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Original Article

Assessment of Serum Biomarkers as Indicators of Treatment Outcome Among Patients with Ischaemic Cerebrovascular Accident in A Tertiary Care Hospital, Kolkata.

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Keywords:
Acute cerebrovascular accidents, NIHS scale, CRP, hsCRP, 3 months and 6 months post-treatment CVA.

ABSTRACT

Background:An estimated 77.2 million people globally suffer from ischemic cerebrovascular accidents but there are no such reliable figures for the prevalence of the disease in West Bengal. Inflammation is an important cause of ischemic cerebrovascular accidents with a strong impact on mortality and post-cerebrovascular accident physical disability. Due to the lack of standard tests for assessment of ischemic cerebrovascular accident evaluation and treatment can be challenging.
Aims: The current study was thus designed and aimed at finding a new set of biological markers along with NIHSS & MRS to aid in the diagnosis, treatment, and follow-up of ischemic cerebrovascular accidents in a non-invasive manner.
Methodology:In an observational case-control study, serum levels of CRP & hsCRP by immunoturbidimetry were measured in 50 clinically and radiologically (CT/MRI) diagnosed untreated patients of ischemic cerebrovascular accident and 50 healthy age & sex-matched control subjects at the pre-treatment stage and in 21 patients and 50 controls after 3 months and 6 months post-treatment stage.
Results:The results of statistical analysis showed that levels of serum CRP and hsCRP were significantly raised ($p < .001$) in patients of ischemic cerebrovascular accident compared to their apparent age and sex-matched controls. It was also found that treated cases showed significantly lower values of serum CRP and hsCRP both 3 months as well as 6 months after completion of therapy as compared to pre-treatment levels.
Conclusion:Both CRP and High-sensitive CRP (hs-CRP) play an important role in ischemic cerebrovascular accident prognosis at discharge, 3 & 6 months follow-up. There was a positive correlation between serum hsCRP levels and functional output as measured by NIHSS in acute ischemic cerebrovascular accidents.

INTRODUCTION

Currently, cerebrovascular accidents are one of the leading causes of death and are responsible for physical and/or mental impairment in low and middle-income countries like India. The prevalence of the disease is increased due to major changes in the main modifiable risk factors[1]. In rural areas, the estimated prevalence rate of cerebrovascular accidents is 84-262/100,000 population whereas in urban areas the value is 334-424/100,000 population. The case fatality rates have a wide variation with the highest being in Kolkata i.e. around 42%[2]. So it is necessary to organize a combined effort from both the government and the private sector to make necessary arrangements for its control and early management in India as well as in its major cities[2].

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Cerebrovascular accident is the sudden occurrence (within minutes to hours) of focal neurological deficits resulting from either hemorrhage or infarction within the brain. In cerebral ischemia reduced blood supply persists for several seconds. If the cerebral ischemia persists for more than a few minutes infarction or death of brain tissue occurs [3]. The signs and symptoms of cerebrovascular accident are highly variable due to the complex anatomical structure and vascular supply of the brain. Despite the decline in overall ischaemic cerebrovascular accident hospitalizations, it has been found that the age-specific acute ischaemic cerebrovascular accident hospitalization rates increased for patients aged 25-¬64years. So it is necessary to predict early outcomes after an acute ischaemic cerebrovascular accident which is clinically very important for optimized care to the patient[4]. Hence, the earlier the diagnosis is made better the outcome in these patients. However, the diagnosis of cerebrovascular accident is critical and its comprehensive diagnosis is based on both clinical and medical imaging studies.

Inflammation plays an important role in the development of atherosclerosis and ischaemic cerebrovascular accident[5]. Several inflammatory markers have been identified as cardiovascular and functional outcome predictors after ischaemic cerebrovascular accidents [6]. C-reactive protein (CRP) is a frequently studied inflammatory biomarker that is involved in all stages of ischaemic cerebrovascular accident. Elevated CRP level is independently associated with an increased risk of ischaemic cerebrovascular accident. However, the different studies on the association between increased CRP levels and the all-cause mortality risk in patients with acute ischaemic cerebrovascular accidents have yielded inconsistent results[4]. High-sensitivity C-reactive protein (hsCRP), a glycoprotein produced by the liver is also a sensitive marker of inflammation and tissue injury in the arterial wall. The hs-CRP measures CRP in the lower range i.e. from 0.5 to 10 mg/L. In this range, the hs-CRP test is used to identify low but persistent levels of inflammation. The hs-CRP is more precise than standard CRP when measuring baseline concentrations. The induction of an hsCRP is rapid and the half-life of hsCRP is long enough in the blood for a steady time course. So hsCRP is very useful for the diagnostic workup of inflammatory and infectious diseases. It plays an important role in the development of atherosclerosis in cerebral and cardiac circulation[7]. As a marker of inflammation and infection, high hsCRP has been associated with acute cerebrovascular accident[8]. Since inflammatory diseases and infections are more common in India in comparison to Western countries, our research question was to investigate any correlation of serum hsCRP levels in patients with ischaemic cerebrovascular accidents [7]. Due to higher levels of infections and infective disorders and a higher risk of cerebrovascular diseases due to infective diseases, India is exposed to a double burden of both communicable and non-communicable diseases. The poor economic population is increasingly affected by cerebrovascular accidents, because of both the changing population exposure to risk factors and, most tragically the inability to bear the high cost of cerebrovascular accident management. The majority of survivors of cerebrovascular accident patients continue their lives with physical disabilities and the continuous rehabilitation expenditure and caring for a long duration are mostly commenced by family members which makes them financial burden[2]. Till now, several studies have indicated this relationship worldwide. Whiteley et al. in 2011 showed that higher levels of hsCRP, along with IL-6 and fibrinogen measured after cerebrovascular accident onset in 817 patients are significantly associated with increased incidence of occlusive vascular events and vascular death along with nonvascular causes of death after cerebrovascular accident[9]. Arenillas et al. showed that hsCRP and plasminogen activator inhibitor-1 measured 3 months after onset of ischemic cerebrovascular accident are highly predictive of intracranial large artery atherosclerosis progression[10]. However, very few studies have highlighted this relationship in our country, particularly in its Eastern part. Based on this lacuna and research question, we hypothesized that there is a direct relationship between the high hs-CRP level and ischemic stroke in India including our study region. Thus, we aimed to analyze the change in hsCRP level with treatment outcome among patients with an ischaemic cerebrovascular accident in a tertiary care hospital, Kolkata, and for this, our objectives were to estimate the levels of hsCRP in clinically & radiologically diagnosed cases of ischaemic cerebrovascular accident and in age & sex matched control and to compare the pre and post-treatment values of the above at 3months and 6months after initiation of treatment.

