

Original Article

Association of Admission CRP Level with Short Term Outcome in Patients with Acute Ischemic Stroke

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Abstract:

Acute ischemic stroke is very common in Bangladesh and one of the most common causes of physical disability and death. This study was performed to determine the prognostic value of CRP measured in the very early phase of ischemic stroke for short term functional outcome of patients with acute ischemic stroke. This observational study was carried out in the departments of Medicine and Neurology of Faridpur Medical College Hospital, Faridpur from July 2012 to December 2012. Total 100 patients of acute ischemic stroke were recruited in this study. Blood sample was collected for CRP level during the time of admission. In this study 26% of patients were in low CRP group (CRP <3 mg/L), 34% of patients were in medium CRP group (CRP 3-9.9 mg/L), 40% of patients were in high CRP group (CRP ≥10 mg/L). According to modified Rankin Scale (mRS) scoring system the high CRP group having a 44% risk for a poor outcome (mRS ≥3) vs 27% for the low CRP group (p = 0.01). According to Barthel Index (BI) scoring system the high CRP group having a 45% risk for a poor outcome (BI <95) vs. 25% for the low CRP group (p = 0.002). Z test of proportion revealed significant association between high CRP level and poor short-term outcome of patients with acute ischemic stroke.

Key words: Ischemic stroke, CRP level, Modified Rankin Scale (mRS) scoring, Barthel Index (BI) scoring.

Introduction:

Stroke is defined as a syndrome of rapid onset of cerebral deficit (usually focal) lasting >24 hrs or leading to death, with no apparent cause other than vascular one¹. Of the patients presenting with stroke, 85% will have sustained a cerebral infarction due to inadequate blood flow to part of the brain and remainder will have an intracerebral hemorrhage. Cerebral Infarction is mostly due to thromboembolic disease secondary to atherosclerosis in major extracranial arteries (Carotid and Aortic arch). About 20% of infarctions are due to embolism from heart

and further 20% are due to intrinsic diseases of small perforating vessels (lenticulostriate arteries) producing so called lacunar stroke. About 5% are due to rare causes, including vasculitis, endocarditis and cerebral venous disease².

According to WHO, of estimated 57 million deaths in 2008 globally, 63% were due to Non communicable Diseases (NCDs). Of NCDs death 22% were due to Coronary Heart Disease (CHD) and 16% due to stroke. The South Asian

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countries account for about a quarter of the world's population and contribute the highest proportion of the burden of cardiovascular diseases as compared with any other region globally³. In Bangladesh, about 8.57% death

occur due to stroke, second to CHD (17.11%)⁴. It is likely that the recent increase in stroke in South Asians is due to lifestyle changes associated with urbanization, perhaps interacting with a genetic predisposition that leads to abdominal obesity, hyperglycaemia, and dyslipidaemia⁵.

There is growing evidence that C-reactive protein (CRP), a peripheral marker of inflammation, is also a marker of generalized atherosclerosis⁶. This relationship between inflammation and atherosclerosis make CRP a potential marker for prognosis after vascular events and a potential predictor of future vascular events.

Elevated serum levels of CRP are found in up to three quarters of patients with ischemic stroke^{7,8}. Increases in CRP may reflect a systemic inflammatory response following ischemic stroke, the extent of tissue injury, or concurrent infections. Moreover, in animal models of focal cerebral ischemia, CRP increased secondary brain damage through activation of the complement system^{9, 10}.

Several studies have assessed the value of CRP in the very early phase of ischemic stroke as a prognostic factor of functional outcome. These studies were either small, included a selected group of patients, or tested only the relation between CRP and mortality instead of functional outcome. The findings were inconclusive as some found a positive association¹¹⁻¹³, but others not^{14,15}.

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. The aim of this study was therefore to determine the prognostic value of CRP measured in the very early phase of ischemic stroke for short term functional outcome of patients with acute ischemic stroke.

Materials and methods:

This observational study was carried out in the departments of Medicine and Neurology of Faridpur Medical College Hospital (FMCH), Faridpur from July 2012 to December 2012. Total 100 samples were taken purposively. Patients who were admitted with sign symptoms of stroke within 24 hours after the onset of symptoms were considered first and CT scan or MRI of brain was done for confirmation of stroke. Blood sample was collected for CRP level during the time of admission. After receiving the investigation report among the patients who were confirmed as acute ischemic stroke were included in this study. Among the patients who were diagnosed as acute hemorrhagic stroke or patients who

recovered completely within 24 hours of onset of symptoms were excluded from this study.

Written informed consent was obtained from patients or their next of kin. Confidentiality and privacy was maintained throughout the study. Participant refusal and withdrawal from the study at any time was accepted. Data was recorded in a pre-designed format with standardized questionnaires after taking history, clinical examination and doing necessary investigations of patients. Poor outcome was defined as mRS ≥ 3 or BI < 95 & short term outcome was defined as functional outcome of patient of acute stroke at 7 days after admission¹⁶.

Data was compiled in a master chart and the data was entered into computer for statistical analysis using computer based software, statistical package for social science (SPSS) version 15. Continuous variable like age was calculated as mean standard deviation. Cross tabulation was performed to get the relation between males and females. Categorical variables like gender, history of hypertension, diabetes mellitus, smoking, dyslipidaemia were presented in frequencies and percentages. Appropriate statistical test was done as required.

