Original Article

Evaluation of Prognostic Role of Serum CRP in Acute Stroke Patients

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Abstract: Cerebrovascular disease includes all disorders in which an area of the brain is transiently or permanently affected by ischemia or bleeding and one or more of the cerebral blood vessels are involved in the pathological process. C-reactive protein (CRP) is one of the first acute phase proteins that increases during systemic inflammation and is also the one that exhibits the most dramatic increase in concentration. The serum CRP is a significant measure that appears to be connected with the neurological outcome of patients who have suffered an acute stroke. This study evaluated the prognostic role of Serum CRP in acute stroke patients. The comparative prospective study was carried out in the department of Biochemistry BSMMU, total N=50 diagnosed acute stroke patients were enrolled in this study. Stroke patients were diagnosed by CT scan or MRI. The age range of the study subjects was 33-80 years. Serum CRP was measured in all the study subjects, post stroke neurological outcome was assessed by mRS (Modified Rankin Scale), four weeks after an acute stroke. Good outcome was considered as mRS <4 (Group-A) & poor outcome mRS >3 (Group-B). Statistical analyses were performed by using SPSS for windows version 12.0. Unpaired 't' test, Mann Whitney U test, Chi-square test and Spearman's rho correlation test were used to see the level of significance 95% confidence limit ($p < 0.05$) was taken as level of significance. With respect to CRP level the median serum CRP concentration in acute patients was median was 3.7mg/l (range 3–45 mg/l), which was much higher than upper reference range (<1 mg/l). A significant high level of serum CRP was found in poor outcome group as compared to good outcome group. There was a significant association of poor neurological outcome with high serum CRP level (X^2 value = 38.57, $p < .001$). Correlation analysis of serum CRP level with mRS score showed a strong positive correlation, which indicate that mRS score increase with increase in serum CRP level. The study concluded that serum CRP concentration increased in stroke patients as well as Serum CRP concentration positively correlated with post stroke neurological outcome as assessed by mRS score. Serum CRP level may be estimated in all stroke patients as prognostic tool to predict post stroke neurological outcome.

Keywords: serum CRP, stroke patients, cerebrovascular disease

1. INTRODUCTION

Cerebrovascular disease refers to any and all conditions in which a region of the brain is affected, either temporarily or permanently, by ischemia or bleeding, and in which one or more of the cerebral blood arteries are implicated in the pathological process [1]. Ischemic stroke, hemorrhagic stroke, and cerebrovascular anomalies including intracranial aneurysm and arteriovenous malformation are examples

