CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
http://doi.org/10.5281/zenodo.3373788

Available online at: http://www.iajps.com *Research Article*

AN ASSESSMENT OF SERUM FIBRINOGEN LEVELS IN PATIENT OF ACUTE STROKE

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Article Received: June 2019 **Accepted:** July 2019 **Published:** August 2019

Abstract:

Objective: *To assess the serum fibrinogen levels in patient of stroke presenting at BVH Bahawalpur.*

Material and methods: *This cross-sectional study was conducted at Department of Pathology, Quaid-e-Azam Medical College/BVH, Bahawalpur from September 2018 to March 2019 over the period of 6 months. Total 50 patients with first-ever stroke admitted within 24 h after stroke onset either male or female were selected for this study. Serum fibrinogen levels were assessed in selected patients.*

Results: *A total of 50 patients of stroke were enrolled and studied. Thirty (60%) cases reported ischemic stroke while hemorrhagic stroke was observed in 20 (40%) cases. Thirteen out of 50 (26%) patients were in the age group of 31-40 years; with age distribution of rest of the participants being relatively evenly distributed. Males (29, 58%) outnumbered females (21, 42%).*

Conclusion: *In conclusion, we report significantly higher than normal mean fibrinogen levels in ischemic and hemorrhagic stroke and fibrinogen levels increased with increasing infarct volume and the correlation between infarct volume and fibrinogen levels being significant in ischemic stroke. In both the groups, the fibrinogen levels in patients who died was insignificantly higher as compared to patients who survived. Limited mortality numbers probably didn't allow the observations of present study to reach the level of significance, which prompts us to recommend similar study with higher numbers.*

Key Words: *Hemorrhagic stroke, Ischemic stroke, Plasma fibrinogen level*

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Please cite this article in press Tahira Jabeen et al., ***An Assessment Of Serum Fibrinogen Levels In Patient Of Acute Stroke.,*** *Indo Am. J. P. Sci, 2019; 06[08].*

INTRODUCTION:

Stroke is a major global public health problem. According to the Global Burden of Diseases (GBD) study in 1990, stroke was the second leading cause of death worldwide.[1] With the rising proportion of mortality, stroke still remains the second leading cause of death worldwide.[2] In sub-continent, the cumulative incidence of stroke was recently reported higher than those of high-income countries, ranging from 105 to 152/100,000 persons per year.[3]

Thus, it becomes imperative to look for factors contributing to the increased chances and severity of stroke. Risk factors include diabetes, hypertension, smoking and hyperlipidemia and these have been linked to abnormalities of coagulation.[4] A number of biological markers such as leptin, high sensitivity C-reactive protein (hs-CRP), insulin, cortisol, fibrinogen, protein C, protein S, Von Willebr and factor, D-dimer, Antithrombin III and MMP-9 have been evaluated for their prognostic values and their relationship with lesion volume in stroke patients.[5,6] Fibrinogen is a plasma glycoprotein that is converted by thrombin into fibrin during blood clot formation. 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.[7,8] In a developing country with limited health care facilities and with neuroimaging being inaccessible in certain areas, plasma fibrinogen can easily be made available and is postulated to be effective parameter for assessing the severity and prognosis in stroke cases.

The present study was undertaken to determine the correlation between mean plasma fibrinogen level and infarct volume on CT scan among patients with acute stroke.

MATERIAL AND METHODS:

This cross-sectional study was conducted at Department of Pathology, Quaid-e-Azam Medical College/BVH, Bahawalpur from September 2018 to March 2019 over the period of 6 months.

Total 50 patients with first-ever stroke admitted within 24 h after stroke onset either male or female were selected for this study. Study was approved by the ethical committee and written informed consent was taken from every patient.

Patients with past history of stroke, active infections or malignancy, renal, cardiac or liver disease, pregnant women, patients with transient ischemic attack, CNS tumours, recent head injury and patients/relatives not willing to participate in the study were excluded.

5ml blood of patients was drawn serum fibrinogen levels were measured. Findings of the test was entered in pre-designed proforma along with demographic profile of the patients.

Operational definitions:

Stroke: Rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin.9 Diagnostic criteria for acute stroke would consist of sudden onset of focal/ global neurologic deficit with objective confirmation of arterial-distribution ischemia/hemorrhage by computed tomography (CT) or magnetic resonance imaging (MRI).

