Print ISSN: 2321-6379
Online ISSN: 2321-595X
DOI: 10.17354/ijss/2018/54

Original Article

C-reactive Protein as a Morbidity Predictor in Ischemic Stroke

C Ilango[1], G Rathnakumar[2], Heber Anandan[3]

[1]Professor, Department of Medicine, Thoothukudi Medical College and Hospital, Thoothukudi, Tamil Nadu, India, [2]Associate Professor, Department of Medicine, Tirunelveli Medical College and Hospital, Tirunelveli, Tamil Nadu, India, [3]Senior Clinical Scientist, Department of Clinical Research, Dr. Agarwal's Healthcare Limited, Chennai, Tamil Nadu, India

Abstract

Introduction: Cerebrovascular accident (CVA) is an important health problem worldwide. Various studies proved that C-reactive protein (CRP) at admission was found to be a predictor of functional disability in ischemic CVA. Inflammation also regulates the production of the acute phase proteins such as CRP, fibrinogen, and serum amyloid A. CRP is one of the substances, present in the atherosclerotic lesion, more specifically in the vascular intima.

Aim: The aim of the study was to evaluate the role of CRP as a morbidity predictor in acute ischemic stroke, to study the CRP level pattern in ischemic stroke and to study the correlation between severity level of stroke and CRP level.

Materials and Methods: The study of CRP in ischemic stroke was carried out in the medical wards of Department of Medicine, Tirunelveli Medical College. We examined the association between the level of CRP at different stages after stroke and outcome.

Results: Among patient with positive CRP, 13 were male and eight were female CRP level status positive in 21 patients. There is no association between age of patient and CRP and age factor does not influence the group pattern. Severe disability is more in CRP positive compared to CRP negative group.

Conclusion: CRP is increased in a significant fraction of ischemic stroke. Patients with increased CRP had invariably more deficit during admission and patients with low CRP had good prognostic outcome 4 weeks after onset of stroke.

Key words: Atherosclerosis, C-reactive protein, Cerebrovascular accident, Ischemic stroke

INTRODUCTION

Cerebrovascular accident (CVA) is an important health problem worldwide. Various studies proved that C- reactive protein (CRP) at admission was found to be a predictor of functional disability in ischemic CVA. Inflammation also regulates the production of the acute phase proteins such as CRP, fibrinogen, and serum amyloid A. CRP is one of the substances, present in the atherosclerotic lesion, more specifically in the vascular intima, where it colocalizes with monocytes, monocyte-derived macro plaques, and lipoproteins.[1] CRP is a phylogenetically, highly conserved plasma protein with homologs in vertebrates and many invertebrates, that is part of the systemic response to inflammation. It is an acute phase protein and a member of the family of pentraxins, CRP was originally observed in 1930 in the plasma of patients with acute infections, where it reacts with the C. Polysaccharide of pneumococcus.[2] The major part of the CRP present in the plasma comes from the liver, where the synthesis of CRP is mainly regulated by interleukin (IL-6), which in turn is unregulated by other inflammatory cytokines such as IL-1 and TNFα. Small amounts of CRP can also be produced locally. CRP had been detected on the surface of about 4% of normal blood lymphocytes, and CRP can be produced locally in the atherosclerotic lesions by smooth muscle cells and monocytic cells. Locally in the atherosclerotic lesions by smooth muscle cells and monocytic cells.[3] The structure of CRP is important for its stability and the execution of its function. CRP is composed of five identical 21,500 Da subunits. On dissociation of its pentameric structure, CRP subunits undergo a spontaneous and irreversible

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www.ijss-sn.com

Month of Submission : 12-2017
Month of Peer Review : 01-2018
Month of Acceptance : 01-2018
Month of Publishing : 02-2018

Corresponding Author: Dr. G Rathnakumar, Department of Medicine, Tirunelveli Medical College and Hospital, Tirunelveli, Tamil Nadu, India. Phone: +91-9894177006. E-mail: drrathnakumar2020@gmail.com

conformational change. The loss of the pentameric structure of CRP results in modified or monomeric CRP (MCRP) which is a naturally occurring form of CRP and is tissue-based rather than the serum-based molecule. MCRP is less soluble than CRP and tends to aggregate, and it has been described to induce mRNA of chemokines and expression of adhesion molecules n human cultured coronary artery endothelial cells.[4] Thus, next to circulating native pentameric CRP, MCRP can also promote a pro-inflammatory phenotype and exert atherogenic effects in human endothelial cells, although it may be in a less potent manner that native CRP. Most recent studies report that CRP is an independent predictor of risk of atherosclerosis, cardiovascular events, atherothrombosis, hypertension, and myocardial infarction. Of several inflammatory markers studies, CRP emerged the most powerful inflammatory predictor of future cardiovascular and cerebrovascular risk. Furthermore, the patient with elevated CRP levels within 72 h of stroke has an increased risk of mortality.[5] CRP in ischemic stroke predicts outcome and identifies patients who are at risk for future vascular events and early mortality. CRP has also been found to be elevated in patients with ischemic stroke, correlating with the size of the infarct as evidenced by CT scan. Levels of CRP are consistently associated with cardiovascular disease and predict myocardial infarctions and stroke. Thus, CRP is useful and a reliable predictor of cerebrovascular events.[6]

Aim

The aim of the study was to evaluate the role of CRP as a morbidity predictor in acute ischemic stroke and the correlation between severity level of stroke and CRP level.