of some of the illnesses that fall under the category of cerebrovascular disease. These are some of the most frequent and debilitating conditions. Stroke is defined by the World Health Organization (WHO) as the fast development of clinical signs of focal (sometimes global) disruption of brain function that lasts for more than twenty-four hours or that results in death and has no apparent cause other than vascular origin. There are two distinct forms of strokes, which are ischemic and hemorrhagic strokes. Stroke caused by ischemia accounts for 85 percent of all cases. Within the category of hemorrhagic stroke, there are two subcategories: intracerebral and subarachnoid. In the event of an ischemic stroke, the disruption of the blood supply to the brain leads to hypoperfusion of the tissues, hypoxia, and ultimately the death of cells as a consequence of a failure in the mechanism that produces energy. Intracerebral hemorrhage is a condition that occurs when a vessel within the brain parenchyma ruptures. The usual rate of cerebral blood flow is fifty milliliters per minute for every one hundred grams of tissue, although there is a significant amount of regional variance between white matter and gray matter as well as within different portions of gray matter [2]. In between four and ten minutes, the death of brain tissue might occur when the cerebral blood flow drops to zero degree. The values of 16 to 18 milliliters per gram of tissue per minute cause infarction within an hour, but the values of 20 milliliters per gram of tissue per minute create ischemia without infarction except for several hours to days [3]. In affluent countries, stroke is the third most prevalent cause of death after heart disease and cancer. It is higher in the Afro-Caribbean population than it is in the Caucasian population. The age-adjusted annual death rate from stroke is 116 per 100000 population in the United States of America and 200 per 100000 population in the United Kingdom. Under the age of 40, stroke is a very infrequent occurrence, and it is more prevalent in males. While the prevalence rate of stroke in India was between 250 and 350 per 100,000 people during the course of the previous decade, there is a lack of reliable and comprehensive data regarding the incidence and death of stroke in Bangladesh. Patients who receive treatment in specialized acute stroke units have a lower risk of passing away, a higher chance of returning home, and a higher chance of being able to function independently three months later [4]. In the majority of clinical trials, approximately fifteen percent of patients who have suffered an ischemic stroke pass away within the first three months [5]. Even though the majority of functional recoveries occur during the first month, it is feasible that some ongoing modest improvement will occur for a period of one year. It was determined that risk variables or risk markers for a first stroke may be characterized according to their potential for modification (nonmodifiable, modifiable, or potentially modifiable) and the degree of evidence (well documented or less well documented) [6]. Age, gender, low birth weight, race or ethnicity, and genetic variables are known to be non-modifiable risk factors. The following are examples of risk factors that have been well-documented and can be modified: hypertension, exposure to cigarette smoke, diabetes, atrial fibrillation and certain other cardiac conditions, dyslipidemia, carotid artery stenosis, sickle cell disease, postmenopausal hormone therapy, poor diet, physical inactivity, obesity, and body fat distribution [7]. The metabolic syndrome, the abuse of alcohol and drugs, the use of oral contraceptives, sleep-disordered breathing, migraine headaches, hyperhomocysteinemia, elevated lipoprotein (a), elevated lipoprotein-associated phospholipase, inflammation, and infection are just some of the risk factors that have received less attention from researchers and may be modifiable. C-reactive protein (CRP) is one of the first acute phase proteins that increases during systemic inflammation and is also the one that exhibits the most dramatic increase in concentration [8]. Inflammatory variables play a significant part in the pathophysiology of ischemic stroke, especially when it comes to the development of the condition. Over the course of a cross-sectional investigation, researchers demonstrated that individuals who had experienced a stroke had significantly higher median CRP values. According to the National Institutes of Health Stroke Scale, a higher CRP

concentration was an independent predictor of mortality, along with age and the severity of the stroke. According to the findings of a study, elevated plasma CRP levels strongly predict the risk of future ischemic stroke and transient ischemic attack in elderly people, regardless of the presence of other cardiovascular risk factors. According to the findings of another study, the CRP level that was evaluated within 12 hours of the beginning of symptoms in an acute ischemic stroke does not have an independent relationship with the long-term prognosis [9]. Contrarily, an increase in CRP between 12 and 24 hours following the onset of symptoms is related with an increased frequency of cerebrovascular and cardiovascular events, and it is a predictor of an unfavorable outcome. There is a correlation between an increase in the production of acute phase reactants (APR) such CRP and a decrease in the production of pre-albumin, albumin, and transferrin [10]. People have been using albumin concentrations as a measure of health and disease for a very long time. There are a number of factors that can cause a decrease in blood albumin concentrations, including undernutrition, catabolism, liver illness, and renal disease. There was a significant difference in the incidence of infective complications and poor functional result during hospitalization between stroke patients with hypoalbuminemia and those with normal or higher blood albumin concentrations, according to the findings of a prospective observational study that comprised hospitalized stroke patients. In addition to being one of the main causes of morbidity and mortality across the globe, cerebrovascular illness also places a significant burden on the health care system overall. The serum CRP is a significant measure that appears to be connected with the neurological outcome of patients who have suffered an acute stroke. It is possible to use these to make a prognosis prediction for people who are suffering from acute stroke, even at secondary hospitals.

