



STUDY OF C-REACTIVE PROTEIN LEVEL IN ACUTE CEREBROVASCULAR ACCIDENTS

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ABSTRACT **BACKGROUND** Stroke is a major cause of death and physical, mental, psychological morbidity worldwide. According to WHO, about 15 million peoples suffer from stroke each year. C- reactive protein (CRP) is a major acute phase protein in humans. The levels of CRP have been found to be raised in atherothrombotic diseases and related to plaque formation. This study was done to assess the levels of CRP (hs-CRP) in various types of stroke patients, and to predict the severity and prognosis. **METHODS** Study was conducted in 90 patients admitted in LLR and associated hospitals, G.S.V.M. medical college Kanpur. All patients of stroke fulfilling the Inclusion and exclusion criteria were enrolled in the study. Serum CRP (hs-CRP) was measured by Turbidimetric immunoassay. Statistical analysis was done by using T test and chi square test. **RESULTS** Our patients were mostly in the age group of 40-79 years with mean age 59 year. Patients were mostly males. hsCRP levels were found to be raised statistically significant in all types of stroke patients as compared to controls. There was significant rise from first day to third day ($P<0.05$). CRP was maximum in patients of cerebral infarction as compared to other types of stroke. Mean CRP of expired patients was higher as compared to whole study group ($P<0.05$). **CONCLUSIONS** We concluded that hsCRP level elevation is common in stroke patients and its evaluation could be an important prognostic parameter in stroke patients.

KEYWORDS : Stroke, Ischemic stroke, hemorrhagic stroke, hsCRP

INTRODUCTION:

Stroke is a leading cause of mortality and morbidity worldwide. According to WHO, about 15 million population suffers from stroke annually and the overall disease burden of stroke is higher in the developing countries [1, 2]. Two thirds of deaths from stroke occur in developing and less developed countries [3]. The overall rate of stroke-related mortality is decreasing but the absolute number of people with stroke, stroke survivors, stroke-related deaths, and the global burden of stroke-related disability is increasing [4]. The incidence of ischemic stroke is 68 percent and the incidence of hemorrhagic stroke is 32 percent worldwide [5]. The incidence is higher in men as compared to the women, and is more common in old age group though it can occur at any age [2,6]. Stroke is defined as sudden onset loss of global or focal cerebral function persisting for more than 24 hours attributable to a focal vascular cause [7]. Thus, the definition of stroke is based on the clinical and imaging studies. When the blood flow is quickly restored, the brain tissue can be recovered and the manifestations are only transient; this is called a transient ischemic attack (TIA).

Inflammation has vital role in the mechanism of atherosclerosis and in ischemic event. Inflammatory markers such as fibrinogen and hsCRP have been reported as predictable marker for stroke severity and prognosis [8]. C- reactive protein is an acute phase protein of hepatic origin that increases following interleukin 6 secretions by macrophages & T cells [9]. Several studies favour the concept that local & systemic inflammation plays a role in initiation & progression of atherosclerosis & its complications. Increased CRP level has been considered as a sensitive but not specific marker of acute inflammatory response. Increased risk of mortality is associated with stroke having elevated levels of CRP within 72 hours of onset. Levels of hsCRP measured after stroke predicted complementary aspects of prognosis that suggests the possibility of elevated levels of hsCRP has direct relation to extent of cerebral tissue injury. Nowadays neuroimaging modalities such as plain CT scan head and diffusion weighted MRI brain are the standard diagnostic test for stroke. Biomarkers can assist with patient care by helping to predict the prognosis. hsCRP is emerging as a prognostic marker in stroke. This study was done to assess the level of C - reactive protein in acute cerebrovascular accidents and to correlate the outcomes with CRP level.

METHODS:

The study was conducted on patients admitted in Medical wards, OPD, ICU and emergency ward of LLR and associated hospitals, GSVM medical college, Kanpur, Uttar Pradesh. 90 patients were included in the study.

