C-REACTIVE PROTEIN – A MARKER TO PREDICT THE OUTCOME OF PATIENTS WITH ACUTE ISCHEMIC STROKE

Sanjay Neeralagi[1], Chandrashekar K[2], Ajmeer Pasha[3], Chetan K. Ganteppanavar[4], Praveen N[5]

[1]Associate Professor, Department of General Medicine, Karnataka Institute of Medical Sciences, Hubli, Karnataka.
[2]Assistant Professor, Department of General Medicine, Karnataka Institute of Medical Sciences, Hubli, Karnataka.
[3]Senior Resident, Department of General Medicine, Karnataka Institute of Medical Sciences, Hubli, Karnataka.
[4]Junior Resident, Department of General Medicine, Karnataka Institute of Medical Sciences, Hubli, Karnataka.
[5]Junior Resident, Department of General Medicine, Karnataka Institute of Medical Sciences, Hubli, Karnataka.

ABSTRACT

BACKGROUND

C-reactive protein is an inflammatory marker. The inflammation plays an important role in the atherogenesis. There is an evidence of the prognostic importance of C-reactive protein (CRP) in ischemic stroke. In this study, we assessed the prognostic values of CRP in ischemic stroke and predicting outcomes.

Aims and Objectives- To evaluate the role of CRP in acute ischemic stroke. To assess the levels of CRP in acute ischemic stroke and in follow-up and CRP as a risk factor in acute ischemic stroke

MATERIALS AND METHODS

We studied 71 patients admitted in department of general medicine, Karnataka Institute of Medical Sciences (KIMS), Hubli, with either hypertension or diabetes or both or none without thrombolysis. Patients with first ever acute ischemic stroke, were examined considering all inclusion and exclusion criteria. CT scan of brain is done in all patients to confirm ischemic stroke and plasma CRP level was measured in all CT confirmed patients, and patients were followed-up for a period of three months and reassessed by NIHS scale and plasma CRP level.

RESULTS

In the ischemic stroke, we found that serum CRP level on admission was predictive of stroke severity (positively correlated with NIHSS), CRP was elevated >6 mg/dl in 50 patients out of 71 patients at the time of admission which was statistically significant. High CRP was associated with high NIHSS and high long-term mortality.

CONCLUSION

The CRP level is significantly higher in ischemic stroke and its elevation between 12-72 hours of symptom onset is a bad prognostic indicator. Elevated CRP level was a risk factor in association with other risk factors like diabetes hypertension.

KEYWORDS

C-Reactive Protein, Ischemic Stroke.

HOW TO CITE THIS ARTICLE: Neeralagi S, Chandrashekar K, Pasha A, et al. C – Reactive Protein – A marker to predict the outcome of patients with acute ischemic stroke. J. Evid. Based Med. Healthc. 2019; 6(6), 357-360. DOI: 10.18410/jebmh/2019/74

BACKGROUND

Stroke is the second common cause of death and fourth leading cause of adult disability in world.[1] Disability is a significant problem in long-term survivors. In previous studies 15–30% are permanently disabled among stroke survivors, and 20% of stroke survivors require hospital care 3 months after stroke.[2,3]

CRP is a systemic inflammatory marker that is produced in large amounts by hepatocytes in response to IL-1, IL-6 and TNF factor.[3,4] Rapid induction of CRP, its long half-life (19 hours) and a lack of alteration during day and night in comparison with other acute phase reactants has introduced CRP as an important factor for evaluation of inflammatory and infectious diseases.[4]

C-reactive protein (CRP is a prognostic marker of ischemic stroke is used for evaluating pathological inflammation and has been studied in relationship to the progression of atherosclerosis.[5]

Patients with ischemic stroke an increased circulatory CRP on hospital admission have greater mortality.[6,7] The prospective study showed that CRP is clinically helpful in predicting the risk of the future cardiovascular diseases.[8]

MATERIALS AND METHODS

71 patients were included in the study and the sample population was collected from admitted patients in KIMS, Hubballi. Clinical history was taken from either patient or

Financial or Other, Competing Interest: None.
Submission 27-01-2019, Peer Review 31-01-2019,
Acceptance 04-02-2019, Published 06-02-2019.
Corresponding Author:
Dr. Sanjay Neeralagi,
Associate Professor, Department of General Medicine,
Karnataka Institute of Medical Sciences,
Vidyanagar, Hubli- 580021, Karnataka.
E-mail: sanjay.neeralagi@gmail.com
DOI: 10.18410/jebmh/2019/74

his/her attender. Personal history regarding dietary habits, smoking, alcohol consumption and tobacco chewing were noted. NIH Stroke Scale was assessed in all patients to assess the neurological disability and its prognosis.

Sampling Method

Convenient sampling method was used. All the cases of ischaemic stroke presented to KIMS, Hubballi were included in the study period of 6 months duration. The study period was from July 2018 – December 2018.

Inclusion Criteria

All the cases of acute ischemic stroke presented to the KIMS Hospital, Hubballi during the study period and aged >18 years were included in the study.