2. MATERIALS & METHOD

The study has adopted the prospective study design, conducted in the Department of Biochemistry of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. Acute stroke patients of both sexes, diagnosis confirmed by CT scan or MRI were the population of the study. Patients were collected from the department of neuromedicine of BSMMU, Dhaka Medical College & Holy Family Red Crescent Medical College & Hospital, Dhaka as well. Data has been collected from N=50 with Purposive and convenient sampling technique from the patients diagnosed acute stroke patients of both sexes confirmed by CT scan or MRI, of 25 to 80 years of age. With all aseptic precaution 5ml fasting venous blood sample was collected from the median cubital vein by disposable plastic syringe from all study subjects within 48 hours of onset of symptoms. Blood was transferred immediately into a dry clean test tube with a gentle push to avoid hemolysis. The test tube was kept in standing position till formation of clot. Then the blood was centrifuged at 3000 rmp for 5 minutes and serum was collected and preserved at -350C until analysis. On the basis of serum CRP level, study subjects were divided into following groups:

Group I (serum CRP level ≤10.1mg/dl)

Group II (serum CRP level >10.1mg/dl)

Post stroke neurological outcome was assessed by Modified Rankin Scale (mRS) four (4) weeks after acute stroke and study subjects were divided into following categories:

Group-A - Good outcome (score <4)

Group-B - Poor outcome (score >3 or death)

Analysis of data was done with the help of computer by using SPSS for windows version 12.0. Unpaired 't' test, Mann Whitney U test, Chi-square test and Spearman's rho correlation test were used to see the level of significance. 95% confidence limit ($p < 0.05$) was taken as level of significance.

3. RESULTS & DISCUSSION

3.1 Result Interpretations

Result showed age & sex distribution of the study subjects, the mean age of the study subjects was 65.86 ± 11.38 years and age range were 33-80 years shown in table 01.

Table 01: Age & sex distribution of the study subjects

Parameter	Mean ± SD (Range)	Male	Female
Age (years)	65.86 ± 11.38 (33-80)	--	---
Sex	---	26	24

It showed the distribution of the study subjects among groups based on neurological out come and biochemical parameters serum CRP level as shown in table.

Table 02: Distribution of study subjects among groups based on neurological out come and biochemical parameters

Parameters	Groups	No of cases	Total
mRS scale	Group-A Good outcome(mRS <4)	28	50
	Group-B Poor out come (mRS > 3)	22	
Serum CRP (mg/l)	Group-I CRP (≤10.1 mg/l)	36	50
	Group-II (CRP >10.1 mg/l)	14	

Table showed serum CRP levels of the study subject, the mean serum CRP level was 7.99 ± 8.39 mg/l and median (range) was 3.7mg/l (3– 45 mg/l) as shown in table below.

Table 03: Serum CRP levels of the study subjects.

Parameter	Mean ± SD	Median (Range)
Serum CRP(mg/l)	7.99 ± 8.39	3.7 (3 – 45)

Table showed distribution & comparison of serum CRP level between good outcome (Group-A) & poor outcome (Group-B) groups. The median (range) of serum CRP level in good & poor outcome groups was 3.55 mg/l (3.0-17.7 mg/l) & 10.35 mg/l (3.3 - 45.9) mg/l respectively. Significantly high level of serum CRP was found in poor outcome group as compared to good outcome group (p <0.01).

Table 04: Distribution & comparison of serum CRP level between good outcome (Group-A) & poor outcome (Group-B) groups.

Parameter	Group-A Good outcome group (mRS <4) (n=28) Median (range)	Group-B Poor outcome group (mRS > 3) (n=22) Median (range)	Mann Whitney U value	p value
Serum CRP(mg/l)	3.55 (3.0-17.7)	10.35 (3.3-45.9)	149	<0.01

p- value reached by Mann Whitney U test & p <0.05 taken as level of significance.

Finding of the study showed association of serum CRP with neurological outcome. Among 50 study subjects, in 36 CRP level was ≤10.1 mg/l (Group-I) & in 14, CRP level was >10.1 mg/l (Group-II). In Group-I, 27 study subjects had good out come & 9 had poor outcome. In Group-II, only one study subject had good out come & 13 had poor outcome. A significant association of poor neurological outcome was found with increase in serum CRP level (p<.001).

