Original Article

C-Reactive Protein in Ischemic Stroke – An Experimental study

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Abstract

Background: There are many studies which predicts the prognostic significance of C-reactive protein (CRP) in ischemic stroke. Taking values at only one point of time is not important as compared to level its concentration at different perids of hospital stay of patient. Therefore we compared the values of CRP Within 24 hrs, 48-72 hrs & at the time of hospital discharge admission and discharge with 1-year outcome.

Methods: Forty eight patients were included in the study and serum CRP values were measured, within 24 hours after ischemic stroke, within 48 to 72 hours, and at hospital discharge and an association was examined between the CRP levels and the time at which these values were taken and analyzed statistically.

Results: 1.5 mg/dL for CRP at discharge provided optimum specificity for adverse outcome. Markers of worse prognosis were the presence of CHD (HR 1.98, 95% CI 1.21 to 3.38; $P = 0.0081$), PAD (HR 2.66, 95% CI 1.32 to 5.69; $P = 0.0082$), age > 70 years (HR 2.28, 95% CI 1.06 to 3.74; $P = 0.0475$). CRP level at hospital discharge (HR 6.82, 95% CI 2.65 to 20.07; $P = 0.0001$) showed the strongest association.

Conclusions: CRP level is a better prognostic indicator of ischemic stroke at the time of discharge and is of greater utility for risk identification. These findings are strongly and statistically significant ($p < 0.005$) and confirm that raised CRP may predict future outcome in terms of mortality and morbidity.

Keywords: IL-6, Prognosis Proteins ischaemia

INTRODUCTION

C-reactive protein (CRP) is considered as a sensitive predictor of both new-onset and recurrent ischemic events.[1-3] C-reactive protein (CRP), levels are associated with different stroke outcomes and further vascular events. CRP is a potential prognostic marker after vascular events and a potential predictor of future vascular events. Many retrospective studies concerning ischemic stroke indicated that recent infections may increase the possible risk for ischemic stroke.[4,5] Several studies have shown elevated levels of C-reactive protein (CRP), among individuals who are at greater risk of ischemic heart diseases.[6-10] Elevated CRP is more reliable predictor than creatine kinase in MI patients.[11] Medical data relating CRP as a prognostic factor in ischemic stroke is very thin.[12,13] Therefore, this prospective study is performed in patients with first-ever ischemic stroke to further analyze the relationship between CRP values measured immediately and at different times.

MATERIAL AND METHODS

All patients (48) who were admitted in department of medicine of Teerthankar Mahaveer Medical College, Moradabad, India, with a diagnosis of ischemic stroke. To maintain the research protocol, consent was taken from all the patients, institutional ethics committee and research committee. A very strict protocol for screening of patients to be included in this study was maintained and monitored, which included thorough history, systematic examination followed by advanced radiological evaluation with the help of department of radio-diagnosis. Radiological findings were classified into infarcts and lucencies. Great emphasis was put on habit of smoking, alcohol, hypercholesterolemia, hyper-triglyceridemia, hypertension and diabetes mellitus. Routine laboratory investigations were done and we tried to keep the patients, away from hospital acquired infections. Exclusion criteria for the present study included those subjects who had stroke, subarachnoid hemorrhage,

vasculitis, renal, hepatic and malignant diseases within 30 days from the time of starting of the study.

RESULTS

After comprehensive evaluation, 48 patients were included in this prospective study. Among 48 patients mean ± SD age was 69.08 ± 6.17 years. The CRP values, within 24 hours, between 48 to 72 hours, and at hospital discharge were 1.4, 1.0 and 0.7 mg/dl, respectively. CRP levels above normal value (>0.5 mg/dL) at entry were significantly associated with larger infarcts ($P < 0.0003$) and cortical involvement ($P = 0.0001$). At discharge, higher CRP levels were also associated with larger infarcts ($P = 0.0041$). Markers of worse prognosis were the presence of CHD (HR 1.98, 95% CI 1.21 to 3.38; $P = 0.0081$), PAD (HR 2.66, 95% CI 1.32 to 5.69; $P = 0.0082$), age >70 years (HR 2.28, 95% CI 1.06 to 3.74; $P = 0.0475$). CRP level at hospital discharge (HR 6.82, 95% CI 2.65 to 20.07; $P = 0.0001$) showed the strongest independent association with the combined end point at 1 year. There was not a significant association between CRP on admission and death.

