ORIGINAL ARTICLE

A COMPARATIVE STUDY OF SELECTIVE INDICATOR PROFILES IN PATIENTS WITH ISCHEMIC STROKE AND HEMORRHAGIC STROKE

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ABSTRACT: BACKGROUND: In Urban India, stroke accounts for 1% mortality in all hospital admissions. The pathogenic role of increased plasma fibrinogen level in causing stroke has been recently reinforced. It was therefore of interest to measure plasma fibrinogen level in patients with ischemic and hemorrhagic stroke and to compare it with lipid profile. Also to sell if fibrinogen levels increase if patient has hypertension, diabetes, smoking and alcohol intake. **METHODS:** The study was conducted in Victoria Hospital and Bowring & Lady Curzon Hospital attached to Bangalore medical college and Research Institute. Study included 30 patients of Ischemic stroke, 20 patients of Hemorrhagic stroke and 50 age and sex matched controls. Plasma Fibrinogen levels and lipid profile were analyzed in cases and controls. Duration of the study was 2 years. **RESULTS:** Most common age group in our study was 61-70 years. Males (62%) were more than females (38%). 16 patients were Diabetics (32%) and 21 were Hypertensives (42%). 40% of patients had elevated total cholesterol, 20% had elevated Triglycerides, 26% had high LDL value, 36% had Low HDL levels, 32% had high VLDL value. Mean fibrinogen levels are significantly raised in cases (411.50+111.56 mg/dl) compared to controls (313.76+71.24 mg/dl). Among patients with Ischemic stroke, mean fibrinogen level was 439.63+106.93 mg/dl and in hemorrhagic stroke mean level was 370.1+105.83 mg/dl. In Correlation of levels of lipid profile with levels of fibrinogen in Ischemic stroke cases, Pearson correlation showed moderate correlation for Fibrinogen vs T chol, small correlation for Fibrinogen vs TGL, Fibrinogen vs LDL and Fibrinogen vs VLDL and negative correlation for Fibrinogen vs HDL in cases and statistically significant difference for Fibrinogen vs T chol. In Hemorrhagic stroke cases, Pearson correlation showed negative correlation for Fibrinogen vs T chol, Fibrinogen vs TGL and Fibrinogen vs HDL, and trivial correlation for Fibrinogen vs LDL and Fibrinogen vs VLDL in cases. There was statistically significant difference in levels of fibrinogen between diabetics and nondiabetics. **CONCLUSION:** Plasma Fibrinogen levels are elevated in patients with Ischemic stroke and Hemorrhagic stroke, to a higher level in Ischemic stroke. Plasma Fibrinogen level correlates with Total cholesterol, Triglycerides, LDL and VLDL cholesterol in Ischemic stroke, whereas it correlates with LDL and VLDL cholesterol in Hemorrhagic stroke. Plasma Fibrinogen levels increase if patient has co morbidities like diabetes mellitus.

KEYWORDS: Ischemic stroke; Hemorrhagic stroke; Fibrinogen; Lipid profile.

INTRODUCTION: In India, Stroke accounts for 1% mortality of all hospital admission, 4% for all medical cases and about 20% of all disorders of central nervous system. Risk factor for stroke includes diabetes, hypertension, smoking and hyperlipidemia and these have been linked to abnormalities of haemorrheology and coagulation such as increased fibrinogen.[1] Stroke and

