ORIGINAL ARTICLE

High Sensitive C - Reactive Protein(HsCRP): A Simplistic Biomarker of Stroke Severity

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Abstract:

Background and Introduction:
Stroke has become an important cause of death as well as disability across the globe. Though the diagnosis of stroke is based on clinical evaluation and imaging, there is need to find biomarkers that can aid in diagnosis, prognosis and overall management of stroke.

Aims & Objectives:
1. To estimate HsCRP level in stroke patients and to correlate it with severity of stroke.
2. To compare the HsCRP level of ischemic with that of hemorrhagic stroke.

Materials and Methods:
This was a prospective clinical study with 50 consecutive patients of acute stroke, admitted to PMCH, Udaipur. Fifty age and sex matched healthy persons were included as controls. Twenty-five patients with ischemic and 25 with hemorrhagic stroke were considered in this study. The severity of stroke was assessed clinically using the National Institutes of Health Stroke Scale (NIHSS). The estimation of serum HsCRP level was done by immunoturbidimetry on Roche analyser.

Results and Conclusion:
The level of HsCRP was found to be higher in stroke patients as compared to the controls and higher in hemorrhagic than the ischemic stroke ($p<0.05$). Moderate correlation was found between HsCRP levels and with stroke severity ($r=0.49$). The ROC curve analyses showed that the patients with severe clinical presentation had higher HsCRP concentrations (>6mg/dl). Thus, assessment of HsCRP level can complement clinical evaluation of stroke and prediction of severity of stroke.

Keywords: HsCRP, Ischemic stroke, Hemorrhagic stroke.

Introduction:
Stroke has become an important cause of death as well as disability across the globe. In developing countries like India there is alarming rise in incidence of stroke to 119-145/100000, which is attributed to the lifestyle changes[1].The initial evaluation of stroke patient includes a detailed history and physical examination, followed by brain imaging and laboratory tests. Neuroimaging modalities like computerized tomography (CT) and magnetic resonance imaging (MRI) are widely used as an aid in the diagnosis and classifying stroke type, to determine the severity outcome, but these are not available at small centers. There is need to find biomarkers that can aid in diagnosis and overall management of stroke[2,3,4]. HsCRP is one such marker of inflammation that might be useful in assessing stroke severity and hence the study was planned to evaluate its utility.

Materials and Methods:
This was a prospective clinical study with 50 consecutive patients of acute stroke, admitted to

PMCH, Udaipur, after getting approval from university ethics committee. Informed, written consent was obtained either from the patient or a relative. Fifty age and sex matched healthy persons were included as controls. Twenty-five patients each of ischemic and hemorrhagic stroke were recruited in this study. Inclusion criterion was first ever episode of stroke, age between 18 and 80 years and, no history of injury to the central nervous system or other incapacitating medical disease. An exclusion criteria was patients with trauma, CNS or systemic infections, encephalopathy, intracranial tumor, organ failure, etc. The clinical examination was followed by the basic laboratory and imaging workup with CT or MRI to determine the underlying pathology. Depending on these findings cases were broadly classified as hemorrhage or ischemic stroke. The severity of stroke was assessed clinically using the National Institutes of Health Stroke Scale (NIHSS), which is a 42-point scale where person having normal functions with no deficit receives a score of zero. NIHSS score >15 were considered as marker of severe stroke[5]. The estimation of serum HsCRP level was done by immunoturbidimetry on Roche fully auto analyser C311.

Statistical analysis:

The data for HsCRP level was compiled in excel sheet, while risk factors conditions were reported as count (n) and percentage (%). Distribution of age of study subjects was reported as median with interquartile range. To assess the statistical significance, t-test was employed. Correlation was assessed using Spearman Rank test. All tests were carried out at 5% level of significance. The statistical analyses of the data was done using SPSS version 16 (SPSS Inc., Chicago).

Results:

The serum HsCRP level in the control group was in the range of 2.82 ± 1.78 mg/L while that of cases was 6.82 ± 3.78mg/L. The level of HsCRP was found to be higher in stroke patients as compared to controls ($p<0.05$). It was also found that HsCRP level was higher in hemorrhagic stroke than the ischemic stroke patients($p<0.05$). Moderate correlation was found between HsCRP level with stroke severity($r=0.49$) as measured by NIHSS score. This correlation was more in hemorrhagic than the ischemic cases. The ROC curve analyses showed that the patients with severe presentation had higher HsCRP concentration (>6mg/dl). (Figure 1)

