ORIGINAL ARTICLE

Association of CRP Level with The Outcome in Patients with Cerebrovasular Accidents: A Case-Control Study

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ABSTRACT

Introduction: Cerbrovascular Accidents (CVA's) are a major burden over the society with highly associated mortality as well as mortality. Therefore it is important to find the markers which may help us in order to determine its prognosis.

Objective: To determine the mortality rate and frequency of poor outcome among patients presenting with CVA along with the relation to higher and normal CRP levels obtained within 24 hours of the start of symptoms

Material and Methods: This case-control study was conducted at Neurology department of Sir Ganga Ram Hospital/ Fatima Jinnah Medical University, Lahore. Total duration of study was 18 months, from January, 2015 to June, 2016. All the patients with CVA presenting in Emergency department of the hospital within 24 hours of start of symptoms were included in the study. Patients underwent CT scan to confirm the diagnosis of CVA. Their blood sample of 3 ml quantity was obtained for CRP levels. According to CRP level, they were dichotomized into 2 groups: ≥6 mg/L (Cases); <6 mg/L (Controls). They were re-assessed after 3 months of presentation using modified Rankin Scale (mRS) for morbidity and the mortality. All data were analyzed by SPSS version 20.

Results: A total of 235 patients were included in the study. They were dichotomized into two groups according to CRP level and 156 patients were in control while 79 patients were in case group. The mean age of patients was found as 63.9 ± 10.9 years and 66.19 ± 12.01 years in both groups. The mRS score was assessed at 3- months follow up and it was found that the mortality occurred among 29 patients (18.5%) in patients in Cases group while in 9 patients (11.3%) in Control group (P = 0.156). Also poor outcome was found in 76 patients (48.7%) in Cases while in 26 patients (32.9%) in Control group (P = 0.020). Odd's Ratio was calculated for poor outcome in both groups and it was found as 1.937 (1.101, 3.406) and 1.776 (0.795, 3.963) for mRS>2 and mortality respectively.

Conclusion: We conclude that CRP level is an easily available test and if it is higher than normal in patients with CVA, it is associated with poor outcome and higher mortality. So we may use this test routinely in order to predict the morbidity of the disease.

Keywords: Cerbrovascular Accident; Ischemic stroke; intracerebral hemorrhage; C-reactive protein; Outcome

INTRODUCTION

There is a continuous research going on to find the prognostic factors for patients having cerbrovascular accidents (CVA). As the population and life expectancy is increasing, so is the incidence of these cerbrovascularaccidents[1]. These accidents lead to a large number of mortality, but also those who survive, most of them suffer from long-term morbidity and place a major burden over the society, hospital as well the care-givers and the family[2, 3]. Among many searched markers for the prognosis of cerbrovascularaccidents including serum calcium level, B-Nitro peptide (BNP) and various cytokines, one is the C - reactive protein (CRP) levels within 24 hours of admission. It has been shown in studies that raised CRP levels may pose as a risk factor for future CVA's[4]. Also another trial has evidently shown that giving the statins and other cholesterol lowering agents may play a significant role for controlling CRP levels and future CVA's[5] .

CRP has not been extensively studied in the literature regarding its role in CVA. A large study has shown that higher CRP levels may help to

predict the future stroke, however it is not efficient for predicting the outcome of current attack[6]. However, the Framingham trial showed that raised CRP level has been associated with higher risk for future CVA[7]. So far, only few studies are available in the literature which have assessed the high CRP level for the prediction of outcome of the current and ongoing stroke event[8-10]. Also the previous studies which have been conducted have different sample sizes and study designs. So there is a lot room in the literature for our study. We planned this study with the objective to determine the mortality rate and frequency of poor outcome among patients presenting with CVA along with the relation to higher and normal CRP levels obtained within 24 hours of the start of symptoms.

