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Role of C - reactive protein as a Potential Prognostic Indicator for Short-term Outcomes in Acute Stroke Patients: an Observational Study

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Abstract

Background: Stroke is a devastating disorder and a significant cause of mortality and morbidity worldwide. In India, stroke prevalence rates vary, making it a major health concern. Elevated levels of inflammatory markers, such as C-reactive protein (CRP), have been associated with an increased risk of cerebrovascular events. While CRP has been studied as a predictive marker for future cerebrovascular events, its role as a prognostic marker for functional outcomes after stroke remains less explored.

Materials and Methods: This observational analytical study was conducted at NMMC Medical College and Hospital in Navi Mumbai. A total of 30 patients with acute stroke were enrolled within 24 hours of symptom onset. Patients were categorized based on age, gender, risk factors, stroke type, and severity using NIHSS. Functional outcomes were assessed using mRS and BI scales. CRP levels were measured on admission using immunoturbidimetry. Statistical analysis was performed using SPSS.

Results: The majority of patients (53%) were in the age group of 41 to 60 years, and 63% were male. Hypertension (47%) was the most prevalent risk factor. Ischemic stroke accounted for 70% of cases. Functional outcomes indicated significant disability in 83% of patients. CRP levels were below 0.6 mg/L in 57% of cases. Correlations between CRP levels and functional outcomes were not statistically significant. However, in the hemorrhagic stroke group, CRP showed a positive correlation with stroke severity (NIHSS) and a negative correlation with functional status (BI), both statistically significant.

Conclusion: Elevated CRP levels were associated with worse outcomes, particularly in hemorrhagic strokes. CRP measurement offers promise as a potential tool in stroke management, but further research is needed to establish its clinical significance. Early identification of elevated CRP levels may aid in risk stratification and guide preventive measures to reduce the burden of stroke and cardiovascular events.

INTRODUCTION

Cerebrovascular disease, including strokes, is a common and devastating disorder, with strokes being the second most common cause of death worldwide. In India, stroke prevalence rates vary depending on the region and time of study, making it a significant cause of mortality and morbidity in the country. [1] The incidence of cerebrovascular diseases increases with age, and as the elderly population grows; the occurrence of strokes is expected to rise as well. Elderly and disabled patients are more susceptible to strokes, and old age is a strong predictor of stroke outcomes and mortality [2,3]. Two major types of strokes are haemorrhagic and ischemic, with the latter being caused by embolic and atherothrombotic factors. Inflammation plays a critical

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role in the pathophysiology of stroke, and elevated levels of inflammatory markers, such as C-reactive protein (CRP), have been associated with an increased risk of cerebrovascular events [4]. CRP is an acute marker of inflammation, and its concentration increases during inflammatory events. It binds to damaged cell membranes and contributes to inflammatory responses. Elevated CRP levels have been linked to coronary heart disease and stroke. Assessing CRP levels using high-sensitivity assays has been recommended for evaluating the risk in ischemic stroke patients. While many studies have shown that elevated CRP is a predictive marker for future cerebrovascular events, its role as a prognostic marker for functional outcomes after stroke remains less explored. The aim of this study is to evaluate the role of CRP assay within 24 hours of stroke onset as a biomarker for predicting disease severity and short-term outcomes (within 1 week). By assessing CRP levels early after the onset of stroke, this research seeks to determine its potential as a prognostic indicator for functional outcomes following a stroke.

MATERIALS AND METHODS

Study Design:

This study was conducted as an observational analytical study.

Study Site:

The study was carried out in the Department of General Medicine at NMMC Medical College and Hospital in Navi Mumbai.

Ethical Committee Approval:

Prior to commencing the study, approval was obtained from the Institutional Ethics Committee. Additionally, all enrolled subjects provided written and signed informed consent.

Study Duration:

The study was conducted over a period of 18 months from the approval of the Institutional Ethics Committee.

Sample Size:

A total of 30 study subjects were enrolled in this research.

Selection Criteria for Study Subjects:

Inclusion Criteria:

Patients who were admitted with their first-ever acute stroke within 24 hours of the onset of symptoms.

Exclusion Criteria:

Patients whose admission occurred more than 24 hours after the onset of stroke symptoms.

Individuals with a recent history of traumatic brain injury, acute coronary syndrome, cerebrovascular events, autoimmune diseases, liver cell failure, and chronic renal failure were excluded from the study.

Method:

Patients admitted to the current tertiary healthcare institute within 24 hours of their first-ever acute stroke were included in the study. The diagnosis of stroke was established based on history, clinical examination, laboratory investigations, and brain CT scan. After excluding patients based on the exclusion criteria, the remaining subjects underwent history taking, clinical examination, and laboratory investigations as per the pre-validated case record proforma. Neurological evaluations were conducted for all patients, and stroke severity at admission was assessed using the National Institute of Health Stroke Scale (NIHSS). The stroke was categorized as mild (NIHSS 0–7), moderate (NIHSS 8–14), or severe (NIHSS >14). Blood samples were collected from the patients on admission for routine laboratory tests and CRP level assay. Three millilitres of venous blood were obtained through venipuncture and sent coded with the patient's number to the laboratory to maintain blinding. The CRP assay was performed using the immunoturbidimetry method, and the normal reference level of CRP in the laboratory was up to 0.60 mg/L.

Statistical Analysis:

Data collection was done using a standard, semi-structured, pre-validated case record proforma and entered into MS Excel software. Statistical analysis was performed using the professional

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statistical Package for Social Science (SPSS). Quantitative data were described as mean (± SD), while qualitative data were presented as frequency and proportion. Pearson correlation coefficient (r) was used to assess the correlation between variables, and the correlation was evaluated based on the r values, ranging from -1 to +1.
Results with a p-value less than or equal to 0.05 were considered statistically significant.