Exclusion Criteria

All cases with significant history of-

1. Autoimmune diseases
2. Rheumatoid arthritis
3. Chronic infectious diseases like HIV, tuberculosis etc.,
4. Acute on chronic systemic illness like inflammatory bowel diseases etc., were excluded from the study and also patients who were found to have newly detected illness which would significantly contribute to changes in acute phase reactants like CRP and ESR were excluded from the study.

Detailed investigations including complete blood count, ESR, fasting blood sugar, serum electrolytes, lipid profile, chest X-Ray, electrocardiography, transthoracic echocardiography, prothrombin time, INR, CRP level, CT brain/MRI brain were done in all patients.

Patients were followed up for a period of three months and all patients were reassessed by using NIH stroke scale to know the clinical improvement or deterioration. Venous blood sample was taken to estimate CRP level at the end of three months follow-up and compared with admission value of CRP and NIH stroke scale.

RESULTS

The maximum ischemic stroke patients are in the age group of 40-60 years constituting 45.1% of total study population. Mean (SD) age of the study participants: 58.01 (13.24).

Age Group	Number	Percentage
<40 Years	8	11.3
40-60 Years	32	45.1
>60 Years	31	43.6
Total	**71**	**100**

Table 1. Age Distribution of Study Group (N =71)

54.9% were males and 45.1% were females. Among 71 patients, 20 patients were smokers constituting 28.2% of study group. 30 patients had past history of hypertension constituting 42.3% of study and 14 patients had a past history of diabetes mellitus constituting 20% of group.

NIHS Categories at Admission	Number	Percentage
Mild Stroke (0-7)	10	14.1
Moderate (8-14)	50	70.4
Severe (>14)	11	15.5
Total	**71**	**100**

Table 2. Distribution Based on NIHS Categories (NIHSS at Baseline/Admission)

Among 71 patients 50 patients had moderate stroke constituting 70.4% of total study group, 11 patients had severe stroke and 10 patients had mild stroke. The mean NIHS at admission was 12.6±6.7.

NIHS Categories at 3rd Month	Number	Percentage
Mild Stroke (0-7)	46	64.8
Moderate (8-14)	18	25.4
Severe (>14)	7	9.9
Total	**71**	**100**

Table 3. Distribution Based on NIHS Categories at the End of Third Month

Among 71 patients 46 patient has shown a significant improvement with only mild impairment in daily activity constituting 64.8% whereas only 7 patients had significant impairment at the end of three months. The mean of NIH at 3rd month is 4±3.1.

CRP Level	Number	Percentage
<6	21	29.6
>6	50	70.4
Total	**71**	**100**

Table 4. Distribution Based on CRP at Admission Category

CRP Level	Number	Percentage
<6	46	64.8
>6	19	26.8
Missing	6	8.5
Total	**71**	**100**

Table 5. Distribution Based on CRP Level at the End of Third Month

In the present study cut off value of 6 mg/dl has been taken since in India as a developing nation there is a high incidence of infectious diseases CRP level of <6 mg/dl is taken as negative and CRP level of >6 mg/dl taken as positive.

CRP was >6 mg/dl in 50 patients constituting 70.4% at the time of admission with mean CRP level at admission of 25.3. At follow up CRP level also reduced to <6 mg/dl constituting 64.8%, and in 19 patients CRP level remained >6 mg/dl. 6 patients expired in period of 3 months.

CRP Level at Admission	NIHSS at Admission Mean (SD)	p-Value (t test)
<6	9.0 (4.69)	0.003
>6	14.1 (6.9)	

Table 6. Association of CRP at Admission with NIHS Score at Admission

CRP Level at 3rd Month	NIHSS at 3rd Month Mean (SD)	P Value (t test)
<6	2.98 (1.97)	<0.001
>6	6.32 (4.04)	

Table 7. Association of CRP and NIHS at the End of Third Month

There is a positive correlation between CRP level and NIH score with a "p" value of 0.03 at admission time which is significant. At the end of three months of follow-up, this also showed a positive correlation with a "p" value of <0.001 which is significant.

DISCUSSION

In the present study ischemic stroke in patients less than 40 years of age constituted 11.3% of all strokes and highest incidence was seen in the age group of 40-60 years, that is 45.1% and followed by age more than 60 years constituting 43.6% and an increased incidence of stroke in both male and females after the age of 60 years with a slight predominance in males. Incidence of stroke in males was 54.9% and that of females was 45.1%.

Acute stroke may trigger an inflammatory response that leads to increased levels of CRP. High levels of CRP may be associated with poor outcome because they reflect either an inflammatory reaction or tissue damage. Elevated serum levels of CRP are found in up-to three quarters of patients with ischemic stroke.

ESR, CRP, Haptoglobin, Fibrinogen etc are many acute phase reactants which are elevated in many conditions like autoimmune diseases, rheumatoid arthritis, connective tissue diseases, inflammatory bowel diseases, acute on chronic infectious diseases like HIV and tuberculosis, Acute on chronic systemic illness. The CRP is the only acute phase reactant studied in association with stroke after ruling out all the above-mentioned causes. Detailed history and relevant investigations were done to rule out the underlying causes which would bias the study.