MATERIAL AND METHODS:

This case-control study was conducted at Neurology department of Sir Ganga Ram Hospital/ Fatima Jinnah Medical University, Lahore. The duration of study was 18 months, from January, 2015 to June, 2016. All the patients with ischemic stroke (IS) or intra-cerebral hemorrhage (ICH) presenting in Emergency department of the hospital within 24 hours of start of symptoms were included in the study. The sample selection technique was non-probability, consecutive sampling. We excluded those patients presenting after 24 hours of start of symptoms, previous history of IS or ICH and those who refused for participation into the study. Baseline information including age, gender, body temperature, systolic blood pressure and history of hypertensionand diabetes mellitis were sought. Patients underwent CT scan to confirm the diagnosis of CVA. Their blood sample of 3 ml quantity was obtained from wither limb after admission into the hospital. These samples were sent to the hematology laboratory of the hospital for CRP levels. This test was performed in the laboratory by technician and report was verified from the consultant pathologist. According to the report obtained for CRP, they were dichotomized into 2 groups: >6 mg/L (Cases); ≤6 mg/L (Controls). Patients were managed as per departmental protocols. They were re-assessed after 3 months of presentation using modified Rankin Scale (mRS) for morbidity and the mortality. Poor outcome was defined if mRS is >2. Outcome was assessed by on duty doctor who was blind about CRP status of the patient. All data were analyzed by Statistical Package for the Social Sciences (SPSS) version 20. Odd's Ratio (OR)were calculated between CRP levels and the outcomes using confidence interval of 95%.

RESULTS

A total of 235 patients were included in the study. Among them 111 patients (47.2%) were having IS while remaining 124 patients (52.7%) had ICH. They were dichotomized into two groups according to CRP level. The mean age of patients was found as 63.9 ± 10.9 years and 66.19 ± 12.01 years in both groups. The other baseline information was also obtained and they were almost comparable in both groups (table 1).

Table 1: Baseline information of the patients in this study

Number of patients	156 (66.3%)	79 (33.7%)	
Age (years) Mean ± SD	63.9 ± 10.9	66.19 ± 12.01	0.176
Gender			
Male	94 (60.2%)	48 (60.7%)	0.94
Female	62 (39.7%)	31 (39.2%)	
Hypertension			
Yes	97	39	0.06
No	59	40	
Diabetes Mellitis			
Yes	68	24	0.049
No	88	55	
Temperature (F)	37.49 ± 0.979	37.3 ± 1.0	0.155
Systolic Blood Pressure (mm of Hg)	170.72 ± 21.1	169.58 ± 19.45	0.964