MATERIALS AND METHODS

The study of CRP in ischemic stroke was carried out in the medical wards of Department of Medicine, Tirunelveli Medical College Single center observation prospective hospital based study. Inclusion criteria: Stroke as defined by the WHO is a rapidly developing clinical signs of focal (at times global) disturbances of cerebral function lasting more than 24 h or leading to death with no apparent cause other than that of vascular origin, all patients with computed tomography (CT) proven case of ischemic stroke, first episodes of ischemic stroke, do not satisfy and of exclusion criteria exclusion criteria: Age >75 or <15 years, patients with Tia, patient with previous H/o stoke, TIA, patients with hemorrhagic stroke, tumor, sub arachnoid hemorrhage, patients with head injury within 3 months, CT negative stroke, patient who reserved aspirin treatment outside, patient with H/o hypertension, diabetes, heart disease collagen disorders, hyperlipidemia, and T.B arteritis were excluded. Clinical history was recorded from either the patient or his/her relatives. Special emphasis was given to presenting complaint, mode of onset, presence or absence of seizures, loss of consciousness, headache, and vomiting. Apart from routine observations, makers of atherosclerosis such as carotid arteries status of peripheral vessels, carotid thrill, and B.P were noted. Each patient was assessed according to a fixed protocol. The first evaluation was conducted 24–48 h after admission. A detailed clinical profile was obtained. Neurological deficits such as aphasia, cranial N Palsies, limb weakness, sensory impairment, cerebellar dysfunction, conjugate gaze deviation, and hemianopia were elicited by a standard comprehensive bedside neurological examination. Functional score was assessed using Barthel index. CRP was measured by the Nephelometric method. Patients were reassessed on the 5th day and condition reviewed. Third evaluation was at 4th week of follow-up. According to the Barthel index, patients were divided into three groups. Barthel index <41 Severely disabled, Barthel index 41–60 moderately disabled, and Barthel index >60 mildly disabled. Detailed analysis of data was performed. Univariate analysis was done by Chi-square test and multivariate analysis by logistic regression.

RESULTS

The following observations were mode out of the 49 patients, 21 patients had an abnormal increased CRP and 28 patient had normal level. Among patient with positive CRP, 13 were male and eight were female CRP level status positive in 21 patients (i.e.,) 42.85% CRP level positive in

Table 1: Sex-wise distribution of CRP level

Sex	CRP negative	CRP positive	Total
Male	18	13	31
Female	10	8	18
Total	28	21	49

CRP: C-reactive protein

Table 2: Age-wise distribution of CRP level

Age	CRP negative	CRP positive	Total
>60	12	10	22
<60	16	11	27
Total	28	21	49

CRP: C-reactive protein

Table 3: Outcome score and CRP

Outcome	Barthel index	CRP positive	CRP negative	Total
Severely disabled	<41	15	7	22
Moderately disabled	41–60	6	17	23
Mildly disabled	>60	0	4	4

males 26.5%, percentage positive female is 16.32% Table 1. There is no statistical significance, hence sex does not influence the CRP of the patient since Chi-square test $\chi^2 = 0.0292$ $P > 0.05$. There is no association between age of patient and CRP Chi-square, test $\chi^2 = 0.109$ $P > 0.05$. Hence, age factor does not influence the group patten (CRP positive) Table 2. Severe disability is more in CRP positive compared to CRP negative group. Barthel index was <41 in severely disabled group. All patients who had aphasia at the time of admission were CRP positive and belonged to the severely disabled group. All patients who had conjugate gaze deviation were CRP positive and belonged to the severely disabled group. All patients with power less than medical research connect grade 4 were CRP positive Table 3.

DISCUSSION

Sikka *et al.* (1960, Kanpur) in their study of ischemic cerebrovascular disease (cerebral thrombosis) found, maximum number of cases fell in 5–6th decades with mean age 61.8 years, this study also confirms the same.[7] A study done in Western European region, male stroke incidence was 33% higher, and stroke prevalence was 41% higher than the female, with large variations between age bands and between population Worldwide, stroke is more common among men, but women are more severely ill.[8]

In an experimental acute stroke, the release of inflammatory mediators (e.g., IL-1, IL-6, and tumor necrosis factor-a) in direct response to brain injury occurs within 2 h of onset of focal ischemia,[9] and anti-inflammatory therapies are neuroprotective.[10,11] Beamer *et al.*[12] found significantly elevated IL-6 in patients after stroke in whom intercurrent infection had been excluded. Elevated IL-6 and CRP concentrations were present in patients with large established infarcts on CT but not in those with lacunar stroke. In our study, patients with elevated CRP had higher NIHSS scores and were more likely to have CT evidence of cortical infarction on scans performed predominantly within 12 h of admission. These findings support the observations of Beamer *et al.* and are consistent with elevated CRP reflecting the extent of brain infarction. However, since a detailed search for concurrent infection was not undertaken in our study, it is impossible to exclude the possibility that an acute infection at the time of sampling was responsible for both the poor clinical state and the elevated CRP.

CONCLUSION

The present study identified elevation of CRP in ischemic stroke and a high CRP is clearly associated with more severe stroke and high mortality. Patients with increased CRP had invariably more deficit during admission. Patients with low CRP had good prognostic outcome 4 weeks after onset of stroke. The further periodic advance and follow-up studies should be needed to sort out the possibility that stroke patients may be at greater risk of subsequent cardiovascular complications or death and severe neurological deficit.

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How to cite this article: Ilango C, Rathnakumar G, Anandan H. C-reactive Protein as a Morbidity Predictor in Ischemic Stroke. Int J Sci Stud 2018;5(11):119-121.

Source of Support: Nil, **Conflict of Interest:** None declared.