myocardial infarction are major thrombotic complications of atherosclerosis and leading causes of morbidity in atherosclerosis of blood lipids and lipoproteins, hypertension, diabetes mellitus, and smoking, as well as the active role of endothelial injury, smooth muscle cell proliferation, and inflammation. The role of hypercoagulability and of plasma fibrinogen, the central protein of the coagulation system, in this complex scenario has been suspected for many years, and has recently been documented by experimental and clinical evidence.[2,3,4] Stroke is characterized by rapidly developing clinical signs and symptoms of focal (and at times global in cases of coma and subarachnoid hemorrhage) disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin.[5] Stroke is one of the leading causes of mortality and morbidity worldwide. Approximately 20 million people each year will suffer from stroke and of these 5 million will not survive.[6] Developing countries account for 85% of global deaths from stroke. Stroke is also a leading cause of functional impairments, with 20% of survivors requiring institutional care after 3 months and 15%-30% being permanently disabled.[7] Stroke is a life-changing event that affects not only the person who may be disabled, but their family and caregivers. Utility analyses show that a major stroke is viewed by more than half of those at risk as being worse than death. Effective screening, evaluation, and management strategies for stroke are well established in high-income countries, but these strategies have not been fully implemented in India.[8,9] Stroke can occur at any age, but half of all strokes occur in people over 70 years old. Stroke is the third leading cause of death next only to ischemic heart disease and cancer. The incidence of stroke is expected to rise dramatically as the population ages because stroke risk increases with age. The risk of stroke doubles for each decade after the age of 55 years. Stroke is a major factor in the late life dementia that affects more than 40% of Americans over the age of 80. One in four men will have a disabling stroke by the age of 80 and one in five woman by the age of 85.[10] Fibrinogen and its derivatives have been shown to be involved in the initiation and growth of atherosclerotic lesions. The coagulation protein fibrinogen has emerged as an important contributor in the development of coronary, peripheral and cerebral vascular disease due to its involvement in both atherogenesis and thrombogenesis.[11]Large scale epidemiological studies have constituently demonstrated that an increased fibrinogen concentration is an independent risk factor for future cardiovascular and cerebrovascular events.[12,13] It is well established that raised fibrinogen levels increase the risk of (CHD) coronary heart disease. For stroke however data are much more limited and restricted to overall stroke.[14] Fibrinogen levels have been shown by a number of research teams to raise about 25 mg/dl per decade of age even if they are described as being in good health. Limited data suggest that it can also predict future mortality in survivors of myocardial infarction and stroke. Despite these observations, the metabolic mechanism responsible for producing hyperfibrinogenemia associated with an increased risk of cerebrovascular complications is yet to be established.[15] The purpose of this cross sectional study was to investigate plasma fibrinogen level in ischemic and hemorrhagic stroke with its association with lipid profile, smoking, diabetes, and hypertension and alcohol intake. The present study aims to study plasma fibrinogen levels in patients with stroke and compare it with lipid profile and to investigate whether these levels increase if the patient has additional risk factors like diabetes, hypertension, smoking and alcohol consumption.

MATERIALS AND METHODS: Total 30 cases of Ischemic stroke, 20 cases of Hemorrhagic Stroke confirmed by CT or MRI brain and 50 age and ex matched controls attending outpatient department or as inpatients in the Department of General Medicine, Victoria hospital and Bowring and Lady Curzon Hospital, BMC&RI, Bangalore between the period of October 2010 to September 2012 were included in the study. Prior approval for the study and protocol was obtained from the Institution ethical committee. After explaining the need of the investigations and the treatment options available, all the cases and controls were included in the study. Informed written consent was obtained from responsible attendant before actual study was performed.

INCLUSION CRITERIA:

1. Patients with Ischemic and hemorrhagic stroke confirmed by CT/MRI brain and Patients age more than 18 years.

EXCLUSION CRITERIA:

1. Patient having evidence of renal disease, active hepatic disease, history of prior MI or surgery within preceding 3 months.
2. Patients with prior history of stroke or TIA's
3. Patients with stroke older than 24 hours.
4. Patients with history of any infection in prior 4 weeks.
5. Patients on any lipid lowering agents including fibrates.
6. Patients with venous stroke.

METHOD OF COLLECTION OF DATA: Detailed history including the presence of hypertension, diabetes, smoking and alcohol intake was considered the following parameters were considered.

a) RBS.
b) Blood urea.
c) Serum creatinine.
d) Serum electrolytes.
e) Complete blood count including ESR.
f) LFT.
g) Chest X-ray.
h) ECG.
i) Echocardiogram.
j) Radio-imaging studies: CT scan/MRI Brain.
k) Fasting lipid profile.
l) Plasma fibrinogen levels.