MATERIALS AND METHODS:

Study design/ experiment design:

It was an observational case-control study.

b) Study setting:

The study was conducted in the Department of Biochemistry and Department of Medicine & Neuromedicine of a tertiary care medical college and hospital after getting approval from the Institutional Ethics Committee.

c) Period of study:

After obtaining the ethical clearance the study was started on 1st January 2020 and continued till 30th June 2021 i.e. for18 months.

d) Study population:

Clinically and radiologically (CT/MRI) diagnosed untreated ischemic cerebrovascular accident patients along with apparently healthy age & sex-matched controls.

e) Sample size:

50 cases of ischemic cerebrovascular accidents were selected depending on the total patients attended in the desired period and the estimated number of samples was calculated by the below-mentioned formula.

$n = Z\alpha\ 2pq/\ (L2)$ Where, n required sample size, $Z\alpha = 1.96$ at 95% confidence interval (CI) $p= 0.154$ (as per Indian Council for Medical Research, 2006), $q= 1-p$ L= absolute precision (10%).

50 age and sex-matched controls were included in the study.

Our study design was consecutive sampling according to inclusion and exclusion criteria:

Inclusion criteria –

1) Diagnosed case of Ischaemic cerebrovascular accident confirmed by clinical and radiological means (CT/MRI) 2) Age between 30 -80 years. 3) Sex both male & female.

Exclusion criteria –

1) Stroke due to any Infectious etiology (meningitis, brain abscess) autoimmune etiology, vasculitis, or coagulopathy. 2) History of any autoimmune disorder, any vasculitis, or any coagulopathy. 3) Iatrogenic stroke. 4) Use of any medication within the last 30 days that can affect the hsCRP value e.g. any steroids or immunomodulatory drug. 5) TIA, recurrent stroke, intracerebral hemorrhage or tumor, subarachnoid hemorrhage, head injury within the past 3 months. 6) Admission to hospital after 72 hours of the onset of stroke. 7) Patients suffering from any infection. 8) Patients with a history of heart disease: any valvular heart disease, infective endocarditis, and myocardial infarction. 9) Pregnant and lactating mother. 10) Patients who have developed an infection within 72 hours of onset of stroke.

Procedural methodology:

All the clinically and radiologically (CT/MRI) diagnosed untreated Ischemic cerebrovascular accident patients were thoroughly examined and grading of severity was done. 6ml whole blood was collected from the Outpatient and Inpatient Department of Medicine & Neuromedicine after obtaining informed consent. Blood was subjected to centrifugation @3000rps, for 10 minutes, in the Department of Biochemistry using the centrifuge instrument (REMI R-4C). The serum was separated and stored at -20ºC for further use in clot vials (VAKU-8). Serum was utilized to estimate levels of CRP and hsCRP using the KONE LAB PRIME 60i Auto analyzer by immunoturbidimetry principle. The values of serum CRP are generated in mg/L units by the system All the parameters were assessed both clinically and radiologically (CT/MRI) diagnosed untreated ischemic cerebrovascular accident cases as well as 3 & 6 months post initiation of treatment. All tests were also performed for recruited controls.

Data collection and interpretation:

Statistical methods applied:

The data obtained from the study and control population were further statistically analyzed by Graph pad Prism (version 8.4.3). To evaluate the difference between cases and controls, we used the parametric test and Unpaired t-test if the data was following Gaussian distribution and Mann Whitney U test if the data was not following Gaussian distribution. A 'p' value of <0.05 was considered to be statistically significant. Pearson r or Spearman r rank order correlation coefficients, whichever is applicable, were used to test correlations between the biomarkers and the National Institute of Health Stroke Scale and Modified Rankin Scale.

Results:

In this study, 50 cases and 50 age-matched controls were included as per inclusion and exclusion criteria after a thorough history, clinical examination, and radiological (CT/MRI) investigation. The details of each patient were recorded in predesigned proforma.

To evaluate the difference between cases and controls, we used the parametric test and the Unpaired t-test if the data was following the Gaussian distribution and the Mann-Whitney U test if the data was not following the Gaussian distribution. Statistical significance was evaluated by 'p' value <0.05 or <0.0001 whichever was applicable. Pearson r or Spearman r rank order correlation coefficients, whichever is applicable, were used to test correlations between the study parameters and the National Institute of Health Stroke Scale and Modified Rankin Scale. The entire statistical analysis was done with the help of GraphPad Prism (version 8.4.3).

Comparison between serum CRP levels in Cases of Ischaemic cerebrovascular accident with age and sex-matched Control:

50 cases of clinically and radiologically (CT/MRI) diagnosed ischemic cerebrovascular accident were taken. The normality of the sample size was tested with the D'Agostino & Pearson omnibus normality test. It was observed that the data were not normally distributed. So, the nonparametric Mann-Whitney test was applied to compare the serum CRP levels in cases of ischemic cerebrovascular accident as opposed to that of the age and sex-matched controls and found to be significantly higher in pre-treatment cases than controls as shown in Table 1.