Table 05: Association of serum CRP with neurological outcome.

Neurological outcome	Group I (CRP ≤10.1 mg/l)	Group II (CRP >10.1 mg/l)	Chi square value	p value
Group-A Good outcome (mRS <4)	27	1	38.57	<0.001
Group-B Poor outcome (mRS > 3)	9	13		

p- value reached by X^2 test & p <0.05 taken as level of significance.

Table-X & Fig-2 showed correlation of serum CRP level with mRS scores. A significant positive correlation, (r 0.401, p <.01) was observed between serum CRP level & mRS scores i.e. mRS scores increase with increase in serum CRP level.

Table 06: Correlation of serum CRP level & mRS score of study subjects.

Independent variable / Dependent variable	r value	p value
CRP level / mRS	0.401	p <.01

p- value reached by Spearman's rho correlation test & p <0.05 taken as level of significance.

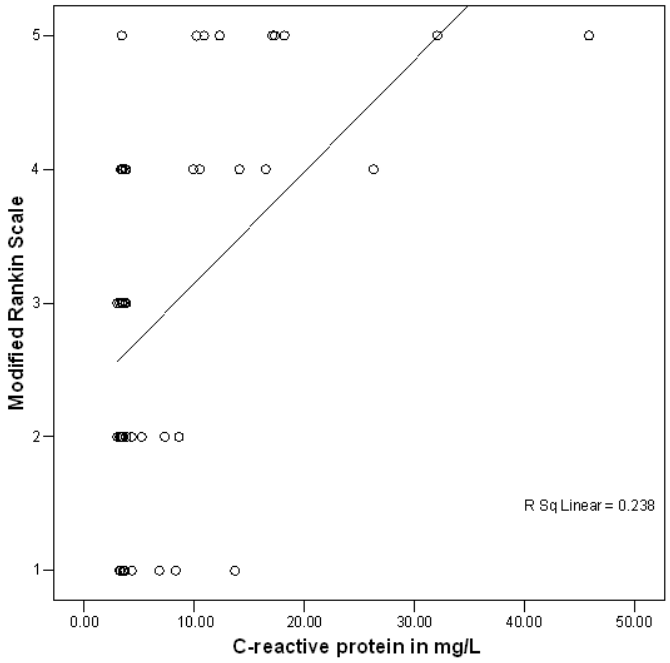

Figure 01: Correlation of serum CRP level with mRS scores of the study subjects

3.2 Discussion

In spite of the fact that stroke therapy has become significantly more advanced over the course of the last decade, there is still a significant risk of death or additional vascular events occurring within the first year following an acute episode. The discovery of new risk markers has the potential to enhance risk classification, as well as the selection of individuals who could potentially benefit from enhanced therapy and the comprehension of pathophysiological mechanisms [11]. In this study, we assessed the amount of CRP in the blood in order to investigate the relationship between hypoalbuminemia and high levels of CRP in the serum and the neurological outcome of patients who had suffered an acute stroke. In accordance with the neurological outcome following a stroke, the participants in the study were separated into two groups: Group A, which had a positive outcome, and Group B, which had a negative outcome. After four weeks had passed since an acute stroke, the mRS score was used to evaluate the neurological outcome. On the basis of biochemical criteria, we had classified the individuals who participated in the study into two groups: Group-I, which had a serum CRP level of less than or equal to 10.1 mg/l, and Group-II, which had a

