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Original Research Article

Association between High-Sensitivity C-Reactive Protein (Hs-Crp) And Acute Ischemic Stroke: A Case-Control Study

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Abstract

Background and Objectives: Acute ischemic stroke (AIS) is a leading cause of morbidity and mortality worldwide. Inflammation plays a crucial role in the pathogenesis of AIS. High-sensitivity C-reactive protein (HS-CRP) is a sensitive marker of inflammation. Use of serum markers has been a established practice in medicine. CRP levels have been known to provide a estimate of inflammation. The present study was formulated to ascertain if levels of CRP in acute ischaemic stroke cases can be a prognostic or diagnostic marker for the condition.

Methods: The study was a prospective case control format and utilized a subject poolof 50 subjects as case and control each. The study observed a significantly elevated level of CRP in cases with an acute ischaemic stroke. The study concluded that use of CRP can be a an effective modality in clinical practice in managing such cases.

To investigate the relationship between HS-CRP levels and AIS.

To evaluate the predictive value of HS-CRP for AIS.

To examine the association between HS-CRP and stroke severity.

Keywords: CRP, Acute Ischaemic Stroke, TOAST.

Introduction

C – Reactive protein is a plasma protein present homogenously in a all vertebrates and some invertebrate species. The CRP plays a role in inflammatory responses to stimuli on a systemic level rather than a local site-based reaction. [1] The molecule of CRP binds to a specific site ofaction which are revealed in the process of cell death or on the cell walls of certain infective pathogenic organisms. Thereafter, it causes a cascade in which the circulating levels of CRP are essentially elevated indicating that a acute inflammatory immune response is active. [2] The elevated levels of CRP in the system can also provide a stimulus for endothelial cells to promote the migration and activation of various adhesion molecules which allow the transport of mononuclear cell and T Cells inside the vessel wall. This migration promotes the formation of atherosclerotic plaques. [3-4]

Additionally it was determined that CRP plays a pivotal role in superoxide ions formation and stimulation of tissue necrosis factors in the system while causing fibrinolysis, endothelial cell lysis and eventually plaque erosion. These are due to its acute inflammatory activity but can lead to an ischemic stroke [4-5] Stroke can be defined as a syndrome characterized by a rapid onset of local or complete loss of brain function for a duration of more than 24 hours or death with no apparent cause apart from vascular origin. [6] In the Indian context, stroke is a disease which has a high mortality rate and in cases where death has not occurred,the disability is long and arduous. Studies have hypothesized that the pathophysiology of stroke is an inflammatory one associated with atherosclerosis. This led to the opinions that a severe stroke will have a elevation of inflammatory markers which if detected can aid in prognostic and diagnostic marking [7-8] With this in mind, the present study was conducted to ascertain if high sensitivity c reactive protein can be used asa marker for acute ischemic events.

Material and Methods

The present study was a double bling randomized control study conducted over a period on 12 months. at Narayan medical college and Hospital, Jamuhar Sasaram, Bihar. and tertiary care hospital in Bihar. The study entailed the inclusion of 50 subjects who fulfilled the inclusion criteria.

Inclusion was done of individuals who had suffered an ischemic stroke, were between 30-70 years of age

and were brought to the hospital within 24 hours of event. The subjects were individuals who had no co morbidities that could alter CRP levels, nor were using steroids for any ailments. If found so, the subjects were excluded from the study. The subjects were individuals who had only a single event of stroke and subjects with a prior h/o stroke or ischemic event were excluded from the study. The study pool also included a pool of age and gender matched controls. These individuals were apparently healthy subjects who had never been in a stroke like condition or had any infective pathology / steroid usage. Stoke diagnosis was made by radiological methods (CT/MRI), as well as history, clinical examination and specific neurological examination. The severity scoring wasbased on NIHSS criteria [9] while etiological classification was done as per TOAST criteria [10] Serum samples for determination of hsCRP level were taken within 24 hours of hospital arrival. hsCRP level was measured using the highly sensitive near-infrared particle immunoassay method which classified hsCRP levels in low risk (< 1 mg/L), moderate risk (1–3 mg/L) and high risk (> 3 mg/L) groups according to American Heart Association and Centers for Disease Control and Prevention criteria[11].

