



ROLE OF PLASMA FIBRINOGEN LEVELS IN CEREBRO VASCULAR ACCIDENTS

General Medicine

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ABSTRACT

Stroke (Cerebrovascular accident) is considered to be one of the most common causes of mortality and long term severe disability.

Aims and Objective : Role of plasma fibrinogen in patients with Cerebrovascular accidents (Stroke).

MATERIAL AND METHODS : It is a hospital based Prospective analytical study, 50 adult patients admitted in medical wards and acute medical care with first episode of stroke between period August 2016 to August 2018 in Sri Venkateswara Ram narain Ruia Government General Hospital, Tirupati, Andhra Pradesh, were included in the study.

RESULTS : Most common in the age group 50-69 years with mean age of 61.56 years. Males are more affected with male to female ratio of 3.5:1. Males have a higher mean fibrinogen levels than females. There is statistically significant raise of fibrinogen levels in smokers and Hypertensives but not in alcoholics and diabetics.

CONCLUSION : Elevated fibrinogen level is one of the independent risk factor for stroke. It is evident from this study that there is increased mortality with increase in fibrinogen levels, higher the fibrinogen levels poorer the outcome.

KEYWORDS

Stroke, Fibrinogen .

INTRODUCTION

Stroke (Cerebrovascular accident) is considered to be one of the most common causes of mortality and long term severe disability. Stroke was defined by World Health Organization criteria as "rapidly developing clinical signs of focal, at times, global disturbance of cerebral function lasting for more than 24 hours or leading to death with no apparent cause other than vascular origin".¹

Fibrinogen is the most haemorrhologically important plasma proteins, which acts as a risk factor for many of clinical conditions, which predicts the future development of complications. Its concentration alters dramatically in association with a wide variety of clinical conditions and it contributes to the difference in viscosity of plasma, leading to peripheral arterial diseases and cerebrovascular diseases.

Normal fibrinogen level is 200-350 mg/dl. Fibrinogen Levels higher than 350 mg/dl is a risk factor for coronary artery disease and stroke.²

The present study aims to estimate plasma fibrinogen levels in cerebrovascular accidents and to correlate the significance between fibrinogen and various parameters including hypertension, diabetes, alcohol, smoking etc.

MATERIALS AND METHODS:

It is a hospital based Prospective analytical study. 50 patients were enrolled in the present study who are admitted in the Medical wards and Acute medical care unit, SVRRGGH, Tirupati between who met the inclusion and exclusion criteria.

INCLUSION CRITERIA:

1. Patients age more than 14 years with first episode of stroke.
2. Patients with stroke confirmed by CT scan or MRI brain.
3. Patients or their attenders who are willing to give informed ,written consent.

EXCLUSION CRITERIA:

1. Patients having evidence of renal disease, active hepatic disease, history of prior MI or surgery within preceding 3 months.
2. Patients with history of any infection in prior 4 weeks.
3. Patients with Trauma, Subdural Haematoma, Tumours.

STUDY METHODS:

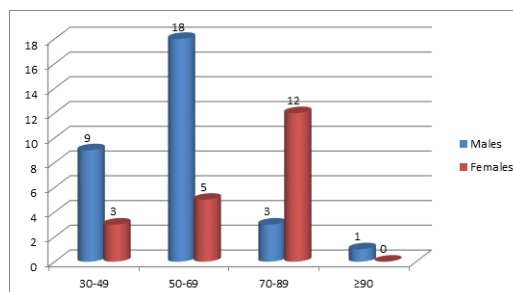
After selection of patients, written informed consent was taken from the patients or their attenders and detailed history and Physical examination was done according to pre structured proforma. All patients were investigated with routine blood tests like CBC, Blood Urea, Serum creatinine, Random blood sugar, CRP, urine Routine Microscopy, ECG, carotid doppler, Lipid profile, CT Brain, MRI Brain done in selected cases. Estimation of Plasma Fibrinogen level was carried between 24-72 hours after the onset of Cerebro Vascular accidents.

