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Association of plasma fibrinogen level with acute ischemic stroke: A comparative study with normal subjects

Dr. Rahil AY[1], Dr. Niranjan S Reddy[2*], Dr. Parameshwarappa SG[3]
[1, 2] Postgraduate Student, Department of , Sri Siddhartha Medical College, Tumakuru. Karnataka, India
[3] Professor, Department of Internal Medicine, Sri Siddhartha Medical College, Tumakuru. Karnataka, India

Abstract
Objective: The present study is designed to evaluate the level of plasma fibrinogen in patients with acute ischemic stroke and controls and also to find the association between them.
Material and Methods: The present study consists of 100 patients among which 50 were controls and 50 were cases including both sexes, aged between 28 to 98 years who had been admitted to medical wards and attended to OPD of Sri Siddhartha Medical College. Age, Sex and BMI was calculated and recorded. All the patients were subjected to blood sugar, and blood pressure. Plasma Fibrinogen was assessed by Clauss Clotting Method and compared to age, sex, BMI and risk factor of matched controls.
Results: In the present study we observed that the mean Plasma Fibrinogen (in mg %) was significantly higher in people with acute ischemic stroke (622.06 ± 112.76) levels than the people with normal CT-MRI findings (255.02 ± 144.99).
Conclusions: In the present study, the mean plasma fibrinogen levels were found to be higher in acute ischemic stroke patients when compared to controls. Hence measurement of plasma fibrinogen levels which is more specific than C-reactive protein to vascular disease is potentially useful to predict the possible outcome.

Keywords: acute ischemic stroke, plasma fibrinogen level, CT scan

Introduction
Stroke is defined as rapidly developing clinical signs of focal disturbance of cerebral function lasting more than 24 hours which distinguishes it from transient ischemic attack (TIA) where neurological deficit lasting less than 24 hours. Many risk factors for stroke includes diabetes, hypertension, smoking and hyperlipidemia were linked to increased fibrinogen levels [1, 2].
Fibrinogen is a plasma glycoprotein and very fundamental element of the coagulation cascade, as well as a major determinant of blood viscosity and blood flow. During blood clot formation, fibrinogen is converted by thrombin into fibrin. The normal serum fibrinogen level is approximately 200-400 mg/dl [3]. Different authors have well acknowledged that the high plasma fibrinogen levels strongly associated with thrombotic complication of atherosclerosis such as stroke and myocardial infarction. Abnormal elevated plasma fibrinogen levels result in changes in the blood rheological properties that aggravate the complications in peripheral blood flow during stroke predisposing to increased mortality [4, 5].
Hence, the present study is designed to evaluate the level of plasma fibrinogen in patients with acute ischemic stroke and controls and also to find the association between them.

Material & Methods
The present study was a case control study consists of 100 patients including both sexes, aged between 28 to 98 years who had been admitted to medical wards and attended to OPD of Sri Siddhartha Medical College (during the two year study period, Oct 2017-Aug 2019). Patients who were newly diagnosed acute ischemic stroke within 24 hours of onset of symptoms with diabetes mellitus and hypertension were considered for study as cases (n=50).
Patients who were accompanying with diabetes and hypertension apparently matched individuals with no previous history of stroke were recruited for control group (n = 50).
Patients with evidence of uremia, infection, active hepatic disease, and who have suffered from myocardial infarction in last three months and who have undergone surgery in last three months were excluded from the present study. After getting approval from Institutional ethics committee and informed consent obtained, the data will be collected from the patients by the detailed clinical history, clinical examination of the patients and relevant investigation in a specially designed proforma.
Age, Sex and BMI was calculated and recorded. All the patients were subjected to blood sugar, and blood pressure. Plasma Fibrinogen was assessed by Clauss Clotting Method and compared to age, sex, BMI and risk factor of matched controls. Data was analysed by using SPSS software version 18.0.

Results
This study consists of 100 patients (58 males and 42 females) with type 2 diabetes mellitus and hypertension includes both rural and urban subjects between 30-98 years of age inclusive. One hundred (100) subjects composed of 50 cases (Acute Ischemic stroke patients) and 50 matched controls were enrolled in the study. Of the 50 cases, 31 (67.4%) were males and 19 (45.2%) were females while in control group 27 (46.6%) were males and 23 (54.8%) were females which showed no statistical significant. The mean (± S.D) age was slightly increased in subjects with acute ischemic stroke patients (62.24 ± 14.87 years) compared to matched controls (59.30 ± 11.02 years) (Table 1).

