



SERUM HSCRP LEVEL AS A PROGNOSTIC INDICATOR IN ISCHEMIC STROKE PATIENTS

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ABSTRACT

Background Stroke is a leading cause of mortality and morbidity worldwide. About 15 million people suffer from stroke each year. hsCRP is a major acute phase reactant in humans. The levels of hsCRP have been found to be raised in atherosclerosis and related to plaque formation. This study was done to assess the levels of CRP (hs-CRP) in ischemic stroke patients, and to predict the prognosis and severity. **Methods** Study was conducted in 42 patients admitted in medical ward and ICU of Medicine department, G.S.V.M. medical college Kanpur. All patients of ischemic stroke who fulfilled 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** Maximum number of our patients were in the age group of 40-79 years with mean age 59 years. Ischemic stroke was more prevalent in males. hsCRP level was observed to be raised statistically significant in ischemic stroke patients as compared to controls. There was significant rise from first day to third day ($P < 0.05$). Mean CRP level of expired patients was elevated as compared to whole study group ($P < 0.05$). **Conclusions** We concluded that rise in hsCRP level is common in ischemic stroke patients and its evaluation could be an important prognostic indicator.

KEYWORDS : Stroke, Ischemic stroke, cerebral infarction, hsCRP

INTRODUCTION:

Stroke is a major cause of death and disability 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]. Deaths from stroke are more common in developing and less developed countries [3]. The overall rate of stroke-associated mortality is decreasing but the absolute number of people with stroke, stroke survivors, stroke-related deaths, and the global burden of stroke-related morbidity is increasing [4]. Ischemic stroke is the most common type of stroke worldwide [5]. The incidence is higher in male as compared to the females, 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 radiological examination. 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).

There are growing evidences that inflammations are involved in atherosclerosis and in ischemic event. Ischemic brain injury secondary to arterial occlusion is associated with local inflammation and rise in inflammatory cytokines. Inflammatory markers such as fibrinogen and hsCRP have been mentioned as predictable marker for stroke severity and prognosis [8, 9]. C-reactive protein is an acute phase protein of produced in liver that increases, following interleukin 6 secretions by macrophages & T cells [10]. Several studies support 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 reaction. Increased risk of mortality is associated with Ischemic 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 association to extent of cerebral parenchymal injury. Currently neuroimaging modalities such as plain CT scan head and diffusion weighted MRI brain are the standard diagnostic test for Ischemic stroke. Biomarkers can assist with patient care by helping to predict the prognosis. hsCRP is emerging as a

prognostic marker in ischemic stroke. This study was done to correlate the level of C-reactive protein with the prognosis of acute ischemic stroke patients.

METHODS:

The study was conducted on 42 patients admitted in Medical wards, OPD, ICU and emergency ward of Medicine department, GSVM medical college, Kanpur, Uttar Pradesh.

Inclusion criteria:

1. All the patients of ischemic stroke of either sex without any recent ischemic cardiac event.
2. Patients of whom the symptoms of stroke have started within 72 hours.

Exclusion criteria:

1. Patients with any recent ischemic cardiac event or cardioembolic stroke.
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 42 patients who fulfilled inclusion criteria were included in the study. Mean age of patients enrolled in the study was 59 years. 76.19 % of the patients were between the ages 40-79 years. In the current study, 25 patients were males and 17 subjects were females [Table I]. Male to female ratio was 1.47:1. 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%), diabetes (17.77%) and chronic alcoholism (10.88%). Clinical presentations in patients included hemiparesis (90.48%), slurring of speech (71.42%) altered sensorium (47.61%), aphasia (26.19%), vomiting (11.90%), and headache (7.14%) etc. Serum CRP level was measured on admission, third and seventh day. Two patients expired till seventh day [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 as compared to controls (6.6mg/L) [Table III]. We also studied the correlation of CT scan findings with CRP level. In our study 18 cases had lesion <2.5 cm in CT scan out of which 58.8% patients had CRP between 3-10 mg/L and 41.2% had CRP between 11-24 mg/L. 24 patients had size of lesion in CT scan more than 2.5cm out of which 21.7% had CRP between 3-10mg/L, 52.2% had CRP between 11-24 mg/L and 26.1% 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 ischemic 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-I Age and sex distribution