RESULTS:

AGE AND SEX DISTRIBUTION:

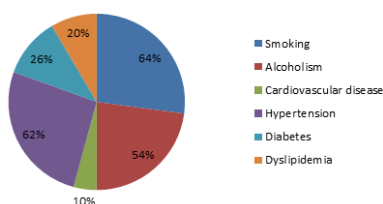
In the present study, the most common age group affected is between 50-69 years (46%), followed by 70-89 years (30%) and 30-49 years (24%). The least common age group observed in the present study is ≥ 90 years (2%). The mean age was 61.56 years. 78 % of patients are male and 22% are female in the present study. Male preponderance is observed in the present study with a male to female ratio of 3.5:1.

Figure 1: Age and sex distribution



RISK FACTORS IN STROKE:

Commonest risk factor observed in the present study is smoking which is seen in 64% of patients followed by hypertension and alcoholism seen in 62% and 54% respectively. Least common risk factor observed is cardiovascular diseases (10%). Other risk factors are Diabetes and Dyslipidemias, observed in 26% and 20% respectively.

Figure 2: Risk factors**TYPE OF STROKE:**

In the present study, Ischemic stroke is seen in 34 (68%) patients and Hemorrhagic stroke in 16 (32%) patients. It shows that ischemic stroke is more common than hemorrhagic stroke.

PLASMA FIBRINOGEN LEVELS IN STROKE:

In the present study 19 (38%) patients have normal fibrinogen levels and 31 (62%) patients have higher fibrinogen levels. Out of 31 patients, 22 (71%) patients are having ischemic stroke (plasma fibrinogen levels ≥ 350 mg/dl) and 9 (29%) are having hemorrhagic stroke.

PLASMA FIBRINOGEN LEVELS IN RELATION WITH RISK FACTORS:**AGE AND SEX:**

When compared age wise, hyperfibrinogenemia is seen in 4 out of 11 patients in the age group of 21-40 years, 15 out of 23 patients in the age group of 41-60 years and 12 out of 15 patients in the age group of 61-80 years. This shows increasing the levels of fibrinogen as age advances. Among male patients, 28 (72%) out of 39 have hyperfibrinogenemia and in female 3 (27%) out of 11 have hyperfibrinogenemia. The mean fibrinogen levels in males and females are 393.38 and 323.18 respectively and is statistically significant (p value is 0.0074).

SMOKING AND ALCOHOL. Out of 50 persons, 32 are smokers and 27 are alcoholics. The mean value of fibrinogen is more among smokers and alcoholics when compared to non-smokers and non alcoholics. There is a statistical significance is observed in smokers with a p value of 0.0201. In alcoholics there is no statistical significance when compared with non alcoholics. (p value is 0.198)

HYPERTENSION AND DIABETES:

Out of 50 persons, 32 (64%) are hypertensive and 14 (28%) are Diabetics. There is a statistical significance is observed between hypertensives and normotensives in mean fibrinogen levels with a P value of 0.0064. There is no statistical significance between diabetics and non diabetics.

TYPE OF STROKE

In the present study, the most common type of stroke is ischemic stroke in 68% and hemorrhagic stroke is seen in 32% of patients. But the mean value of fibrinogen is almost similar to both ischemic (384.9) and hemorrhagic (380.5) strokes. It is not statistically significant (P value is 0.84).

STROKE OUTCOME IN RELATION WITH FIBRINOGEN LEVELS:

Out of 50 patients, 7 patients expired and 43 patients survived. Among deceased 4 patients had ischemic stroke and 3 patients had hemorrhagic stroke. All non survivors have higher fibrinogen level.