Table 1: Serum level of CRP (mg/L) in Pre-treatment Cases and Controls by Mann-Whitney test.

CRP (mg/L) Pre-treatment		**No.**	**Median value**	**P value**
	Case	50	53.06	**<.001**
	Control	50	7.356	

P value considered to be significant at P<.05 for a 95% confidence interval

The data distribution of the CRP values in case and control groups has been also depicted in the Box whisker plot in Figure 1:

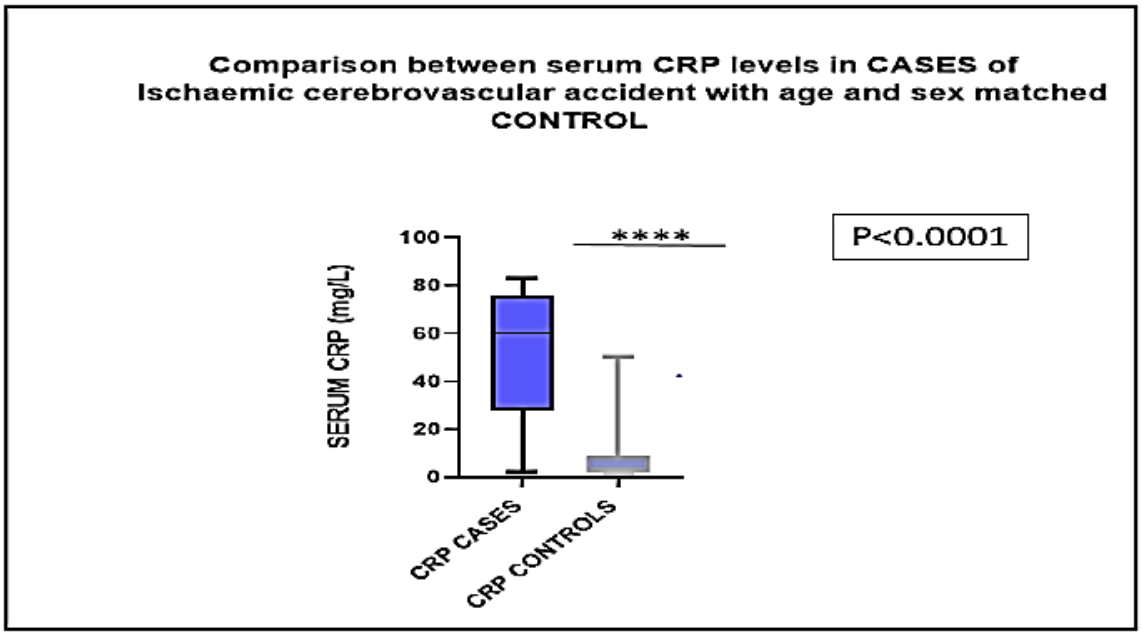

Figure 1: Box whisker plot showing data distribution of serum CRP levels in the case and control groups.

Comparison between serum hs-CRP levels in Cases of Ischaemic cerebrovascular accident with age and sex-matched Controls:
50 cases of clinically and radiologically (CT/MRI) diagnosed ischemic cerebrovascular accident were taken. The normality of the sample size was tested with the D'Agostino & Pearson omnibus normality test. It was observed that the data were normally distributed. So, an unpaired t-test was applied to compare the serum hsCRP levels in cases of ischemic cerebrovascular accident as opposed to that of the age and sex-matched controls and found to be significantly higher in pre-treatment cases than controls. Results are shown in Table 2 as follows:

Table 2: Serum level of hs-CRP (mg/L) in Pre-treatment Cases and Controls by Independent t-test:

CRP (mg/L) Pre-treatment		**No.**	**Mean ± SD**	**P value**
	Case	50	1.439 ± 0.48	**<.001**
	Control	50	0.404 ± 0.28	

P value considered to be significant at P<.05 for a 95% confidence interval

The data distribution of the CRP values in case and control groups has been also depicted in the Box whisker plot in Figure 1:

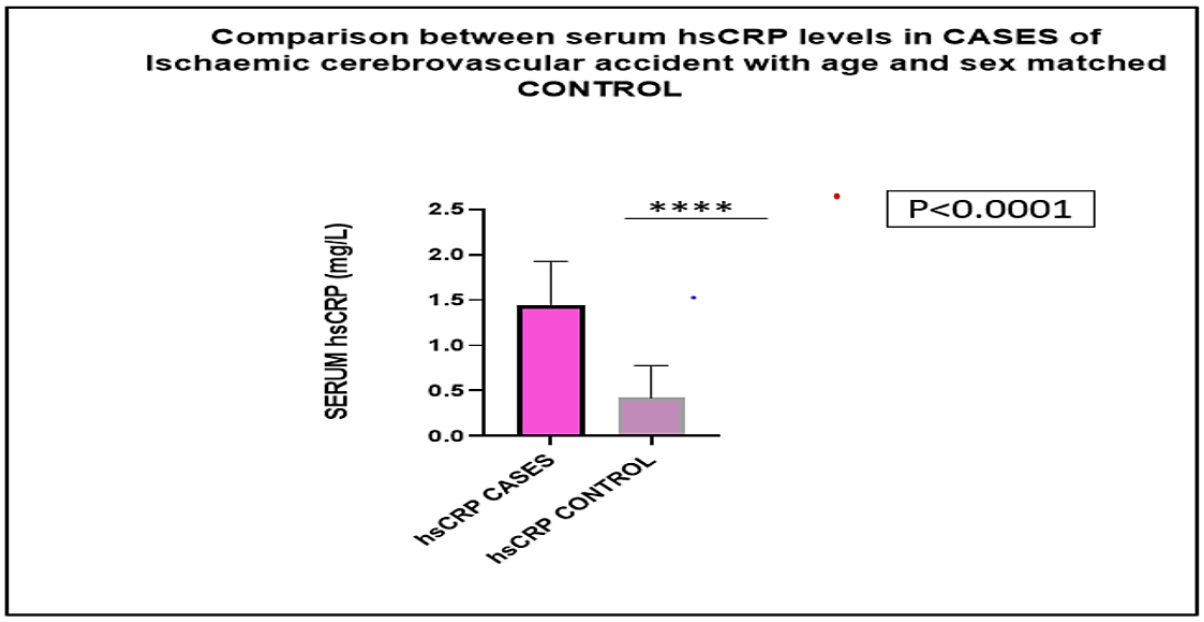

Figure 2: Box whisker plot showing data distribution of serum hsCRP levels in the case and control groups.

Comparison between serum CRP (mg/L) levels in Pre-treatment and 3 months Post-treatment cases of Ischaemic cerebrovascular accident:

50 cases of clinically and radiologically (CT/MRI) diagnosed ischemic cerebrovascular accident were taken. 29 cases were found to be expired in 3 months follow up. The normality of the sample size was tested with the D'Agostino & Pearson omnibus normality test. It was observed that the data were not normally distributed. So, the Wilcoxon Signed Rank test was applied to compare the serum CRP levels in Pre-treatment cases and 3-month Post-treatment cases of ischemic cerebrovascular accidents. Results are shown in Table 3.

Table 3: Comparison of serum CRP (mg/L) levels in Pre-treatment and 3 months Post-treatment Cases of Ischemic cerebrovascular accident:

		No.	**Median**	**P value**
CRP (mg/L) Pre-treatment	Case	50	53.06	**<.001**
CRP (mg/L) 3months Post-treatment		21	5.98	

P value considered to be significant at P<.05 for a 95% confidence interval

Distribution of these data in the case group at their pre-treatment and 3 months post-treatment levels are shown in the Box whisker plot in Figure 3:

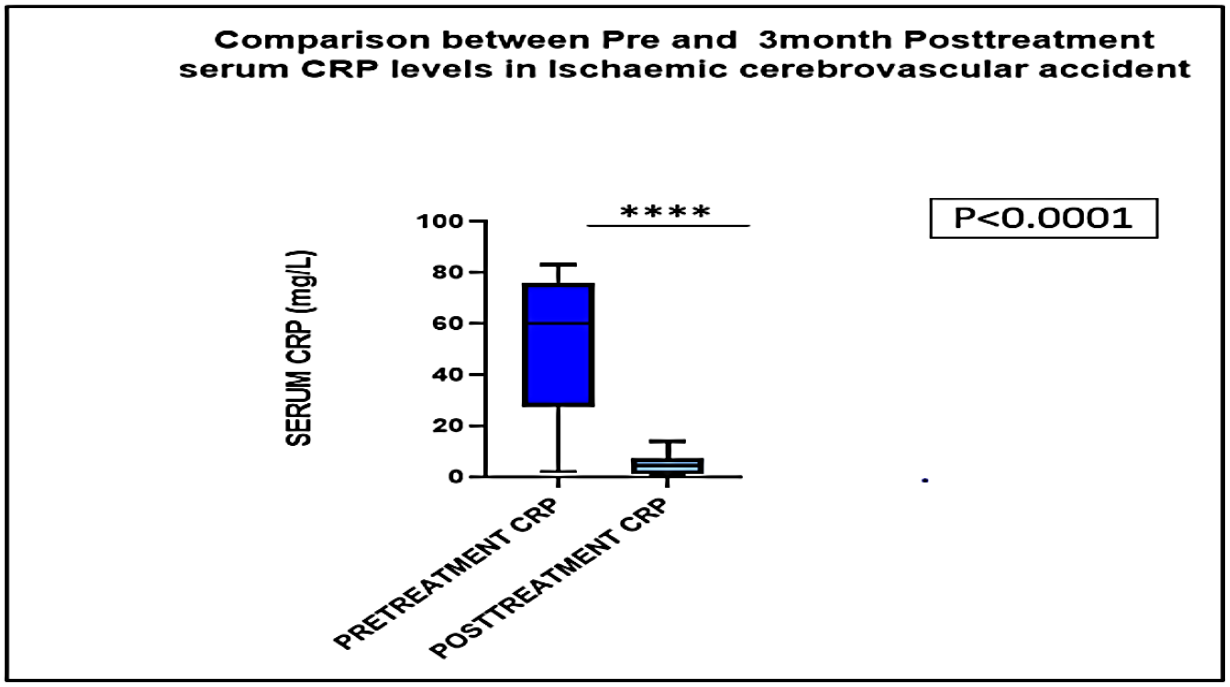

Figure 3: Box and Whisker plot showing the comparison between Pre-treatment serum CRP levels (Median = 53.06) and 3 months Post-treatment serum CRP levels (Median = 5.986) in Cases of Ischaemic cerebrovascular accident.