Increases in CRP may reflect a systemic inflammatory response following stroke, the extent of tissue injury, or concurrent infections. Several studies have assessed the value of CRP in the very early phase of stroke as a prognostic factor of functional outcome.[9] Verification of the role of CRP as an early prognostic factor of functional outcome after ischemic stroke may be of clinical importance, because it is an easily-measured and readily available inflammatory marker.

Anuradha Bharosay et al[10] studied 46 Patients admitted in neurology department SAIMS, Indore with first ever ischemic stroke within 72 h of onset and correlated serum Interleukin 6, high sensitivity C reactive protein at the time of admission with neurological worsening assessed by NIHSS at the time of admission and 7 days after admission and they observed that disability was associated with higher concentrations of IL-6 and hsCRP in plasma and early neurological deterioration was too observed in cases with high levels of hsCRP and IL-6.

Mahapatra SC et al[11] observed CRP value 76 mg/dl in 64 patients out of 80 total thrombotic stroke patients (p<0.001). The study was undertaken to assess the role of inflammation in pathogenesis of ischemic stroke

Rathore HS et al[12] performed a study to measure and compare CRP levels in the cortical and lacunar infarct and to find out their diagnostic importance at an early stage of stroke

M.A. Shoaeb, M.A. Shehata[13] et al in their study classified Severity of stroke by using NIHSS, there was a strong positive correlation between disease severity assessed by NIHSS and Serum CRP level, was positively correlated.

Mario Di Napoli et al[14] studied, the risk of CRP in 72% of patients (p=0.0001) out of 473 first ever ischemic stroke patients and suggested CRP as an independent marker of underlying chronic inflammatory process in atherosclerosis

When we followed the patients for a period of three months and patient's disability was reassessed by using NIHSS and CRP level, the association between the two was compared. Severity of stroke assessed by NIHSS revealed a mean score of 4±3.1, with 7 patients (9.9%) stratified as severe, 18 patients (25.4%) as moderate, and 46 patients (64.8%) as mild, and there was a strong positive correlation between disability severity assessed by NIHSS and Serum CRP level at the end of three months, correlated positively with NIHSS (r = 0.62, P <0.001).

CONCLUSION

CRP is a very useful marker to assess the severity of the disease and for prognosis of the disability in patients with acute ischemic stroke.

REFERENCES

[1] Rajput MR, Lakhair MA, Shaikh MA, et al. C-Reactive Protein (CRP) and other risk factors in acute ischemic stroke patients. JLUMHS 2011;10(3):131-133.

[2] Asplund K, Stegmayr B, Peltonen M. From the twentieth to the twenty-first century: a public health perspective. Cerebrovascular Disease: Pathophysiology, Diagnosis, and Management. Blackwell Science 1998.

[3] Lloyd-Jones D, Adams RJ, Brown TM, et al. Executive summary: heart disease and stroke statistics--2010 update: a report from the American Heart Association. Circulation 2010;121(7):948-954.

[4] Song IU, Kim JS, Kim YI, et al. Relationship between high-sensitivity C-reactive protein and clinical

functional outcome after acute ischemic stroke in a Korean population. Cerebrovasc Dis 2009;28(6):545-550.
[5] Calabro P, Golia E, Yeh ET. Role of C-reactive protein in acute myocardial infarction and stroke: possible therapeutic approaches. Curr Pharm Biotechnol 2012;13(1):4-16.
[6] Anuk T, Assayag EB, Rotstein R, et al. Prognostic implications of admission inflammatory profile in acute ischemic neurological events. Acta Neurol Scand 2002;106(4):196-199.
[7] Rallidis LS, Vikelis M, Panagiotakos DB, et al. Inflammatory markers and in hospital mortality in acute ischaemic stroke. Atherosclerosis 2006;189(1):193-197.
[8] Tanne D, Benderly M, Goldbourt U, et al. C-reactive protein as a predictor of incident ischemic stroke among patients with pre-existing cardiovascular disease. Stroke 2006;37(7):1720-1724.
[9] Idicula TT, Brogger J, Naess H, et al. Admission C-reactive protein after acute ischemic stroke is associated with stroke severity and mortality: the Bergen stroke study. BMC Neurol 2009;9:18.
[10] Bharosay A, Saxena K, Varma M, et al. Correlation between Proinflammatory serum markers: high sensitivity C-reactive protein, interleukin-6 with disability score in acute ischemic stroke. Indian J Clin Biochem 2011;26(3):279-282.
[11] Mahapatra SC, Pillai PK, Hui PK, et al. C-reactive protein in thrombotic stroke. JAPI 2002;50:1512.
[12] Rathore HS. Role of C-reactive protein estimation in early diagnosis of cortical and lacunar infarct. JAPI 2002;50:1516.
[13] Shoaeb MA, Shehata MA, Taema KM, et al. CRP in cerebrovascular stroke: prognostic implications. The Egyptian Journal of Critical Care Medicine 2014;2(1):43-52.
[14] Di Napoli M, Papa F. Inflammation, hemostatic markers and antithrombotic agents in relative to long-term risk of new cardiovascular events in first-over ischemic stroke patients. Stroke 2002;33(7):1763-1771.