



## CORRELATION OF SIZE AND VOLUME OF CT SCAN LESION WITH SYSTEMIC INFLAMMATORY RESPONSE IN ACUTE CEREBROVASCULAR ACCIDENTS

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### ABSTRACT

**Background** Acute cerebrovascular accidents (CVA) are the leading cause of mortality and morbidity worldwide. CVA is now considered to produce an inflammatory response in brain and periphery in form of rise in inflammatory markers. CT scan head is an initial investigation of choice in acute cerebrovascular accidents (stroke). This study was done to correlate the size and volume of CT scan head lesion with inflammatory response in acute cerebrovascular accidents. **Methods** Study was conducted in 90 patients of acute CVA admitted in LLR and associated hospitals, G.S.V.M. medical college Kanpur. All patients of CVA (stroke) fulfilling the Inclusion and exclusion criteria were enrolled in the study. CT scan head was done as an initial investigation to confirm the diagnosis. To assess the inflammatory response Serum CRP (hs-CRP) level 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 with male predominance. CRP levels were found to be elevated statistically significant in all types of CVA 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. Observation showed higher CRP level in patients with larger lesion in CT head. Mean CRP of expired patients was higher as compared to whole study group ( $P < 0.05$ ). **Conclusions** We concluded that CRP level was much elevated with increase in size and volume of lesion in CT head in patients of CVA indicating the magnitude of inflammatory response, assessing severity and outcome.

**KEYWORDS :** Stroke, cerebrovascular accidents, inflammatory markers

### INTRODUCTION:

Acute cerebrovascular accidents (CVA) are the leading causes of deaths and disabilities worldwide. About 15 million populations suffer 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 incidence of ischemic stroke is 68 percent and the incidence of hemorrhagic stroke is 32 percent worldwide [4]. CVA initiates an inflammatory response in the brain with induction of a various cytokines and inflammatory markers, including interleukin-6 (IL-6), a pleiotropic cytokine implicated in varied inflammatory functions [5, 6]. In some experimental studies, there is elevated IL-6 concentrations in cerebrospinal fluid (CSF) of acute stroke patients correlate with infarct volume [5]. Inflammation has vital role in the mechanism of atherosclerosis and in ischemic event. Inflammatory markers such as fibrinogen and CRP have been reported as predictable marker for stroke severity and prognosis [7]. C-reactive protein is an acute phase protein of hepatic origin that increases following interleukin 6 secretions by macrophages & T cells [8]. Increased CRP level has been considered as a sensitive but not specific marker of acute inflammatory response. Nowadays neuroimaging modalities such as plain CT scan head and diffusion weighted MRI brain are the standard diagnostic test for CVA. In patients with acute ischaemic stroke, in some studies associations have been reported between circulating IL-6 concentration and brain infarct volume, stroke severity, or outcome up to 6 months.

Conversely, other studies have reported no association between serum IL-6 concentration and infarct volume or stroke severity at 3 months.[3] Biomarkers can assist with patient care by helping to predict the prognosis. CRP is emerging as a prognostic marker in stroke. The aim of the present study was to examine the relationship between the magnitude of the systemic inflammatory response by measuring the routinely available inflammatory parameters such as C-reactive

protein (CRP) with the size and volume of lesion in CT head and to establish severity and outcome in CVA patients.

### 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, connective tissue 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. To assess the inflammatory response serum CRP level was measured by Turbidimetric immunoassay. It is a method of quantitative estimation of CRP in serum. Size and volume of lesion in CT head was measured. 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 dyslipidemia (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 CRP 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 CRP 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 CRP 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 CRP 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 CRP 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 CRP 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 <2.5cm (<8 cc) in CT scan out of which 23 (63.88%) patients had CRP between 3-10 mg/L and 13(36.22%) had CRP between 11-24 mg/L. 32 patients had size of lesion 2.5 to 4.5 cm(8 -45 cc), in which 14 patients had CRP 3 -10 mg/L (43.75%), 15 patients had 11-24mg/L (46.87%) and 3 patients had 25-36mg/L (9.37%). 18 patients had lesion more than 4.5cm (>45cc), out of which 3 patients (16.66%) had CRP between 3-10mg/L, 9 patients (40%) had CRP between 11-24 mg/L, 2 patients (11.11%) had CRP 25-36mg/L, 3 (16.66%) patients had CRP level 37-48mg/L and one patient (5.55%) had the CRP more than 48mg/L [Table V]. 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 VI].