Inclusion criteria: 1. All patients of stroke (ischemic, hemorrhagic, embolic, SAH, TIA) of either sex without any recent ischemic cardiac event

2. Patients of whom the symptoms of stroke have started during the previous 72 hours.

Exclusion criteria:

1. Patients with any recent ischemic cardiac event.
2. Patients with recent bacterial infection.
3. Patients of stroke due to any inflammatory pathology in brain or meningitis or encephalitis or neurocysticercosis.
4. Patients with autoimmune disease i.e. rheumatoid arthritis etc.

The patients and controls were subjected to detailed history, clinical examination and investigations as per the Performa. Neurological deficit was scored by using the Scandinavian stroke Scale. Serum CRP level was measured by Turbidimetric immunoassay. It is a method of quantitative estimation of CRP in serum. Statistical analysis was done by using tools like T test, chi square test to assess the significance or difference between study and control group and between the subgroups of study group.

RESULTS:

A total of 90 patients who fulfilled inclusion criteria were included in the study. Mean age of patients enrolled in the study was 59 years. 76.66 % of the patients were between the ages 40-79 years. In the current study, 52 patients were males and 38 subjects were females [Table I]. Male to female ratio was 1.36:1. The most common addiction was smoking comprised 41.11 % of patients. Hypertension was the most common risk factor with 66.66 % of the patients having it. The other comorbidities in their order of prevalence were dyslipidemias (31.11%), chronic alcoholism (18.88%) and diabetes (7.77%). Ischemic stroke was present in 46.66 % of the patients, 33.33% of the patients had intra cerebral haemorrhage. Embolic stroke was in 12.22%, sub arachnoid hemorrhage in 3.33% and TIA in 4.44%

patients. Clinical presentations in patients included hemiparesis (96.66%), altered sensorium (65.55%), vomiting (46.66%), and headache (43.33%), slurring of speech, aphasia (7.77%) etc. Mean CRP level in the stroke patients was 15.09 mg/L on first day, 22.73 mg/L on third day and 23.03mg/L on seventh day as compared to control (6.6mg/L)[Table II]. Mean hsCRP level in the ischemic stroke patients was 17.42 mg/L on first day, 26.68 mg/L on third day and 27.50mg/L on seventh day[Table III].The mean hsCRP levels in patients with haemorrhagic stroke was 14 mg/L on first day, 19.38 mg/L on third day and 19.03 mg/L on seventh day[Table IV]. Mean hsCRP level in the embolic stroke patients was 11.63 mg/L on first day, 20.63 mg/L on third day and 21.81mg/L on seventh day. Mean hsCRP level in the TIA patients was 11.00 mg/L on first day, 17.50 mg/L on third day and 14.00 mg/L on seventh day. Mean hsCRP level in sub arachnoid hemorrhage patients was 11.33 mg/L on first day, 16.66 mg/L on third day and 16 mg/L on seventh day. The hsCRP level was more elevated in ischemic stroke patients as compared to other types of cerebrovascular accidents. We also studied the correlation of CT scan findings with CRP level. In our study 36 cases had lesion <2.5 cm in CT scan out of which 63.88% patients had CRP between 3-10 mg/L and 36.22% had CRP between 11-24 mg/L. 50 patients had size of lesion in CT scan more than 2.5cm out of which 34% had CRP between 3-10mg/L, 48% had CRP between 11-24 mg/L and 18% patients had the CRP more than 24mg/L. The above observations showed that CRP level increases with increase in size of lesion. CRP level was found to be raised statistically significant in all types of stroke as compared to controls. There was significant rise from first day to third day (P<0.05). There was no significant difference in CRP from third day to seventh day (P>0.05).Mean CRP of expired patients was significantly higher as compared to the mean CRP of whole study group (P<0.05) [Table V].