Hyperfibrinogenemia: Plasma fibrinogen concentration >3.5g/L (as determined by modified Clauss method).[10,11]

All the participants were subjected to radiological examination (CT scan or MRI) for confirmation, as relevant. Routine haematological and other investigations were conducted in all the participants. Blood sample for plasma fibrinogen concentration was withdrawn at the time of admission after stabilization of the patient. Clinical course of patients during the admission as well as the outcomes were assessed by relevant parameters.

All the collected data was entered in SPSS version 18 and analyzed. Mean and SD was calculated for numerical data and frequencies and percentages were calculated for categorical data.

RESULTS:

A total of 50 patients of stroke were enrolled and studied. Thirty (60%) cases reported ischemic stroke while haemorrhagic stroke was observed in 20 (40%) cases. Thirteen out of 50 (26%) patients were in the age group of 31-40 years; with age distribution of rest of the participants being relatively evenly distributed. Males (29, 58%) outnumbered females (21, 42%).

Right sided hemiparesis was observed in 27 cases (54%) while left sided hemiparesis was found in 21 cases (42%). Headache (29, 58%) was the commonest symptom followed by vomiting (26, 52%) and altered sensorium (20, 40%) in all types of stroke patients. Atherosclerosis was observed to be the most common cause of ischemic stroke (70%) followed with

cardiogenic embolism (26.7%) and sickle cell disease (3.3%); whereas hypertension was found present in majority of haemorrhagic stroke patients (12, 60%) along with other conditions (AV malformation, Moya Moya disease, Warfarin toxicity and preeclampsia in 2 patients each).

Assessment of risk factors revealed that out of 4 peripartum females, 3 suffered ischemic stroke and 1 had haemorrhagic stroke. Similar were the findings for patients on oral contraceptive pills (OCP). Obesity and abnormal lipid profile were found to be more associated with occurrence of ischemic stroke. Rheumatic valvular heart disease (RVHD), smoking, alcohol consumption and tobacco use was found to be similar across all groups (Table 1).

The mean fibrinogen levels in ischemic (584±62mg/dl) and haemorrhagic stroke (52±28mg/dl) were found to be significantly higher ($p<0.05$) than normal range of (200-400 mg/dl). The mean infarct volume in patients with Ischemic Stroke was 62.79±9.51cm3 while mean plasma fibrinogen level was 584±62mg/dl. It was observed that fibrinogen level increased with increasing infarct volume. There was significant correlation between infarct volume in patients with Ischemic Stroke and fibrinogen levels (r coefficient =0.61; $p<0.05$).

The mean infarct volume in patients with Haemorrhagic Stroke was 60.58±10.52cm3 while mean plasma fibrinogen level was 552±28mg/dl. It was observed that fibrinogen level did not increase with increasing infarct volume and there was no significant correlation between infarct volume in patients with Haemorrhagic Stroke and fibrinogen levels (r coefficient =0.3; $p>0.05$) (Table 2).

Seven and five patients with ischemic and haemorrhagic stroke respectively died in the present study. There was no significant association between mortality and occurrence of specific type of stroke. The fibrinogen levels in patients who died was higher as compared to patients who survived. Although fibrinogen levels were higher in patients who died, the association of fibrinogen levels with mortality was not significant ($p>0.05$) (Table 3).

Table 1: Association of risk factor in different types of stroke.

Risk Factors	Ischemic		Hemorrhagic		Total		P value
	N	%	N	%	N	%	
Peripartum	3	10	1	5	4	8	p>0.05
Obesity/ overweight	15	50	6	30	21	42	
RVHD	9	30	7	3	16	32	
Smoking	11	36.7	7	35	18	36	
Alcohol	7	23.3	6	30	13	26	
Tobacco	6	20	6	30	12	24	
DM	3	10	3	15	6	12	
Abnormal lipid profile	12	40	5	25	17	34	
OCPs	3	10	2	10	5	10	

Table 2: Association of fibrinogen level with infarct volume in stroke patients.

Infarct volume range (cm3)	Infarct volume (cm3)		Fibrinogen level (mg/dl)		r coefficient	P value
	Mean	SD	Mean	SD		
Ischemic stroke						
30-40	38.85	0.71	480.5	3.53	0.61	p<0.05
40-50	48.34	0.44	509.3	2.08		
50-60	58.56	1.12	520.3	5.75		
60-70	68.92	1.17	626.79	28.12		
Total	62.79	9.51	584	62		
Haemorrhagic stroke						
30-40	37.80	0.63.	557	48.08	0.3	p<0.05
40-50	47.58	1.36	550	49.49		
50-60	57.81	1.39	551.8	31.62		
60-70	68.35	1.23	551.54	23.72		
Total	60.58	10.52	552	28		

Table 3: Association of fibrinogen level with mortality in stroke patients.