serum CRP level that was greater than or equal to 10.1 mg/l. Our investigation revealed that there was no statistically significant difference in age or blood pressure between the groups with a favorable outcome (mRS < 4) and those with a poor outcome (mRS > 3). There is some degree of compatibility between our findings and the research presented in [12]. The researchers discovered a significant difference in the age distribution, but they did not discover a significant difference in the SBP or DBP levels between the groups with good outcomes and those with bad outcomes. Within forty-eight hours of the beginning of stroke, we examined the amount of CRP in the serum for our study. All of the participants in the study had a considerably elevated serum CRP level (median value, 3.7 mg/l), which is much higher than the reference range [13]. All of them discovered that patients who had suffered a stroke had a greater CRP level than those who had not suffered a stroke. The purpose of the study was to investigate whether or not there is a correlation between the levels of serum CRP in patients who had suffered an acute stroke and their post-stroke neurological outcome, which was measured by the mRS score four weeks after the stroke had begun. We discovered that the group with poor outcomes had a significantly higher level of serum CRP than the group with good outcomes (the Mann Whitney U value was 149.00, and the p-value was less than.001) [14]. According to the findings of the study, which claimed that increased levels of CRP are associated with a worse prognosis in patients who have suffered an ischemic stroke [15], this conclusion is in agreement with the findings. According to the findings of a study [16], survival rates were significantly worse in those with high CRP levels at compared to those with low CRP levels. There was a noteworthy correlation between an elevated blood CRP level and a negative outcome in neurological conditions (X2 value = 38.57, p <0.001). There is a strong correlation between elevated blood CRP levels and the neurological result that occurs after a stroke, according to a number of writers [17]. The investigation of correlation between serum CRP level and mRS score revealed a noteworthy positive association, with a correlation coefficient of 0.401 and a p-value of less than.01. This suggests that the mRS score increases in tandem with the serum CRP value. In patients who have suffered a stroke, a high mRS indicates a poor neurological outcome [18]. It appears from this that serum CRP has the potential to serve as a predictive marker for determining the neurological outcome following a stroke. A similar finding was published [19], which was that there is a direct association between rising levels of CRP and rising levels of Rankin score. When CRP levels rise, the likelihood of experiencing disability also rises [20]. According to the findings of a study, elevated CRP levels following the commencement of a stroke are a strong indicator of further cardiovascular or cerebrovascular events, as well as a poor prognosis [21].

4. CONCLUSIONS

A comparative prospective study was carried out in the department of Biochemistry, BSMMU to evaluate the role of serum CRP level with post stroke neurological outcome of acute stroke patients. A total number of 50 diagnosed acute stroke patients were enrolled in this study. Stroke patients were diagnosed by CT scan or MRI. The age range of the study subjects was 33-80 years. By history and clinical examination renal failure, hepatic failure, recent MI, trauma, pregnancy, infectious disease and inflammatory disorders were excluded. Sample was collected within forty eight hours of admission. Serum CRP was measured in all the study subjects, post stroke neurological outcome was assessed by mRS (Modified Rankin Scale), four weeks after an acute stroke. Good outcome was considered as mRS <4 (Group-A) & poor outcome mRS >3 (Group-B). On the basis of serum CRP concentration study subjects were divided into two groups-Group-I (n=36) with serum CRP concentration ≤10.1mg/l & Group-II (n=36) with serum CRP concentration >10.1mg/l. Statistical analyses were performed by using SPSS for windows version 12.0. Unpaired ‘t’ test, Mann Whitney U test, Chi-square test and Spearman’s rho correlation test were used to see the level of

significance 95% confidence limit ($p < 0.05$) was taken as level of significance. With respect to CRP level the median serum CRP concentration in acute patients was median was 3.7mg/l (range 3–45 mg/l), which was much higher than upper reference range (<1 mg/l). A significant high level of serum CRP was found in poor out come group as compared to good outcome group. There was a significant association of poor neurological outcome with high serum CRP level (X^2 value = 38.57, $p < .001$). Correlation analysis of serum CRP level with mRS score showed a strong positive correlation, which indicate that mRS score increase with increase in serum CRP level. The study concluded that serum CRP concentration increased in stroke patients as well as Serum CRP concentration positively correlated with post stroke neurological outcome as assessed by mRS score. Serum CRP level may be estimated in all stroke patients as prognostic tool to predict post stroke neurological outcome.

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