Age	Male	Female	Total	Percentage
10 - 19	0	0	0	0
20 - 29	1	0	1	2.38
30 - 39	3	1	4	9.52
40 - 49	3	2	5	11.90
50 - 59	4	3	7	16.66
60 - 69	7	6	13	30.95
70 - 79	4	3	7	16.66
80 - 89	3	2	5	11.90
90 - 99	0	0	0	0
Total	25	17	42	

Table II hsCRP level in Ischemic stroke patients (n = 42)

CRP(mg/L)	On admission	III day	VII day
3-10	18(42.85%)	10(23.80%)	8(19.04%)
11-24	18(42.85%)	12(28.57%)	8(19.04%)
25-36	4(9.52%)	10(23.80%)	14(33.33%)
37-48	1(2.38%)	9(21.42%)	8(19.04%)
49-60	1(2.38%)	0	2(4.76%)
>60	0	1(2.38%)	0

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 Cases(n=42) on III day	17.42 26.68	11.91 14.81	t=3.11 P<0.005
Cases(n=42) on III day Cases(n=40) on VII day	26.68 27.50	14.81 13.88	t=0.36 P>0.05
Cases(n=42) on admission Cases(n=40) on VII day	17.42 27.50	11.91 13.88	t=3.48 P<0.005

DISCUSSION:

The study was a conducted in department of Medicine, GSVM medical college Kanpur in 42 patients diagnosed with ischemic stroke. Stroke is the third leading cause of death in India according to CDC 2012 and major cause of morbidity [1]. The hsCRP level was measured on admission, third day

and seventh day in all ischemic stroke patients fulfilling inclusion criteria. Correlation between serum hsCRP level and neurological outcome in terms of improvement, morbidity and 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 [11] Similar results were observed in studies done by SD Bhaire et al [2], PT Mishra et al [12] JR Chaudhuri et al [13] S Kumar et al, [14] DS Rana et al, [15] Jayachandra et al, [16] the Mumbai Stroke Registry [17] and Y Wakugawa in the Hisayama Study [18]. In this study there was male preponderance with 59.52% cases being males and 40.47% were females. Male to female ratio in the current study was 1.47:1. Male sex is also considered as a non modifiable risk factor for stroke [11]. Similar results were observed in the studies conducted by Sujit Kumar et al [14], Davinder Singh Rana et al[15] and Jayachandra et al [16] 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 included in study was tobacco smoking with a prevalence of 41.11%. This is substantiated by findings in studies conducted by DS Rana et al [15] and JR Chaudhuri et al [13]. 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 as compared to control (6-6mg/L). This shows that hsCRP levels are increased in case of acute ischemic stroke. In the study by Yoshiyuki Wakugawa et al, [18] 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. This suggests that higher hsCRP levels are associated with severe neurological deficit and thus poor outcome. Ischemic Stroke patients were classified on the basis of Scandinavian Stroke Scale into minor, moderate and severe stroke. Patients with minor ischemic stroke had lower hsCRP values as compared to patients with severe stroke. Thus, higher hsCRP levels were associated with poor 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 [16]. Thus there was a relation between high hsCRP and mortality. We also studied the correlation of CT scan findings with CRP level. Our observations showed that CRP level increases with increase in size of lesion in CT scan head. Our observations were similar to previous studies done by Audebert HJ et al [19], Guo Y, et al [20] 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 related to the extent of necrosis in the brain parenchyma and somewhat unknown determinants of intensity and concentration of acute phase reactants. The prognostic importance of hsCRP with respect to neurological deficits and mortality as outcomes of ischemic strokes may help clinician to offer realistic expectations to families of stroke sufferers. Thus hsCRP can be measured in practice for all ischemic stroke patients to provide a statistically significant level of prognostic information.

CONCLUSIONS:

In our study hsCRP level was elevated in ischemic stroke patients. 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 indicator for assessing the outcome in acute ischemic stroke.

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