TABLE-I Age and sex distribution

Age	Male	Female	Total	Percentage
10 - 19	2	0	2	2.22
20 - 29	1	1	2	2.22
30 - 39	3	4	7	7.77
40 - 49	6	8	14	15.55
50 - 59	9	6	15	16.66
60 - 69	16	9	25	27.77
70 - 79	9	6	15	16.66
80 - 89	6	3	9	10
90 - 99	0	1	1	1.11
Total	52	38	90	

TABLE – II Statistical analysis of CRP in all CVA cases

GROUP	MEAN CRP(mg/L)	S.D.	STATISTICAL VALUES
Control (n=20) Cases (n=90) On admission	6.6 15.09	1.795 10.31	t=3.82 P=<0.005
Cases (n=90) On admission	15.09	10.31	t=4.34
Cases(n=90) on III day	22.73	12.99	P<0.005
Cases(n=90) on III day	22.73	12.99	t=0.152
Cases(n=85) on VII day	23.03	12.66	P>0.05
Cases(n=90) on admission	15.09	10.31	t=4.52
Cases(n=85) on VII day	23.03	12.66	P<0.005

TABLE- III Statistical analysis of CRP level in Ischemic Stroke

GROUP	MEAN CRP(mg/L)	S.D.	STATISTICAL VALUES
Control (n=20) Cases (n=42) On admission	6.6 17.42	1.795 11.91	t=3.98 P<0.005
Cases (n=42) On admission	17.42	11.91	t=3.11
Cases(n=42) on III day	26.68	14.81	P<0.005

Cases(n=42) on III day	26.68 27.50	14.81 13.88	t=0.36 P>0.05
Cases(n=40) on VII day			
Cases(n=42) on admission	17.42	11.91	t=3.48
Cases(n=40) on VII day	27.50	13.88	P<0.005

TABLE-IV STATISTICAL ANALYSIS OF CRP IN INTRACEREBRALHEMORRHAGE

GROUP	MEAN CRP(mg/L)	S.D.	STATISTICAL VALUES
Control (n=20) Cases (n=30) On admission	6.6 14	1.795 9.92	t=3.23 P<0.005
Cases (n=30) On admission	14	9.92	T=1.85
Cases(n=30) on III day	19.38	12.02	P<0.05
Cases(n=30) on III day	19.38	12.02	T=0.10
Cases(n=27) on VII day	19.03	11.72	P>0.05
Cases(n=30) on admission	14	9.92	t=1.72
Cases(n=27) on VII day	19.03	11.72	P<0.05

TABLE-V Mortality in patients in various CRP level (on admission)

CRP (mg/L)	Total number of patients	Number of patients expired	Percentage
3-10	41	5	12.19%
11-24	40	18	45%
25-36	5	3	60%
37-48	3	3	100%
49-60	1	1	100%
>60	0	0	0

DISCUSSION:

The study was a conducted at LLR and associated hospitals, GSVM medical college Kanpur in 90 patients diagnosed with stroke. Stroke is the third major cause of death in India according to CDC 2012 and leading cause of morbidity [2]. The hsCRP level was measured on admission, third day and seventh day in all types of stroke patients. Correlation between CRP level and neurologic outcome in terms of discharge or mortality was studied'. The age distribution of patients was from 10-19 years to 90-99 years age groups with mean age of 59 years and maximum numbers of patients were of 40-79 years age group. Age is usually considered as a non-modifiable risk factor for stroke [10] Similar results were found in studies done by SD Bhaiare et al [1], PT Mishra et al [11] JR Chaudhuri et al [12] S Kumar et al, [13] DS Rana et al, [14] Jayachandra et al, [15] the Mumbai Stroke Registry [16] and Y Wakugawa in the Hisayama Study [17]. In this study there was male preponderance with 57.77% cases being males and 42.22% were females. Male to female ratio in the current study was 1.36:1. Male sex is also considered as a non modifiable risk factor for stroke [10]. Similar results were found in the studies conducted by Sujit Kumar et al [13], Davinder Singh Rana et al(14) and Jayachandra et al (15) which having male preponderance. The most common modifiable risk factor in the study was hypertension (66.66%) followed by dyslipidemias (31.11%). The most common addiction in patients enrolled in study was tobacco smoking with a prevalence of 41.11%. This is substantiated by findings in studies conducted by DS Rana et al [14] and JR Chaudhuri et al[12]. Mean CRP level in the stroke patients was 15.09 mg/L on first day, 22.73 mg/L on third day and 23.03mg/L on seventh day as compared to control (6.6mg/L). This shows that hsCRP levels are increased in case of cerebrovascular accidents. Mean hsCRP level in the ischemic stroke patients was 17.42 mg/L on first day, 26.68 mg/L on third day and 27.50mg/L on seventh day. the mean hsCRP levels in patients with haemorrhagic stroke was 14 mg/L on first day, 19.38 mg/L on third day and 19.03 mg/L on seventh day. Mean hsCRP level in the embolic stroke patients was 11.63 mg/L on first day, 20.63 mg/L on third day and 21.81 mg/L on seventh day. Mean hsCRP level in the TIA patients was 11.00 mg/L on first day, 17.50 mg/L on third day and 14.00 mg/L on seventh day. Mean hsCRP level