S.no	Fibrinogen(mg/dl)	Survivors	Non survivors
1	200-349	19	-
2	350-449	19	3
3	450-549	05	4

DISCUSSION:**AGE:**

Age is a non modifiable risk factor for stroke and stroke is commonly seen in individuals with age more than 55 years. For each successive 10 years of age, the stroke rate more than doubles in both men and women.³ In the present study, patients are in the age group of 30-90 years, with mean age of 61.56 years. the similar results were observed by Kamalchandra et al, Narayanaswamy et al, Ramanamurthy et al and Venkata Madhav et al where the mean age was 58.52 yrs, 59.5+11.8 yrs, 58.52 yrs and 56.26 respectively. The mean age was higher in the studies done by Jaroslaw Pniewski et al (68.27 years), Bruce M Coull et al (67 years) and Swarowska et al (69 years). The higher mean age

may be due to more number of elderly patients in their study. The mean age was lower in the study done by Venkateswarlu et al (49.22) as more number of younger patients were enrolled in their study.

SEX:

Male sex is a risk factor for stroke. Sex hormones like oestrogen is said to have protective against the development of atherosclerosis and stroke in females. Atherosclerosis process is more severe in men than women.

Stroke incidence rates are 1.25 times greater in men⁴. In the present study of stroke males constitute 78 % of study population and 22 % are females. The male to female ratio is 3.5 : 1. Similar observations were made by Bruce M Coull et al with male to female ratio of 4:1. Male to female ratio is lower in the study of Haritha et al and Perumall et al (1.9:1). Venkateswarlu et al and Ahmed et al (1.08) observed more or less equal involvement in both sexes in their studies.

RISK FACTORS:**SMOKING:**

Mechanism by which tobacco smoke exposure can increase the risk of stroke and heart disease are numerous and include carboxyhemoglobinemia, increased platelet aggregability, increased fibrinogen levels, reduced HDL-cholesterol, and direct toxic effects of compounds such as 1,3-butadiene, a vapor phase constituent of environmental tobacco smoke that has been shown to accelerate atherosclerosis. In our study, smoking is the most common risk factor and is observed in 64 % of the patients. Similar results were reported by Haritha et al, Kamalchandra et al and Appuraj et al. A higher incidence of smoking is reported by Shrestha et al (75%) compared to present study. A lower incidence of smoking is reported by Venkateswarlu et al and Narayanaswamy et al, this may be due to less number of male subjects in their studies compared to the present study.

ALCOHOL:

Alcohol consumption is an independent risk factor for both ischemic stroke and hemorrhagic stroke. In the present study, alcohol is the third most common risk factor and is observed in 54% of study subjects. Most of the previous studies showed lesser incidence of alcohol as risk factor.

HYPERTENSION:

Hypertension is the strong risk factor for stroke. The incidence of stroke increases with rising blood pressure levels. About 40% of strokes can be attributed to a systolic blood pressure of more than 140 mm Hg^{7,8,9,10}. Second most common risk factor observed in the present study is hypertension which is seen in 62% of patients. Similar observations were made by Haritha et al (70%) and Perumalla et al (53.3%). The incidence of hypertension was lower in study of Appuraj et al (44%), Narayanaswamy et al (42%). Higher incidence of hypertension was observed in the study of Shrestha et al (82.5%).

DIABETES MELLITUS

Diabetes mellitus is one of the risk factors for stroke and abnormal lipoprotein profile in diabetes accounts for the elevated risk of stroke. In the present study, Diabetes is the fourth common risk factor and is present in 26% of subjects. Similar results were observed in studies by Venkateswarlu et al (28%), Kamal chanda et al (30%), Appuraj et al (30%) and Narayanaswamy et al (32%). A higher incidence of Diabetes is observed in the study by Seong et al (39.6%) but a lower incidence of Diabetes is documented in the study of Haritha et al (10%).

DYSLIPIDEMIA:

Dyslipidemia in the form of high total and LDL cholesterol is an important risk factor in the development of stroke, be it an infarct or hemorrhage. It is the fifth common risk factor observed in the present study and is present in 20% of study subjects. The incidence of Dyslipidemia in the study by Appuraj et al (30%) and Perumalla et al (31.6%) more or less correlate with the present study. A higher incidence of Dyslipidemia was seen in Haritha et al study (78%).