Comparison between serum hs-CRP (mg/L) levels in Pre-treatment and 3 months Post-treatment cases of Ischaemic cerebrovascular accident:
50 cases of clinically and radiologically (CT/MRI) diagnosed ischemic cerebrovascular accident were taken. 29 cases were found to be expired in 3 months follow up. The normality of the sample size was tested with the D'Agostino & Pearson omnibus normality test. It was observed that the data were normally distributed. So, a Paired t-test was applied to compare the serum hsCRP levels in Pre-treatment cases and 3 months Post-treatment cases of ischemic cerebrovascular accident. Results are shown in Table 4 as follows:

Table 4: Comparison of serum hs-CRP (mg/L) levels in Pre-treatment and 3 months Post-treatment Cases of Ischemic cerebrovascular accident:

		No.	Mean ± SD	P value
CRP (mg/L) Pre-treatment	Case	50	1.43 ± 0.48	<.001
CRP (mg/L) 3months Post-treatment		21	0.84 ± 0.35	

P value considered to be significant at P<.05 for a 95% confidence interval

Distribution of these data in both pre-treatment and post-treatment groups are shown in the Box whisker plot as follows:

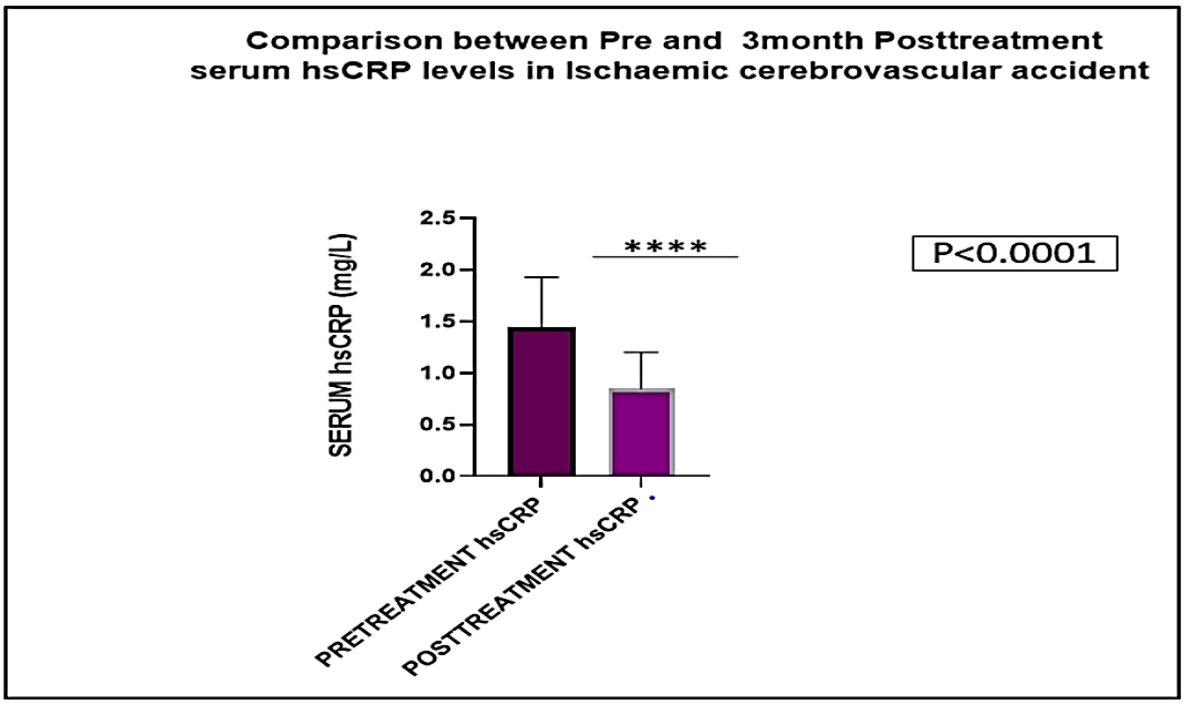

Figure 4: Box and Whisker plot showing the comparison between Pre-treatment serum hs-CRP levels and 3 months Post-treatment serum CRP levels in Cases of Ischaemic cerebrovascular accident.

Correlation of Pre-treatment and post-treatment (3 months and 6 months) serum hs-CRP levels with NIHS Scale of performance status:
After confirmation of the normal distribution of the data, Pearson's correlation study was performed to find the correlation between the pre-treatment and post-treatment (3 months and 6 months) serum hs-CRP levels with the NIHS Scale of performance status. Results are shown in Table 5 as follows:

Table 5: Correlation between pre-treatment serum hsCRP levels and post-treatment serum hsCRP levels (3 and 6 months) with NIHS Scale of performance status in cases of clinically and radiologically (CT/MRI) diagnosed ischemic cerebrovascular accident.

NIHSS Vs. serum hs-CRP (Pre-treatment)	Case	No.	Pearson Rank Order Correlation Coefficient (r)	P value
		50	0.3647	0.0092
NIHSS Vs. serum hs-CRP (3 months post-treatment)		21	0.6267	0.0024
NIHSS Vs. serum hs-CRP (6 months post-treatment)		21	0.5484	0.0101

P value considered to be significant at P<.05 for a 95% confidence interval

Data distribution of all three groups have been shown in the scatter plot as follows:

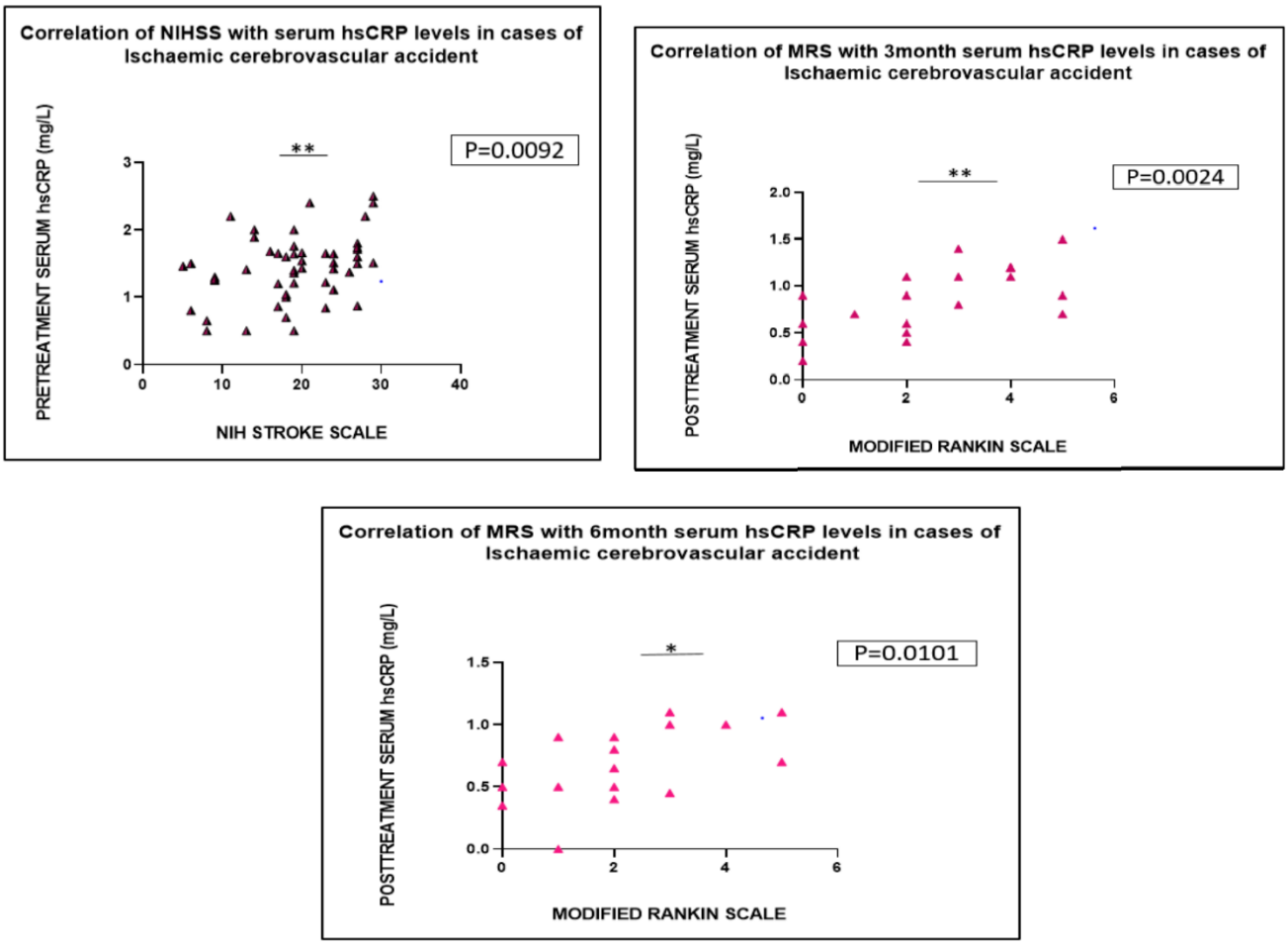

Figure 5: Scatter plots showing the correlation between pre-treatment serum hsCRP levels and post-treatment serum hsCRP levels (3 and 6 months) with NIHS Scale of performance status in cases of clinically and radiologically (CT/MRI) diagnosed ischemic cerebrovascular accident.

DISCUSSION:

Several studies have assessed the value of serum CRP level as a prognostic factor of functional outcome in the very early phase of cerebrovascular accident. These studies were either, tested only the relation between serum CRP level and mortality instead of functional outcome or small, including a selected group of patients. The findings were inconclusive as some found a positive association of serum CRP level[11, 12] but others did not[13, 14]. In this study, patients with high serum CRP levels within 72 h of ischemic cerebrovascular accident onset had a significantly increased risk of poor functional outcome or death at 3 months and 6 months, even after adjustment for potential confounders. In addition, a level-risk relationship was found between serum CRP level and poor outcome and death. Mann-Whitney U test was applied to compare the pre-treatment serum CRP levels in cases (Mean ± SD = 53.06 ± 25.65) of ischemic cerebrovascular accident as opposed to that of the age and sex-matched controls (Mean ± SD = 7.356 ± 9.821) and found to be significantly higher in pre-treatment cases than controls. 29 cases were found to be expired in 3 months follow up. Comparison between Pre-treatment serum CRP levels (Mean ± SD = 53.06 ± 25.65) and 3 months Post-treatment serum CRP levels (Mean ± SD = 5.986 ± 6.326) done. Wilcoxon Signed Rank test was applied & showed a significantly lower level of serum CRP in 3 months Post-treatment cases as compared to Pre-treatment cases. Comparison between Pre-treatment serum CRP levels (Mean ± SD = 53.06 ± 25.65) and 6 months Post-treatment serum CRP levels (Mean ± SD = 2.929 ± 2.696) done. Wilcoxon Signed Rank test was applied & showed a significantly lower level of serum CRP in 6 months Post-treatment cases as compared to Pretreatment cases[15]. A study of ischemic cerebrovascular accident patients identified admission cerebrovascular accident severity as measured by the NIH Stroke Scale (NIHSS) as the strongest predictor of 3-month mortality[16] and another one concluded that it was the only independent predictor of 30-day mortality[17]. We found in our study that the serum CRP level is a predictor for severity and outcome in ischemic cerebrovascular accidents. It was positively correlated with the NIH Stroke Scale and Modified Rankin Scale. The NIHSS was used in this study to evaluate the cerebrovascular accident severity and was developed and validated for assessing the initial cerebrovascular accident severity. Our study showed that the NIHSS is a strong predictor for poor outcomes in ischemic cerebrovascular accident patients. Spearman Rank Order Correlation test was applied to correlate between pretreatment serum CRP levels and the NIH Stroke scale on admission which showed a significant correlation of pre-treatment serum CRP levels with the NIHS scale [p value = 0.0009, r = 0.4561]. den Hertog et al. (2009)showed the relation between higher levels of CRP within 12 h onset of ischemic cerebrovascular accident and poor outcome (modified Rankin Scale score >2) or death at 3 months[18]. In our study Spearman Rank Order Correlation test was applied to correlate between 3 months Post-treatment serum CRP levels according to the Modified Rankin Scale of performance status which showed a significant correlation of 3 months Post-treatment serum CRP levels with Modified Rankin Scale [p value < 0.0001, r = 0.8085]. Spearman Rank Order Correlation test was applied to correlate between 6 months Post-treatment serum CRP levels according to the Modified Rankin Scale of performance status which showed a significant correlation of 6 months Post-treatment serum CRP levels with Modified Rankin Scale [p value < 0.0001, r = 0.9297]. Elkind et al concluded that serum

