value	P value
	Non diabetic	diabetic	Non diabetic	Diabetic		
Plasma fibrinogen	568.87 ± 170.3	378.17 ± 100.8	295.07 ± 77.38	295.07 ± 77.38	36.64	< 0.001

**Table 10. Demonstrating the present study with earlier studies**

Author/ study	Study population	Mean Fibrinogen mg% Case group	Mean Fibrinogen mg% control group	'p' value
Mistry <i>et al.</i> 1990	56 patients 40 controls	531±74	445.78±92.28	< 0.01
Hazra <i>et al.</i> 1997	63 patients 30 controls	378.67	216.67	< 0.01
Bots <i>et al.</i> 2002	521 Cases 215 Controls	340.0	260.0	< 0.05
Beg <i>et al.</i> 2007	56	326.45 mg/dl,	202.23 mg/dl	< 0.001
Balachandiran <i>et al.</i> 2012	30 Cases 30 controls	362.41±89.56*	298.96±85.97	< 0.05
Anbuselvan <i>et al.</i> 2013	50 patients 26 control	547.5 ± 167mg/dl	326.8 ± 55mg/dl	< 0.001
Swarowska <i>et al.</i> 2014	266 Cases	340	270	< 0.01
Haritha <i>et al.</i> 2015	105	498.1	118.22	< 0.001
Naraina Swamy <i>et al.</i> 2015	30 20	411.50+111.56 370.1+105.83	313.76+71.24	< 0.05
Santhi <i>et al.</i> 2015	50 Cases 30 Control	492.1 mg/dl	318.33mg/dl	< 0.005
Present study	100 cases 50 controls	523.1± 175.9	292.22±73.7	< 0.001

\*45 sustained rise in fibrinogen, 221 non sustained rises in fibrinogen levels

(Table 1) There was no difference between gender variation, BMI measurement, smoking and alcohol consumption in this study (Tables 2, 3, 4, 5). 40 cases were hypertensive in stroke group while 32 were hypertensive in control (Table 6), 28 cases were diabetics as against 24 in control group (Table 7); both these risk factors did not show any difference in present study. Table 8 shows the plasma fibrinogen levels in both the groups. Mean plasma fibrinogen level amongst cases was 523.1 mg/dL in stroke patients as against 292.22 mg/dL with a 't' value 8.55 and 'p' value <0.001. Group A and B were subdivided into presence and absence of risk factors and an analysis of variance (ANOVA) was done to compare the role of fibrinogen in each group in the presence of risk factors. In the present study it was observed (Table 8) that plasma fibrinogen was significantly more in the non-diabetic study group compared to others (F = 36.64, p< 0.001). A post hoc analysis was done in ANOVA it was observed that fibrinogen levels significantly more in non-diabetic cases compared to diabetic cases, diabetic controls, non-diabetic controls p< 0.001. Plasma fibrinogen levels significantly more in diabetic cases compared to non-diabetic controls (p = 0.03), there was no statistical significance in plasma fibrinogen levels between diabetic controls and non-diabetic controls, and diabetic cases and diabetic controls. 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) (Table 6). 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 5). It was observed that plasma fibrinogen was significantly more in the non-smoker study group compared to others (F = 24.38, p< 0.001) (Table 4). There was no statistical significance in plasma fibrinogen levels between nonsmoker 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 controls (Table 4).

## DISCUSSION

Because fibrinogen is an acute phase reactant, elevated fibrinogen levels may be associated with severity of the ischemic event (Gregory J. del Zoppo *et al.*, 2009). The normal fibrinogen level is 400 mg/dl. From our study we concluded that Fibrinogen level in stroke patients was 40% higher than the fibrinogen level in normal subjects. The fibrinogen level linearly increased with the increase with age, similar to earlier study by Di. Mino Get...al in 1990 from their study they stated that increase in fibrinogen level by 25 mg/dl in every 10 years of increase in age. This proves that elderly people at higher risk of getting stroke and again the probable mechanism could be through the increased fibrinogen level in blood. The level of the increased fibrinogen level in blood. The level of fibrinogen is high in males than females. Though the variables like

diabetes and hypertension contributed individually to the increase in plasma fibrinogen, it is observed that the group in which both these two variables individually to the increase in plasma fibrinogen, it is observed that the group in which both these two variables existed together they have an additive effect on the plasma fibrinogen. The group in which there were no known risk factors like smoking, hypertension and diabetes also had increased fibrinogen level, which indicated that increased fibrinogen level alone could cause development of stroke. Similar observation was found in the study by Kayoed *et al* in 2003. 7, 8. By keeping age as a factor, Quzilbash *et al* conducted a study in 1995 they correlated the incidence of stroke and cardio vascular dysfunction by keeping age as a factor which proves that increased in plasma fibrinogen level is the voluntary potential factor for episodes of stroke. Fraser Bremen *et al* ...in 2000 correlated the Relation between circadian patterns in levels of circulating Lipoprotein (a), Fibrinogen, Platelets and related lipid variables in men, they stated that role of fibrinogen in stroke is by narrowing the blood vessels. Apart from fibrinogen other risk factors such as smoking, blood pressure, hematocrit, can favor the incidence of stroke in old age people (Turaj *et al.*, 2006).

In our study, mean fibrinogen levels are significantly raised in cases (411.50+111.56 mg/dl) compared to controls (313.76+71.24 mg/dl) with statistically significant difference. Among patients with Ischemic stroke, mean fibrinogen level was 439.63+106.93 mg/dl (with statistically significant difference compared to controls) and in hemorrhagic stroke mean level was 370.1+105.83 mg/dl (with statistically significant difference compared to controls) with statistically significant difference between two types of stroke. The following table shows the present study compared with earlier studies.

### Summary and Conclusion

In this study, mean plasma fibrinogen levels were significantly higher in ischemic stroke patients when compared to controls.

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**Conflicts:** Nil

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