TYPE OF STROKE:

The most common type of stroke is ischemic compared to hemorrhagic stroke¹¹. The present study shows ischemic stroke in 68% of study subjects and hemorrhagic stroke in 32%. More or less similar results were reported by Narayanaswamy et al and Shrestha et al. Higher incidence of ischemic

stroke was observed by Ramanamurthy et al (90%) and Kamalchandra et al (88%).

Lower incidence of ischemic stroke was observed by Ahmad et al (40%).

PLASMA FIBRINOGEN LEVELS AND TYPE OF STROKE:

In the present study, mean plasma fibrinogen levels are slightly higher in ischemic stroke (384.9) than hemorrhagic stroke (380.5). Similar results were observed in the studies done by Kamalchandra et al, Narayanaswamy et al. But mean plasma fibrinogen levels are lower in ischemic stroke (348) compared to hemorrhagic (381) in a study done by Ahmad et al.

Haritha et al and Venkateswarlu et al conducted studies only in ischemic stroke and their mean fibrinogen levels were 498.1 mg/dl and 523.1 mg/dl respectively, these values are higher compared to the present study.

PLASMA FIBRINOGEN LEVELS AND AGE:

It has been observed in various epidemiological studies that plasma fibrinogen level increases with increasing age. Spada et al¹² have shown that patients with ischemic stroke have an earlier and more evident age related increase in fibrinogen values than controls, showing that fibrinogen is an important risk factor in elderly for stroke. Kamalchandra et al¹³ also have shown that fibrinogen levels increase with age.

PLASMA FIBRINOGEN LEVELS AND SEX:

In the present study increased fibrinogen levels are seen in males (72%) compared to females (27%). A.R. Kumar et al¹⁴ in their study showed elevated fibrinogen levels were seen in 80% of male subjects and 50% of female. Haritha et al¹⁵ observed elevated plasma fibrinogen levels in 73% of males and 59% of females in their study. In contrast to this higher fibrinogen levels are seen in female subjects observed by P S V Ramana Murthy et al¹⁶ Appuraj et al¹⁷.

SMOKING AND FIBRINOGEN LEVELS

There is a positive correlation between smoking and plasma fibrinogen levels.

Hunter et al, Shrestha et al, Haritha et al and Appuraj et al demonstrated that smoking is associated with increased plasma fibrinogen levels. The present study shows higher plasma fibrinogen levels in smoker compared to non smokers and correlates with other studies.

ALCOHOL AND FIBRINOGEN LEVELS

Binge drinking is an independent risk factor for all strokes. The present study demonstrated that fibrinogen levels are higher in non alcoholics compared to alcoholics similar to studies done by Appuraj et al and venkateswarlu et al

HYPERTENSION AND FIBRINOGEN LEVELS

Fibrinogen levels are higher in hypertensives than in normotensives. In the present study, plasma fibrinogen levels are higher in hypertensives than normotensives. Anjulajain et al, Lee AJ and Shrestha et al demonstrated higher fibrinogen levels in hypertensives.

DIABETES AND FIBRINOGEN LEVELS

In the present study, plasma fibrinogen levels are higher in non-diabetics than Diabetics. Archana Kamalchandra et al have shown that mean fibrinogen levels in diabetics is 545.3 mg/dl compared to 648.6 mg/dl in non diabetics. Appuraj et al and Ramanamurthy et al observed higher plasma fibrinogen levels in non diabetics compared to diabetic. These studies correlate with the present study.

OUTCOME AND FIBRINOGEN LEVELS

The present study shows higher mean fibrinogen levels in non survival group compared to survival group. High mean fibrinogen levels are associated with poor outcome. Swarowska M et al, Appuraj et al showed that sustained increase of plasma fibrinogen during ischemic stroke predicts worse outcome independently of baseline fibrinogen level.

LIMITATIONS:

Small Sample size and the findings are based on single time measurement of fibrinogen rather than serial measurements of fibrinogen.

CONCLUSIONS

Elevated fibrinogen level are one of the independent risk factor for

stroke. High fibrinogen levels are seen in increasing Age, Male sex, smoking and hypertension. It is evident from this study that there is increased mortality with increase in fibrinogen levels and higher the fibrinogen levels, poorer the outcome.

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