hs-CRP level, an acute phase reactant increases with cerebrovascular accident severity and may be associated with mortality to a greater extent than recurrence[19]. Chaudhuri et al. (2013) in their study found that serum hs-CRP level was significantly higher in cerebrovascular accident patients than in controls[20]. Cai et al concluded that high serum hs-CRP levels are associated with worse outcomes in acute ischemic cerebrovascular accident patients[21]. In our study, the Unpaired t-test was applied & showed a significantly higher level of serum hs-CRP (Mean ± SD = 1.439 ± 0.4881) in pretreatment cases as compared to age and sex-matched Controls (Mean ± SD = 0.4048 ± 0.2843). 29 cases were found to be expired in 3 months follow up. 99 Comparison between Pre-treatment serum hsCRP levels (Mean ± SD = 1.439 ± 0.4881) and 3 months Post-treatment serum hsCRP levels (Mean ± SD = 0.8476 ± 0.3516) in Cases Paired t-test showed significantly lower level of serum hsCRP in 3months Post-treatment cases as compared to Pre-treatment cases. Comparison between Pre-treatment serum hsCRP levels (Mean ± SD = 1.439 ± 0.4881) and 6 months Post-treatment serum hsCRP levels (Mean ± SD = 0.6576 ± 0.2888) in Cases Paired t-test also showed significantly lower level of serum hsCRP in 6months Post-treatment cases as compared to Pre-treatment cases. Peycheva et al showed that serum hs-CRP level correlated positively with the neurological assessment made by the NIH Stroke Scale and negatively with cerebrovascular accident evolution[22]. These findings support other investigations that the hs-CRP level can predict the severity of the ischemic cerebrovascular accident, the occurrence of a new cerebrovascular accident, and an unfavorable cerebrovascular accident outcome[22]. Indicula et al found that increased levels of hs-CRP were associated with cerebrovascular accident severity and mortality rate[23]. Our study showed that the pre-treatment serum hsCRP levels significantly correlated with the NIH Stroke scale [Pearson Rank Order Correlation test: p-value 0.0092, r = 0.3647]. Kumar SR et al showed that higher serum hs-CRP levels correlated with the higher Modified Rankin Scale on day 90 in ischemic cerebrovascular accidents [24]. In our study, 3 months Post-treatment serum hsCRP levels according to Modified Rankin Scale showed a significant correlation [Pearson Rank Order Correlation test: p-value = 0.0024, r = 0.6267] and 6 months Post-treatment serum hsCRP levels according to Modified Rankin Scale also showed significant correlation [Pearson Rank Order Correlation test: p-value = 0.0101, r = 0.5484]. Ischemic cerebrovascular accident is the most common type of cerebrovascular accident which accounts for about 80%–85% of cerebrovascular accident cases. Inflammation has been proposed to play an important role in the pathogenesis of acute ischemic cerebrovascular accidents over the last few decades. C-reactive protein (CRP), an acute phase reactant protein, has been the most extensively studied biomarker of inflammation in cardiovascular disease and Ischemic cerebrovascular accident. An increased level of CRP remarkably associated with the functional prognosis of acute ischemic cerebrovascular accident was observed in multiple studies[25]. Halvor et al. found that serum CRP and homocysteine levels were associated with long-term mortality in young ischemic cerebrovascular accident patients[26]. Huang et al. revealed that serum hs-CRP was related to a worse prognosis risk of all-cause death within three months after the acute ischemic cerebrovascular accident in Chinese patients[27]. To the best of our knowledge, we studied the relationship between serum biomarkers (CRP and hsCRP) and discharge outcome with 3 & 6 months follow-up of ischemic cerebrovascular accident for the first time. To prove the independent association between biomarker level and poor outcome, we strictly selected the inclusion and exclusion criteria to obtain homogenous data and to avoid potential confounding factors. The use of biomarkers as predictors of ischemic cerebrovascular accident prognosis is becoming increasingly important, as they may be valuable tools in the search for optimal management of ischemic cerebrovascular accident patients. The present study confirms results from previous studies that have advocated serum CRP and hsCRP levels as a powerful prognostic marker in patients with ischemic cerebrovascular accidents. 102 It was seen that there was a positive correlation between serum CRP levels and NIHSS values in acute ischemic cerebrovascular accident patients, which was statistically significant. This means that the higher the serum CRP level, the greater the NIHSS value, and also found a significant relation between CRP and MRS in 3 & 6 months follow-up cases. In our study, serum hsCRP levels correlated positively with the neurological assessment made by NIHSS and MRS, positively with the time of hsCRP testing, and an unfavorable ischemic cerebrovascular accident outcome.

So, measuring serum levels of hsCRP and CRP (where hsCRP is not available), would not only identify patients being at high risk but would also provide an opportunity for intervention. Similarly, we found that a high CRP level was related to the poor outcome at discharge and 3 months & 6 months follow even after adjustment for other significant co-variables.

Limitations of the study:

The present study was conducted under various time and material constraints. A longer period with more access to various nutritional and other inflammatory markers would have given a clearer picture.