**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)	6.6	1.795	t=3.82
Cases (n=90) On admission	15.09	10.31	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)	6.6	1.795	t=3.98
Cases (n=42) On admission	17.42	11.91	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	14.81	t=0.36
Cases(n=40) on VII day	27.50	13.88	P>0.05
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 Intracerebral Hemorrhage**

GROUP	MEAN CRP(mg/L)	S.D.	STATISTICAL VALUES
Control (n=20)	6.6	1.795	t=3.23
Cases (n=30) On admission	14	9.92	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 Correlations of CT scan (size and volume of lesion) with CRP level**

CRP (mg/L)	<2.5 cm (<8cc)	2.5-4.5 cm (8-45cc)	>4.5cm (>45cc)	Normal scan
3-10	23	14	3	1
11-24	13	15	9	3
25-36	0	3	2	0
37-48	0	0	3	0
>48	0	0	1	0

**Table-VI 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, G SVM medical college Kanpur in 90 patients diagnosed with acute cerebrovascular accidents (CVA). Stroke is the third major cause of death in India according to CDC 2012 and leading cause of morbidity [2]. The CRP level was measured on admission, third day and seventh day in all types of CVA patients. Correlation between CRP level and size and volume of lesion in CT scan head in relation with neurologic outcome 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. 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. 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%. 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 CRP levels are increased in case of cerebrovascular accidents. Mean CRP 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 CRP 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 CRP 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 CRP 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 CRP 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 CRP 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 [9] and R Lal et al [10]. Stroke patients were classified on the basis of Scandinavian Stroke Scale into minor, moderate and severe stroke. Patients with minor stroke had lower CRP values as compared to patients with severe stroke. Mean CRP of expired patients was significantly higher as compared to the mean CRP of whole study group ( $P < 0.05$ ). Thus, higher CRP levels were associated with worse prognosis. Similar results were found in study by Jayachandra et al [11]. We studied the correlation of CT scan findings (size and volume of lesion) with CRP level. In our study 36 cases had lesion  $< 2.5\text{cm}$  ( $< 8\text{ cc}$ ) in CT scan out of which 23 (63.88%) patients had CRP between 3-10 mg/L and 13(36.22%) had CRP between 11-24 mg/L. 32 patients had size of lesion 2.5 to 4.5 cm(8-45 cc), in which 14 patients had CRP 3-10 mg/L (43.75%), 15 patients had 11-24mg/L (46.87%) and 3 patients had 25-36mg/L (9.37%). 18 patients had lesion more than 4.5cm ( $> 45\text{cc}$ ), out of which 3 patients (16.66%) had CRP between 3-10mg/L, 9 patients (40%) had CRP between 11-24 mg/L, 2 patients (11.11%) had CRP 25-36mg/L, 3 (16.66%) patients had CRP level 37-48mg/L and one patient (5.55%) had the CRP more than 48mg/L. These observations showed that CRP level increases with increase in size of lesion. Our observations were in accordance to previous studies done by Audebert HJ, et al [6], Iyigun I, et al [12], who concluded that patients with large infarcts had higher CRP concentration as compared to patients with smaller infarcts and controls. Craig J Smith et al demonstrated significant correlations between peak plasma IL-6, an inflammatory marker in the first week of ischemic stroke with both brain infarct volume and outcome at 3 months [5]. These observations show that elevation of inflammatory parameters in the acute ischemic stroke is a well-known phenomenon and may result from infectious complications or from the inflammatory reaction of the damaged brain parenchyma. Audebert HJ et al found significant correlation between lesion size and CRP in first 5 days after onset [6]. Our study showed the there is rise in CRP level with the larger the size and volume of lesion in CT head of stroke patients. This is similar to the previous studies depicting that rise in inflammatory markers was correlated with the size and volume of lesion and this may be associated to the extent of necrosis in the brain parenchyma.

#### CONCLUSIONS:

CRP level was elevated with larger the size and volume of CT scan lesion in all types of acute cerebrovascular accidents as compared to small lesion, indicating the aggravated systemic inflammatory response. CRP was significantly higher in

expired patients and with severe neurological deficit and with large lesion. Therefore, the association between lesion size and elevated inflammatory parameters in acute cerebrovascular accidents can be predictive for the functional outcome.

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