in sub arachnoid patients was 11.33 mg/L on first day, 16.66 mg/L on third day and 16 mg/L on seventh day. The hsCRP level was more elevated in ischemic stroke patients as compared to other types of cerebrovascular accidents. These results are similar to the findings of Y Wakugawa et al in the Hisayama study [17] and R Lal et al [18]. In the study by Yoshiyuki Wakugawa et al, (17) high hsCRP levels were observed as an independent risk factor for ischemic stroke in males but not for haemorrhagic stroke in either men or women. In the study by Ritesh Lal et al [18], mean hsCRP levels in ischemic stroke were higher than in haemorrhagic stroke. This suggests that higher hsCRP levels are associated with severe neurological deficit and thus worse outcome. Stroke patients were classified on the basis of Scandinavian Stroke Scale into minor, moderate and severe stroke. Patients with minor stroke had lower hsCRP values as compared to patients with severe stroke. Thus, higher hsCRP levels were associated with worse prognosis. In the current study, the hsCRP levels were correlated with outcomes in terms of death. Mean CRP of expired patients was significantly higher as compared to the mean CRP of whole study group ($P < 0.05$). Similar results were found in study by Jayachandra et al [15]. Thus there was a relation between high hsCRP and mortality. We also studied the correlation of CT scan findings with CRP level. In our study 36 cases had lesion < 2.5 cm in CT scan out of which 63.88% patients had CRP between 3-10 mg/L and 36.22% had CRP between 11-24 mg/L. 50 patients had size of lesion in CT scan more than 2.5cm out of which 34% had CRP between 3-10mg/L, 48% had CRP between 11-24 mg/L and 18% patients had the CRP more than 24mg/L. The above observations showed that CRP level increases with increase in size of lesion. Our observations were in accordance to previous studies done by Iyigun I, et al [19], Guo Y, et al [20], Audebert HJ, et al [21], who concluded that patients with large infarcts had higher CRP concentration as compared to patients with smaller infarcts and controls. The prognostic importance of hsCRP may be associated to the extent of necrosis in the brain parenchyma and somewhat unknown determinants of intensity of acute phase reactants. The prognostic importance of hsCRP with respect to neurological deficits and mortality as outcomes of stroke helps clinician to offer pragmatic expectations to families of stroke victims. Thus hsCRP can be measured in routine for all cerebrovascular accidents patients to provide a statistically significant level of prognostic information.

CONCLUSIONS:

CRP (hsCRP) level was elevated in all types of acute cerebrovascular accidents. The rise in hsCRP level was more in ischemic than in hemorrhagic stroke. CRP was significantly higher in expired patients and with severe neurological deficit large lesion. Higher hsCRP level had poor prognosis as compared to patients with lower hsCRP. Thus, level of hsCRP can be used as a prognostic parameter for assessing the outcome in acute cerebrovascular accidents.

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