Patients were followed up till their discharge from the hospital. Age, sex and risk factor matched controls not suffering from any medical illness were taken.

METHOD OF STATISTICAL ANALYSIS: Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean+SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. The following assumptions on data are made,

ASSUMPTIONS: 1) Dependent variables should be normally distributed, 2) Samples drawn from the population should be random, and cases of the samples should be independent. Students t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups Inter group analysis) on metric parameters. Leven's test for homogeneity of variance has been performed to assess the homogeneity of variance. Chi-square/Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Pearson correlation of fibrinogen with lipid parameters is done to find the relationship.

RESULTS AND ANALYSIS:

STUDY DESIGN: A Comparative two group clinical study with 50 cases (Ischemic and Hemorrhagic stroke) and age and sex matched controls in undertaken to study the levels of fibrinogen and lipid profile.

Age in years	Cases		Controls	
	No.	%	No.	%
30-40	4	8.0	4	8.0
41-50	7	14.0	7	14.0
51-60	14	28.0	14	28.0
61-70	18	36.0	18	36.0
>70	7	14.0	7	14.0
Total	50	100.0	50	100.0
Mean + SD	**59.50 + 11.80**		**59.50 + 11.80**	

Table 1: Age distribution of cases and controls

Gender	Cases		Controls	
	No.	%	No.	%
Male	31	62.0	31	62.0
Female	19	38.0	19	38.0
Total	50	100.0	50	100.0

Table 2: Gender distribution of cases and controls

Samples are gender matched with P = 1.000.

Gender	Cases		Controls	
	No.	%	No.	%
Unskilled	12	24.0	5	10.0
Businessman	5	10.0	11	22.0
Service	7	14.0	1	2.0
Housewife	19	38.0	18	36.0
Retired	7	14.0	15	30.0
Total	50	100.0	50	100.0

Table 3: Distribution of occupation of cases and controls

Gender	Cases		Controls	
	No.	%	No.	%
Rural	22	44.0	23	46.0
Urban	28	56.0	27	54.0
Total	50	100.0	50	100.0

Table 4: Distribution of region of cases and controls

Region distribution is statistically similar with P = 1.000.

Complaints	Number of patients (n=50)	%
1. Right hemiparesis	17	34.0
2. Left hemiparesis	14	28.0
3. Right hemiparesis and aphasia	7	14.0
4. Altered sensorium	5	10.0
5. Left hemiplegia	2	4.0
6. Right hemiparesis and altered sensorium	2	4.0
7. GTCS one episode	1	2.0
8. Headache, giddiness, vomiting	1	2.0
9. Right hemiplegia	1	2.0

Table 5: Distribution of Complaints in cases

Co-morbid condition	Cases (n=50)		Controls (n=50)	
	No.	%	No.	%
Diabetes				
Yes	16	32.0	16	32.0
1-2 years	3	6.0	8	16.0
3-5 years	7	14.0	8	16.0
6-10 years	6	12.0	-	-
No	34	68.0	34	68.0
Hypertension				
Yes	21	42.0	21	42.0
1-2 years	10	20.0	6	12.0
3-5 years	5	10.0	15	30.0
6-10 years	6	12.0	-	-
No	29	58.0	29	58.0

Table 6: Distribution of co-morbid conditions in cases and controls

Habits	Cases (n=50)		Controls (n=50)		P Value
	No	%	No	%	
Smoking					
Yes	8	16.0	8	16.0	1.000
No	42	84.0	42	84.0	
Alcohol					
Yes	4	8.0	4	8.0	1.000
No	46	92.0	46	92.0	

Table 7: Distribution of Habits of cases and controls

DISCUSSION: The present study was done to determine the levels of fibrinogen and lipid profile in stroke as well as determine the relation between fibrinogen levels and lipid profile in stroke. Our study compared the fibrinogen levels with lipid profile in patients with ischemic stroke and hemorrhagic stroke. The study included 30 patients of ischemic stroke, 20 patients of hemorrhagic stroke and 50 age and sex matches controls. Patients were evaluated with detailed history, meticulous examination and laboratory investigations. Laboratory investigations included mainly fasting lipid profile and plasma fibrinogen levels. In our study, age group distribution was between 30 years to 87 years. Mean age of patients with stroke was 59.5+11.8 years. Mean age of patients in control group was 59.5+11.8 years. Both the case and control group included 31 males and 19 females.