REFERENCES

1.Bonita R, Beaglehole R. Stroke prevention in poor countries. Time for action. Stroke. 2007; 38:2871-2872. .

2.Pandian JD, Sudhan P. Stroke Epidemiology and Stroke Care Services in India. Stroke. 2013; 15(3):128-134.

3.Wade S. Smith, S. Claiborne Johnston, J Claude Hemphill. Cerebrovascular Diseases. Kasper DL, Hauser SL, Jameson JL et al editors. Harrison's Principles of Internal Medicine. 19th edition. New York: Publisher Mc Graw Hill Education; 2015; 2559-2565.

4.Yu B, Yang P, Xu X and Shao L. C-reactive protein for predicting all-cause mortality in patients with acute ischemic stroke: a meta-analysis. Bioscience Reports 2019; 39:1-8.

5.Chamorro A. Role of inflammation in stroke and atherothrombosis. Cerebrovasc. Dis.2004; 17:1–5.

6.Whiteley W., Chong W.L., Sengupta A. and Sandercock P. Blood markers for the prognosis of ischemic stroke: a systematic review. Stroke.2009; 40:e380– e389.

7.Chaudhuri J R, Mridula K R, Umamahesh M, Swathi A. High sensitivity C-reactive protein levels in Acute Ischemic Stroke and subtypes: A study from a tertiary care center. Ir J neurol 2013; 12(3):92-97.

8.Huang Y, Jing J, Zhao XQ, Wang CX, Wang YL, Liu GF, et al. High-sensitivity C-reactive protein is a strong risk factor for death after acute ischemic stroke among Chinese. CNS Neurosci Ther 2012; 18(3):261-6.

9.Whiteley W, Jackson C, Lewis S, et al. Association of circulating inflammatory markers with recurrent vascular events after stroke: a prospective cohort study. Stroke 2011; 42:10–6.

10.Arenillas JF, Alvarez-Sabín J, Molina CA, et al. Progression of symptomatic intracranial large artery atherosclerosis is associated with a proinflammatory state and impaired fibrinolysis. Stroke 2008; 39:1456–63.

11.Masotti L, Ceccarelli E, Forconi S, et al. Prognostic role of C-reactive protein in very old patients with acute ischaemic stroke. J Intern Med. 2005;258:145–152.

12.Montaner J, Fernandez-Cadenas I, Molina CA, et al. Post-stroke C-reactive protein is a powerful prognostic tool among candidates for thrombolysis. Stroke. 2006;37:1205-1210.

13.Topakian R, Strasak AM, Nussbaumer K, et al. Prognostic value of

admission C-reactive protein in stroke patients undergoing IV thrombolysis. J Neurol. 2008;255:1190–1196.

14.Winbeck K, Poppert H, Etgen T, et al. Prognostic relevance of early serial C-reactive protein measurements after first ischemic stroke. Stroke. 2002;33:2459-2464.

15.Zhiyou Cai, Wenbo He, Feng-Juan Zhuang. The role of high-sensitivity C-reactive protein levels at admission on poor prognosis after acute ischemic stroke. International Journal of Neuroscience. 2018;129(5):423-429.

16. Chang KC, Tseng MC, Tan TY, Liou CW. Predicting 3-month mortality among patients hospitalized for first-ever acute ischemic stroke. J Formos Med Assoc 2006;105(4):310–7.

17.Henon H, Godefroy O, Leys D, Mounier-Vehier F, Lucas C, Rondepierre P, et al. Early predictors of death and disability after an acute cerebral ischemic event. Stroke 1995;26(3):392–8.

18.den Hertog HM, van Rossum JA, van der Worp HB. C-reactive protein in the very early phase of acute ischemic stroke: association with poor outcome and death. J Neurol. 2009 Dec;256(12):2003-8.

19.Elkind MS, Tai W, Coates K, Paik MC, Sacco RL. High-sensitivity C-reactive protein, lipoprotein-associated phospholipase A2, and outcome after ischaemic stroke. Arch Intern Med. 2006;166(19):2073-80.

20.Chaudhuri JR, Mridula KR, Umamahesh M. High sensitivity C-reactive protein levels in acute ischemic stroke and subtypes: A study from a tertiary care center. Iran J Neurol. 2013;12:92-97.

21. Zhiyou Cai, Wenbo He, Feng-Juan Zhuang. The role of high-sensitivity C-reactive protein levels at admission on poor prognosis after acute ischemic stroke. International Journal of Neuroscience. 2018;129(5):423-429.

22.M. Peycheva, T. Deneva, Z. Zahariev. High-sensitive CRP in ischaemic stroke patients –from risk factors to evolution. Cesk Slov Neurol N 2019; 82(5): 549-555.

23.Idicula TT, Brogger J, Naess H, et al. Admission C-reactive protein after acute ischaemic stroke is associated with stroke severity and mortality: the Bergen stroke study. BMC Neurology 2009; 9: 18.

24.Sonal Rajesh Kumar, T. A. Vidya. High sensitivity C-reactive protein level in cerebrovascular accident. Int J Adv Med. 2020 Apr;7(4):666-672.

25.Geng HH, Wang XW, Fu RL, et al. The Relationship between C-Reactive Protein Level and Discharge Outcome in Patients with Acute Ischemic Stroke. Int J Environ Res Public Health. 201613(7): 636.

26.Naess H., Nyland H., Idicula T., Waje-Andreassen U. C-reactive protein and homocysteine predict long-term mortality in young ischemic stroke patients. J. Stroke Cerebrovasc. Dis. 2013;22: e435–e440.

27.Huang Y., Jing J., Zhao X.Q., et al. High-sensitivity C-reactive protein is a strong risk factor for death after acute ischemic stroke among Chinese. CNS Neurosci. Ther. 2012;18: 261–266.

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