Figure 1: Outcome comparison in both groups

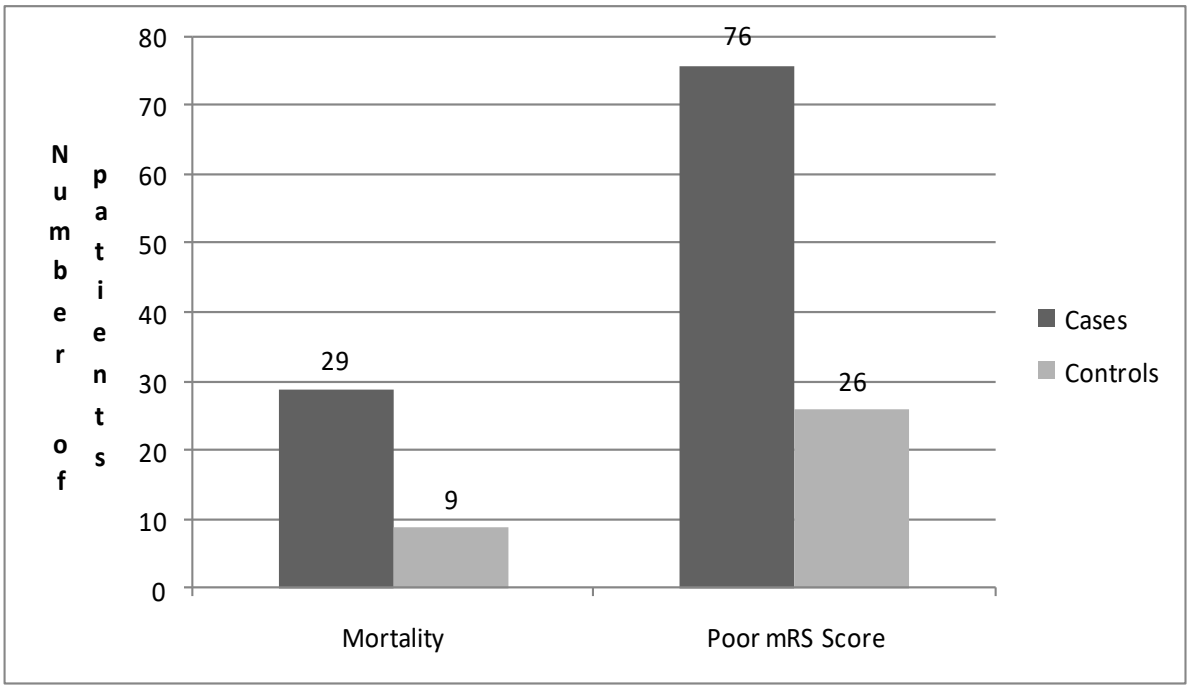

Table 2: Association between poor outcome and CRP levels

mRS>2	1.937 (1.101, 3.406)
Mortality	1.776 (0.795, 3.963)

Also the mRS score was assessed at 3-months follow up and it was found that the mortality occurred among 29 patients (18.5%) in patients in cases group while in 9 patients (11.3%) in Control group (P = 0.156). Also poor outcome was found in 76 patients (48.7%) in Cases while in 26 patients (32.9%) in Control group (P = 0.020). All the data are given in figure 1. OR was calculated for poor outcome in both groups and it was found as 1.937 (1.101, 3.406) and 1.776 (0.795, 3.963) for mRS>2 and mortality respectively (Table 2).

DISCUSSION

CRP has been shown to be associated with inflammation and atherosclerosis. Due tothis fact, CRP had been proposed as a potential marker for CVA and other vascular events[11, 12]. Our study was planned with the objective to determine the mortality rate and frequency of poor outcome among patients presenting with CVA along with the relation to higher and normal CRP levels obtained within 24 hours of the start of symptoms. We had found that higher CRP levels at the time of admission are associated with poor outcome at 3-months follow up in terms of mRS score and also the mortality rate was higher in those patients having higher CRP levels.

Many theories have been proposed to identify the association between high CRP levels and the poor outcome in stroke patients; however none of them has been proved to be true yet. A possibility may be that higher CRP level is the result of tissue injury during stroke and therefore, higher CRP levels indicate the more injury and hence poor outcome [13]. Also at the same time, another possibility may be that higher CRP levels indicate the higher levels of inflammation and the underlying process leading to stroke is sever in higher CRP level patients, so it may lead to higher injury scores. Many studies have tried to see the result of stroke on CRP levels after the event and they have produced mixed results that either this rise might in small units [14] or there may be a large increase [15]. This riddle also remains unsolvable in these studies.

Some studies have shown the association between high CRP levels and the outcome of the patients after stroke. In a study by Hertog et al, the outcome of patients with higher CRP levels was significantly worse than those with lower CRP levels. They had found a fairly significant

difference in mortality rate and poor outcome percentages in both groups. These results are in line with our results[16]. Also in a study by Christensen and Boysen, it was found that early rise in CRP levels is significantly associated with higher mortality rate among patients with stroke [17].

The strengths of this present studyinclude that it had a large sample size and was properly planned study. The outcome tool utilized was fully validated tool. Also many other demographic details were assessed according to local norms. However, there were some limitations also. It was a single center study and we haven't dichotomized the timing since the start of symptoms. Secondly we haven't addressed the confounders in this study as it was beyond the scope and objectives of our study.

We conclude on the basis of this study that higher CRP levels are associated with higher mortality and poor outcome. So if we routinely perform CRP levels of the patients with CVA at the time of admission, we may be able to counsel them in a better way regarding the outcome according to evidence based medicine.

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