56% of the cases were from urban areas and 44% of the cases were from rural areas. Most common presenting complaint in our study was hemiparesis (right/left) (76%) followed by altered sensorium (10%). In this study, 16 patients were Diabetics (32%) and 21 were Hypertensives (42%). 6(12%) patients were both Diabetics and Hypertensives. In our study, there was statistically significant difference in levels of fibrinogen between diabetics and non-diabetics in cases but no difference in controls, with higher levels in diabetics. The exact mechanism of increased fibrinogen in diabetics is unknown, possible mechanisms include. Endothelial dysfunction is common in diabetics, which causes decreased fibrinolytic activity and hence increased plasma fibrinogen levels. Thus, insulin concentrations need to be maintained at the lowest possible levels in type 2 diabetics to prevent increased fibrinogen synthesis and concentrations. In our study, among cases, 8 were Smokers and 4 were chronic alcoholics. Among smokers one was Diabetic, one Hypertensive and one more was both diabetic and hypertensive. Among alcoholics one was diabetic and one was hypertensive.38 patients (76%) had systolic BP more than 140 mmhg, 27 patients (54%) had diastolic BP more than 90 mm hg at presentation. Both Systolic and significant values. Most common radiologic finding noted was MCA infarct (42%) followed by Capsuloganglionic bleed (14%) and putaminal bleed (12%).In our study, 40% of patients had elevated total cholesterol (mean level 182.72+37.64), 20% had elevated Triglycerides (mean 130.44+49.46), High LDL value (mean 111.97+30.74) was seen in 26% of cases, Low HDL levels (mean 44.75+16.62) was seen in 36% of cases, High VLDL value (mean 33.19+15.46) was seen in 32% of cases with HDL, LDL and VLDL levels statistically

significant. In Comparison of lipid profile between cases and controls, statistically significant difference was noted in Mean LDL and VLDL levels. In study done by M Balachandiran et al, mean total cholesterol was 211.48+39.86 mg/dl, mean triglycerides was 158+72.87, mean LDL was 136.51+31.92, mean HDL was 43.72+13.12 and mean VLDL was 31.6+14.57 mg/dl. In Comparison of lipid profile between cases and controls, statistically significant difference was noted in Mean LDL and Total Cholesterol levels. 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. In study done by M. Balachandiran et al, mean plasma fibrinogen level was 362.41+89.56 mg/dl in cases and 298.96+85.97 mg/dl in controls with statistically significant difference. In our study, in Correlation of levels of lipid profile with levels of fibrinogen in Ischemic stroke cases, Total cholesterol levels correlation with fibrinogen was statistically significant. None of the other correlations were statistically significant. In study done by Dotevall A et al[16], plasma fibrinogen and its association to other risk factors for cardiovascular disease was investigated in a random sample of 691 men and 739 women, aged 25 to 64 years, participating in the Goteborg MONICA survey. In both genders univariate analyses revealed significantly positive correlations between plasma fibrinogen and age, body mass index (BMI), waist/hip radio (WHR), systolic blood pressure, serum cholesterol and triglycerides and a negative correlation to high-density lipoprotein (HDL) cholesterol.

CONCLUSION: Plasma Fibrinogen levels are elevated in patients with Ischemic stroke and Hemorrhagic stroke, to a higher level in Ischemic stroke than Hemorrhagic stroke. Plasma Fibrinogen level correlates with Total cholesterol, Triglycerides, LDL and VLDL cholesterol in Ischemic stroke. Smoking, hypertension and alcohol intake did not influence fibrinogen levels. Hence, along with lipid profile estimation, Fibrinogen level needs to be estimated and treated to improve the outcome of the patient.

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