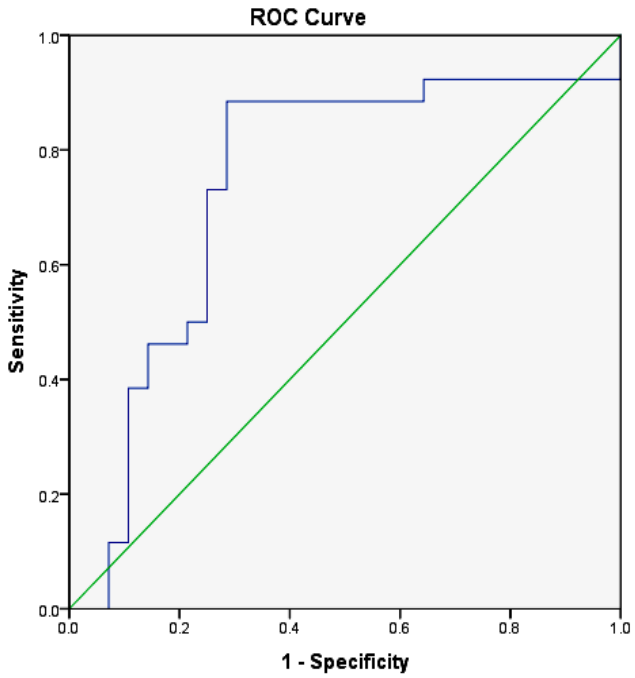

Figure 1: ROC curve analyses of HsCRP concentration NIHSS (>15). The area under the curve was 0.71 (95% CI 0.57-0.85 p=0.008). Cut off of 6mg/L at 68% sensitivity and 78% specificity.

Table No.1: **Profile of stroke cases**

Demographics	**All stroke cases (n=50)**	**Hemorrhagic cases (n=25)**	**Ischemic cases (n=25)**
Age in years (Interquartile range)	60.28(20)	56.3(28)	64.3(15)
Gender-Male (%)	35(70%)	15(60%)	10(40%)
Risk factors	**Number (%)**	**Number (%)**	**Number (%)**
Hypertension	35(70%)	23(92%)	12(48%)
Diabetes mellitus	20(40%)	5(20%)	15(60%)
Hyperlipidemia	30(60%)	15(60%)	15(60%)
Smoking	20(40%)	12(48%)	8(32%)
Alcoholic	25(50%)	8(32%)	17(68%)
Serum HsCRP level	**Mean±(SD)**	**Mean±(SD)**	**Mean±(SD)**
Cases(mg/L) *	6.82 ± 3.78	8.22 ± 2.2	4.6 ± 3.5
Control group(mg/L)	2.82 ± 1.78		
Clinical scale scores	**Mean± Range**	**Mean± Range**	**Mean± Range**
NIHSS admission *	24.5±7.5(17-32)	28.5±3.5(25-32)	21± 4(17-25)
Correlation of HsCRP with NIHSS*	r=0.49	r=0.59	r=0.41

*** = p<0.05 statistically significant result**

Discussion:

A stroke biomarker can be defined as a measurable substance that marks the manifestation of stroke[4]. Several stroke biomarkers have been identified but none has found a place in clinical practice as interpretation of results is confounded by factors like slow rise, blood brain barrier, and diverse etio-pathogensis[6-10]. Hence this study was designed to evaluate the status of HsCRP in acute stroke patients and its utility in assessing severity of stroke.

In ischemic stroke, the arterial flow obstruction causes cerebral infarction. The brain injury is due to the deprivation of metabolic substrates to nervous tissue. Neurons have a high energy requirement; hence, rapid depletion of oxygen and energy supply leads to damage to neurons. On the other hand there is direct cut off of the blood supply in hemorrhagic stroke due to the rupture of vessels. Moreover, the active inflammation and oxidative stress accelerates neuronal damage leading to apoptosis[6-11].

HsCRP is an acute phase protein produced in liver in response to active inflammation. It is expected to be increased in stroke patients too due to the ongoing damage to the brain tissue. It promotes thrombosis by inducing monocytes to express tissue factor, which is a coagulant. It also stimulates the endothelial cells to produce adhesion molecules, which attract inflammatory cells[7-12]. The cardiovascular risk is determined as low if HsCRP level is less than 1.0 mg/L, high risk if HsCRP level is more than 3.0

mg/L[6]. The mean HsCRP concentrations in the cases were high as compared to the controls indicating the active production of HsCRP in stroke patients. This was higher in hemorrhagic than ischemic stroke due the underlying pathology. We found that the stroke severity, as measured by NIHSS on admission was high in those patients having higher HsCRP level. There was a positive correlation of NIHSS at admission and HsCRP level. It was moderate correlation but statistically significant. This is again an indication of greater inflammation and more damage to the brain tissue. The HsCRP level was higher in hemorrhagic stroke and those patients having severe presentation at the time of admission. The results of our study match with previously published data, where the HsCRP level rises proportionately with the disease severity. This might help in assessing the type of pathology and severity of stroke in resource restricted hospitals.

Conclusion:

Thus estimation of HsCRP level can help in etio-pathological assessment of stroke in resource limited centers. It may also help in predicting the severity of stroke and ultimately the management of the disease. However, larger studies are required to justify and validate the results of our study.

Limitations: Small sample size.

Conflict of Interest - Nil
Sources of Support - Nil

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