DISCUSSION

The aim of the study was to predict the relationship between CRP and prognosis after ischemic stroke. Our data indicate that patients with ischemic stroke who have CRP levels >1.4 mg/dL at discharge have a significantly worse outcome. Several previous studies have reported elevated CRP values in patients with ischemic stroke. [8,9,14-19] Variations in CRP level in ischemic stroke not previously analyzed in detail. According to this study a different prognostic significance can be elucidated: a benign, consisting of either constantly normal or decreasing values from admission through to discharge, and another pattern, represented by those patients with constantly elevated or increasing values from the time of admission to discharge. Constantly elevated levels of CRP represent either an ongoing inflammatory process or the extension of cerebral ischemia.[15] Many previous studies indicate that inflammatory mechanisms contribute to secondary neuronal injury after cerebral ischemia.[4,5,20-24] Rise in CRP levels is not only associated with immediate consequences but also remains elevated in stroke survivors.[10] Many previous studies have also indicated that rise in fibrinogen levels are also associated with higher CRP levels.[25,26] However we didn't find any association between fibrinogen and CRP levels. CRP in structure is protein and its synthesis is controlled at the level of transcription.[3,27,28] and IL-6 is key regulatory factor in this phenomenon.[29] Raised levels of CRP reflect the extent of brain infarction in the form of large sized infarcts. Our findings of large sized infarcts are consistent with previous studies.[15] Patients in whom the CRP levels remain persistently elevated have worst prognosis. The mechanism remains unexplained why the values of CRP at the time of discharge remains lower as compared to entry levels.

Table 1: Different CRP levels at different times

S.N.	Duration	Values (mg/dl)
1.	Within 24 hrs	1.4
2.	48-72 hrs	1.0
3.	At the time of hospital discharge	0.7

Table 2: Markers of worst prognosis

S.N.	Markers of worse prognosis	HR (Hazard ratio)
1.	CHD	1.98
2.	PAD	2.66
3.	Age>70 yrs	6.82

CONCLUSION

From above results and discussion it is certain that elevation of CRP is common in ischemic conditions and more so over CRP levels classify stroke patients into high and low-risk groups patients. These observations also raise the possibility that ischaemic patients are at greater risk of subsequent associated complications.

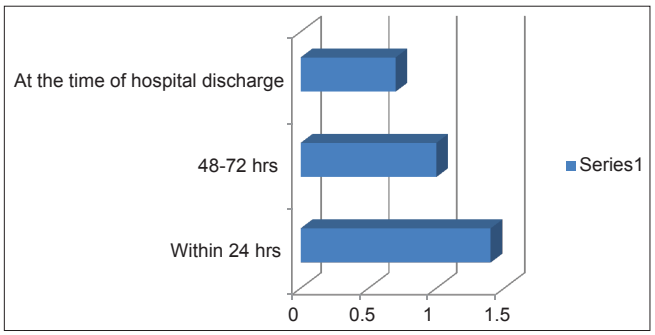

Figure 1: Different CRP levels at different times

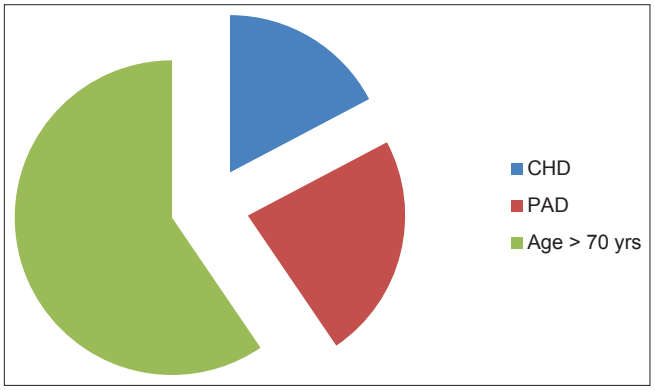

Figure 2: Markers of worst prognosis

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