The demographic details, medical and personal history as well as examination findings were recorded in pre-designedtabular format. The tabulations were analyzed in consultation with institutional statistician using SPSS ver12 software.

Results

The results revealed that the mean age of the patients is 58.57 ± 10.24 years, while the mean age of the controls was 58.22 ± 9.87 years. The gender distribution and age of thecase and control group was comparable. (Table 01)

Table 1: Comparison of Subjects and Controls

	Subjects	Controls	P Value
Number	50	50	
Mean Age	58.57 ± 10.24	58.22 ± 9.87	0.870
hsCRP (mg/dl)	2.23 ± 3.11	0.47 ± 0.55	<0.001

Among the selected study subjects, in the patients group, the commonest risk factor was elevated BP. Hypertension was seen in 66% (n=33) subjects. The second commonest factor was dyslipidemia which comprised of 60 % cases (n=30). Other risk factors were smoking, diabetes and LV dysfunction.

Among the patients, occlusion was dominantly in smallvessels and comprised 36 cases (72 %). Cardio-embolic etiology was commonest among the subjects comprising of 58 % (n=29) cases. Majority of the subjects had a stroke in their anterior circulation territory composed of 88 % (n=44)cases. Based on NIHSS grading, the commonest condition at time of admission was moderate (66%, n=33), followed by mild grade (20%, n=10). The mean hsCRP levels were found to be higher in subjects with hypertension. Based on serum levels, high hsCRP was found in 84 % cases (n=42) as compared to only 6 % in control subjects. Statistical analysis using chi square test revealed a p value of <0.001 between elevated hsCRP and stroke severity.

Discussion

In the present study, we determined that the commonest etiological risk factor for stroke was hypertension. This is inconcurrence with studies by various authors in India and abroad. [12-14)] Hypertension has been the most common and important treatable risk factor for stroke in most of the other epidemiology studies including ICASS and the INTERSTROKE study. [13,14] Among our 50 patients with ischemic stroke, the most common TOAST class was small-vessel occlusion followedby large-artery atherosclerosis. Our findings are consistent with findings from a study by Sharma et al. [15], whoobserved in their study that lacunar stroke was the most frequent stroke subtype. However our results are not inconcurrence with Kaul et al. [16] who performed a study, inwhich 392 patients with ischemic stroke, consisting of 282 men and 110 women, aged 54 (range 2–97 years) years were included. They found that majority of patients had large-artery atherosclerosis. Among patients included in this study, most of them had anterior circulation stroke, In a study by Sivanandy et al. [16] it was found anterior circulation involvement in 73.9% of studied patients was seen. This is in concurrence with our study. Melakea et al. [17] found anterior circulation involvement in 75% of studied patients in similar picture to our study.

The serum hsCRP levels in patients with ischemic stroke had high hsCRP (≥ 1 mg/L) levels compared to 6% healthy controls. Chaudhuri et al. in their study found that hsCRP level was significantly higher in stroke patients than incontrols. Other studies have shown varying prevalence. Rajput et al. performed a study in stroke patients from Pakistan and found that 132 (88%) patients had elevated CRP level (> 10 mg/L). [7,18]

Conclusion

Significantly high hsCRP prevalence among patients in our study suggests the important role of inflammation in isch- emic stroke pathogenesis. It

needs to be further evaluated whether some infectious agents trigger a proinflammatory response besides the conventional risk factors in patients with ischemic stroke. High hsCRP level may be a marker toinitiate primary and secondary preventive strategies. The study is limited by a small sample size and further large-scale studies can be conducted to effectively analyse the efficacy of using CRP as a standard prognostic tool in acute ischaemic events.

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