Mortality	Status	Fibrinogen level (mg/dl)		P value
		Mean	SD	
Ischemic stroke	Died	588.08	58.08	p>0.05
	Alive	571.29	81.39	
Ischemic stroke	Died	552.4	26.01	
	Alive	550.8	35.25	

DISCUSSION:

Present study entailed assessment of 50 consecutive patients with first-ever stroke admitted within 24 h after stroke onset and trying to establish correlation between their plasma fibrinogen levels and various acute stroke parameters.

At the outset, as far as subtyping the stroke from prognostic point of view is concerned, it is believed that comparisons between hemorrhagic (HS) and ischemic stroke (IS) are hampered by the disproportionate distribution of the 2 types of stroke, with IS being 10-times more frequent than HS in Western countries.[12-15] Even in large stroke cohorts absolute numbers of HS are low, rendering statistical validation of differences between the 2 types of stroke difficult.[14,15] So, any difference observed between the two stroke variants needs to be looked at with this caveat in mind.

In the present study, 40% patients reported embolic stroke while thrombotic and haemorrhagic stroke were observed in 30% of patients each. A study by Nayak SD et al observed thrombotic and haemorrhagic stroke to be occurring in 24% and 25% patients respectively.[16] While in the study of Andersen KK et al, 35491 (89.9%) had IS whereas 3993 (10.1%) had HS.[17] Twenty six percent patients were in the age group of 31-40 years. 26 out of 30 (52%) patients reported with stroke were females and 24 (48%) were male. This is similar to the study of Azam R et al.[18]

Atherosclerosis (ATH) was the most common cause of ischemic stroke (70%) followed with cardiogenic embolism (26.7%) and sickle cell disease (3.3%). This is concordant to the findings of Tripathi M. et al.[19] Smoking has previously been observed to be significantly associated with ischemic stroke.[20,21] This is similar to the finding in present study that reports significant difference in occurrence of ischemic stroke in patients with history of smoking as compared to haemorrhagic stroke.

The mean fibrinogen levels in ischaemic and haemorrhagic stroke was found to be significantly higher than normal, which correlates well with the findings of Narayanaswamy M et al.[22] The mean infarct volume in patients with Ischemic Stroke was 62.79±9.51cm3 while mean plasma fibrinogen level was 584±62 mg/dl. It was observed that fibrinogen level increased with increasing infarct volume. There was significant correlation between infarct volume and fibrinogen levels (r coefficient =0.61; p<0.05); whereas in a study done by Azam R et al, the mean infarct volume was 64.32+1.15 cm3 while mean plasma fibrinogen level was 4.78+1.43 mg/dl, correlation coefficient r value was 0.5 while p value was 0.02.[18] The mean haemorrhage volume in patients with Haemorrhagic Stroke was 60.58±10.52cm3 while mean plasma fibrinogen level was 552±28mg/dl. It was observed that fibrinogen level did not increase with increasing haemorrhage volume. There was no significant correlation between haemorrhage volume and fibrinogen levels (r coefficient =0.3; p>0.05).

Seven and five patients with ischemic and haemorrhagic stroke respectively died in present study. No significant association was observed between mortality and occurrence of specific type of stroke. Andersen KK et al, had observed that; compared with ischemic strokes, hemorrhagic stroke was associated with an overall higher mortality risk (HR, 1.564; 95% CI, 1.441-1.696).[17] The increased risk was, however, time-dependent; initially, risk was 4-fold, after 1 week it was 2.5-fold, and after 3 weeks it was 1.5-fold. After 3 months stroke type did not correlate to mortality. It was observed in both the groups that the fibrinogen levels in patients who died was higher as compared to patients who survived. Although fibrinogen levels were higher in patients who died, the association of fibrinogen levels with mortality was not significant. This was also corroborative of the finding of Andersen KK et al.[17]

CONCLUSION:

In conclusion, we report significantly higher than normal mean fibrinogen levels in ischemic and haemorrhagic stroke and fibrinogen levels increased with increasing infarct volume and the correlation between infarct volume and fibrinogen levels being significant in ischemic stroke. In both the groups, the fibrinogen levels in patients who died was insignificantly higher as compared to patients who survived. Limited mortality numbers probably didn't allow the observations of present study to reach the

level of significance, which prompts us to recommend similar study with higher numbers.

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