Table 1: Distribution of age and sex in the study population

Parameters	Acute ischemic stroke (n=50)	Normal (n=50)	P value
Age (years) (Mean ± SD)	62.24 ± 14.87	59.30 ± 11.02	0.18
Sex			
Male (n)	31 (53.4%)	27 (46.6%)	0.418
Female (n)	19 (45.2%)	23 (54.8%)	

Table 2 shows the random blood glucose level (RBS), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), and BMI among the study groups. The mean random blood glucose level and systolic blood pressure level were higher in patients with acute ischemic stroke than control group but the difference was not significant. The mean diastolic blood pressure and BMI was found more in control group than the cases. The results showed no significant differences in both study groups. In the present study we observed that the mean Plasma Fibrinogen (in mg %) was significantly higher in people with acute ischemic stroke (622.06 ± 112.76) levels than the people with normal CT-MRI findings (255.02 ± 144.99).

Table 2: Comparison of mean of Anthropometric parameters and plasma fibrinogen among the study population

Parameters	Acute ischemic stroke (n=50) (Mean± SD)	Normal (n=50) (Mean± SD)	P value
RBS	247.74 ± 70.27	231.6 ± 57.18	0.211
SBP	153.4 ± 16.11	149.8 ± 10.59	0.190
DBP	92 ± 10.1	93 ± 6.47	0.557
BMI	27.42 ± 2.67	27.98 ± 2.64	0.294
Plasma Fibrinogen in mg%	622.06 ± 112.76	255.02 ± 144.99	<0.001

Table 3 shows the relation of risk factors like smoking and alcohol with mean plasma fibrinogen level. There were 48 smokers among the study groups. In the present study, non-smokers had higher mean fibrinogen levels than the smokers which were not statistically significant. Among alcoholic patients, the mean plasma fibrinogen level was higher than the non-alcoholic patients.

Table 3: Relation of risk factors with mean plasma fibrinogen level

Risk Factors	No. of cases	Mean Plasma Fibrinogen in mg%	P value
Smoking			
Yes	48	419.71 ± 206.66	0.425
No	52	455.92 ± 241.77	
Alcohol			
Yes	32	466.34 ± 226.29	0.400
No	68	425.46 ± 225.18	

Discussion

A study conducted by Nandyala V *et al*. reported that the fibrinogen level will linearly increased with the increase in age [6]. Mistry P *et al* did a similar study on 56 patients with acute ischemic stroke and reported that increase in fibrinogen level by 25 mg/dl in every 10 years. He also stated that elderly people at higher risk of getting stroke [2]. But in contrary, we didn't find any association of plasma fibrinogen level with age.

The present study has revealed a very high level of mean plasma fibrinogen in patients with acute ischemic stroke which was significantly different from those of normal group. Our results are in agreement with previous studies as shown in table 4. The disparity in the plasma fibrinogen level in the above said studies may be due to difference of the study populations.

Table 4: shows the mean plasma fibrinogen values among the study population in different authors

Authors	Case group		Control group		p value
	n	Mean Fibrinogen mg%	n	Mean Fibrinogen mg%	
Mistry *et al*. 1990 [2]	56	531 ± 74	40	445.78 ± 92.28	<0.01
Hazra *et al*. 1997 [7]	63	378.67	30	216.67	<0.01
Balachandiran *et al*. 2012 [8]	30	362.41 ± 89.56	30	298.96 ± 85.97	<0.05
Anbuselvan *et al*. 2013 [9]	50	547.5 ± 167	26	326.8 ± 55	<0.001
Santhi *et al*. 2015 [10]	50	492.1	30	318.33	<0.005
Nandyala V *et al* 2016 [6]	100	523.1 ± 175.9	50	292.22 ± 73.7	<0.001
Appuraj A T *et al* 2016 [11]	50	612.2 ± 186.06	50	296.8 ± 134.85	0.001
SK Mandal *et al* 2017 [3]	50	190.6	50	177.0	<0.001
Khandait *et al* 2019 [12]	30	584 ± 62	-	-	-
Present study 2020	50	622.06 ± 112.76	50	255.02 ± 144.99	<0.001

Ischemic stroke is an active vascular clinical event with signs of focal disturbance of cerebral function leading to fetal morbidity and mortality [11]. The pathophysiology may include both cerebral infarction and intracerebral or subarachnoid haemorrage. In the pathogenesis of vascular stroke, inflammation plays an important role wherein ferrtin, fibrinogen, C-reactive proteins (CRP), and other inflammatory reactants are involved.

Exacerbation of fibrinogen together with leukocytosis and increased leukocyte aggregation increases blood viscosity and leading to formation of blood clots resistant to fibrinolysis, predisposing to increased mortality [3]. Hence measurement of plasma fibrinogen levels which is more specific than C-reactive protein to vascular disease is potentially useful to predict the possible outcome.

Conclusion

In the present study, the mean plasma fibrinogen levels were found to be higher in acute ischemic stroke patients when compared to controls. It is advisable to patients who are at high risk for life style modification such as cessation of smoking, reduction of weight with physical activity and control of underlying diabetes and hypertension, which helps in decrease of plasma fibrinogen level, thereby reducing the incidence of acute ischemic stroke. Therefore, measurement of plasma fibrinogen can be used as diagnostic or prognostic tool

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