Result:

Total 100 patients of acute ischemic stroke were recruited in this study. Mean age was 56 years \pm SD 12.5. Majority of the patients in this study were above 40 years (94%), 24% patients were in the 5th decade, 25% were in the 6th decade and 29 % were in the 7th decade. Male were predominantly affected (71% patients were male and 29% patients were female) and male female ratio was 2.45:1. According to occupation most of the patients were farmer (41%) followed by businessman (22%) and then service holder (20%). Among risk factors smoking 65%, hypertension 31%, diabetes 16% and dyslipidaemia was 62% (Table I).

Table I: General characteristics of the study population (n=100)

Variable	Value
Age	Mean (56 years) \pm SD 12.5 Range (31-85 years)
Sex:	
Male	71%
Female	29%
Family history of stroke risk	30%
Smoking	65%

In this study 26% of patients were in low CRP group (CRP <3 mg/L), 34% of patients were in medium CRP group (CRP 3-9.9 mg/L), 40% of patients were in high CRP group (CRP ≥10 mg/L). Among high CRP group 56% were female, 44% were male. Most of the patients with high CRP level were ≥70 years (34%) followed by 60-69 years (23%) and then <50 years (22%).(Table II).

Table-II: Distribution of patients according to level of CRP (n=100)

Category of CRP level(mg/L)	No. of patient (%)
Low (<3)	26 (26)
Medium (3-9.9)	34 (34)
High (≥10)	40 (40)

According to mRS scoring¹⁶ system the high CRP group having a 44% risk for a poor outcome (mRS ≥3) vs. 27% for the low CRP group (p=0.01) (Table III).

Table-III: Outcome of patients according to mRS scoring (n=100)

Category of CRP level (mg/L)	mRS scoring		Z-value	p-value
	0-2	3-6		
Low (<3)	19 (73%)	7 (27%)	2.6	0.01 (S)
Medium (3-9.9)	23 (69%)	11 (31%)		
High (≥10)	22 (56%)	18 (44%)		

*Z test of proportion was done to analyze the data. Level of significance was 0.05.

n: Number of patients, **0-2:** Good outcome, **3-6:** Poor outcome, **S:** Significant

According to BI scoring^{17,18} system the high CRP group having a 45% risk for a poor outcome (BI <95) vs. 25% for the low CRP group (p=0.002). Z test of proportion revealed significant association between high CRP level and poor short-term outcome of patients with acute ischemic stroke(Table IV).

Table-IV: Outcome of patients according to BI scoring (n=100)

Category of CRP level (mg/L)	BI scoring		Z-value	p-value
	>95	<95		
Low (<3)	20 (75%)	6 (25%)	3.0	0.002 (S)
Medium (3-9.9)	24 (71%)	10 (29%)		
High (≥10)	22 (55%)	18 (45%)		

*Z test of proportion was done to analyze the data. Level of significance was 0.05.

n: Number of patients, **>95:** Good outcome, **<95:** Poor outcome, **S:** Significant

Discussion:

In this study 26% of patients were in low CRP group (CRP <3 mg/L), 34% of patients were in medium CRP group (CRP 3-9.9 mg/L), 40% of patients were in high CRP group (CRP ≥10 mg/L). Winbeck et al.¹⁴ showed 25% of patients were in low CRP group, 37% of patients were in medium CRP group, 38% of patients were in high CRP group. Pepys et al.¹⁰ showed 29% of patients were in low CRP group, 35% of patients were in medium CRP group, 36% of patients were in high CRP group. Our current study is similar to above studies.

In current study among high CRP group, 56% were female and 44% were male. Di Napoli et al.⁷ showed 59% were female and 41% were male. Pepys et al.¹⁹ showed 60% were female and 40% were male. Our current series is similar to above two studies.

Among high CRP group according to age distribution 34% were ≥70 years age, 23% were 60-69 years age, 21% were 50-59 years age, 22% were <50 years age which are in conformity with the observation of the respective Framingham study²⁰ and study done by Masotti et al¹².

In the present study two scoring system of short-term functional outcome were assessed. One was mRS, another was BI. This study, according to mRS scoring system showed the high CRP group having a 44% risk for a poor outcome (mRS ≥3) vs. 27% for the low CRP group; according to BI scoring system the high CRP group having a 45% risk for a poor outcome (BI <95) vs. 25% for the low CRP group. The Bergen stroke study²¹ showed on mRS with the high CRP group having a 47% risk for poor outcome vs. 26% for the low CRP group; on BI with the high CRP group having a 40% risk for poor outcome vs. 24% for the low CRP group. So these observations are in consistent with that of the present study. Z test of proportion was done to analyze the data between high and low CRP groups to compare short-term outcome of stroke and revealed statistically significant differences between them. So in the present study there is a positive association between high CRP level and poor short-term outcome of patients with acute ischemic stroke.

Conclusions:

There is a crude association between high CRP level and poor short-term outcome of patients with acute ischemic stroke. Elevated CRP levels in the very early phase of acute ischemic stroke are independent prognostic factors for poor outcome. In clinical practice we may consider high CRP as a "red flag" marker of high morbidity and mortality, but the therapeutic implications of this finding remain uncertain.

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