RESULTS

Demographic Characteristics:

The study included a total of 30 patients with acute stroke, and they were categorized into different age groups. The majority of patients (53%) fell into the age group of 41 to 60 years, followed by 23% in the age group of 61 to 80 years. Patients aged 20 to 40 years accounted for 17% of the cases, while those above 80 years constituted 7%. In terms of gender, 63% were male, and 37% were female.

Risk Factors:

Hypertension was the most prevalent risk factor, present in 47% of the cases. Diabetes mellitus was reported in 23% of patients and 10% had coronary artery disease (CAD). However, no cases of atrial fibrillation were observed in the study. Left ventricular hypertrophy (LVH) was present in 30% of the patients.

Stroke Types:

Among the total cases, 70% had ischemic stroke, while 30% experienced hemorrhagic stroke.

Severity Assessment:

The National Institute of Health Stroke Scale (NIHSS) was used to assess stroke severity. Among the patients, 27% had mild strokes (NIHSS 0-7), 27% had moderate strokes (NIHSS 8-14), and 47% had severe strokes (NIHSS >14).

Functional Outcomes:

The Modified Rankin Scale (mRS) was utilized to assess functional outcomes. The majority of patients (83%) had a mRS score greater than 2, indicating significant disability, while only 17% had a mRS score less than 2, indicating a relatively favorable outcome. The Barthel Index (BI) was also used to assess functional status, with 90% of patients having a BI score less than 95, indicating significant dependence on activities of daily living.

CRP Levels:

C-reactive protein (CRP) levels were measured as a marker of inflammation. Among all cases, 57% had CRP levels less than 0.6 mg/L, while 43% had CRP levels higher than 0.6 mg/L.

End Points:

At the end of the study period, 87% of the patients were discharged; indicating improvement in their condition, while 13% of patients experienced mortality during their hospital stay.

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Table 1: Age distribution of patients

Age Group	Ischemic Stroke	Hemorrhagic Stroke	Total
20 to 40 years	4 (18%)	1 (13%)	5 (17%)
41 to 60 years	12 (55%)	4 (50%)	16 (53%)
61 to 80 years	5 (23%)	2 (25%)	7 (23%)
81 years & above	1 (5%)	1 (13%)	2 (7%)
Total	22 (100%)	8 (100%)	30 (100%)

Table 2: Sex distribution of patients

Gender	Ischemic Stroke	Hemorrhagic Stroke	Total
Male	14 (64%)	5 (63%)	19 (63%)
Female	8 (36%)	3 (38%)	11 (37%)
Total	22 (100%)	8 (100%)	30 (100%)

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Table 3: Distribution of Risk Factors

Risk Factors	Ischemic Stroke	Hemorrhagic Stroke	Total
Hypertension	9 (41%)	5 (63%)	14 (47%)
Diabetes Mellitus	6 (27%)	1 (13%)	7 (23%)
Coronary Artery Disease	2 (9%)	1 (13%)	3 (10%)
Atrial Fibrillation	0 (0%)	0 (0%)	0 (0%)
Left Ventricular Hypertrophy	5 (23%)	4 (50%)	9 (30%)
Total	22 (100%)	8 (100%)	30 (100%)

It is observed that there is negligible correlation in NIHSS and CRP, mRS and CRP & BI and CRP when all patients are taken into consideration and all correlations are insignificant. In the Ischemic group of patient there is negligible negative correlation between NIHSS and CRP but is insignificant, also there is very poor correlation between mRS and CRP as well as BI and CRP which are also statistically not significant. In haemorrhage group there is high degree of correlation between NIHSS an CRP while there is strong negative correlation between BI and CRP an both are statistically significant, also mRS and CRP has negative correlation but is insignificant. Table 4

Patients	Correlation between	Correlation value	p - value
TOTAL	**NIHSS vs CRP**	0.03	0.87
mRS vs CRP	0.13	0.49	
BI vs CRP	0.05	0.79	
ISCHEMIC group	**NIHSS vs CRP**	-0.0083	0.9
mRS vs CRP	0.20	0.17	
BI vs CRP	0.19	0.46	
HAEMORRHAGE group	**NIHSS vs CRP**	0.88	<0.05
mRS vs CRP	-0.35	0.06	
BI vs CRP	-0.82	<0.05	

DISCUSSION

Stroke is a leading cause of disability in both developing and developed countries, and early identification of biomarkers for predicting disease severity and short-term outcomes is crucial for better management and prognosis [5-8]. In this study, C-reactive protein (CRP) was evaluated as a potential biomarker for predicting stroke severity and short-term outcomes. The inflammatory response plays a central role in the initiation, development, and rupture of atherosclerotic plaques, which are a common cause of stroke. The recruitment of immune cells, such as macrophages and T-cells, into the plaques leads to the secretion of various inflammatory mediators, promoting plaque rupture and thrombosis. Additionally, brain damage caused by ischemic or hemorrhagic stroke stimulates the mobilization and migration of immune cells into the brain, leading to a systemic inflammatory response [9]. The study found that the majority of patients were in the age group of 41 to 60 years, consistent with previous studies showing a higher prevalence of stroke in middle-aged individuals. The male-to-female ratio was approximately 1.72:1, which aligns with other stroke studies that have reported a higher incidence in males. Hypertension was the most common risk factor observed in 47% of the cases, followed by diabetes mellitus in 23% of patients. The coexistence of hypertension and diabetes was found to significantly increase the risk of stroke, consistent with previous studies showing the combined effect of these risk factors. The

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study showed that 30% of patients had LVH, which is an indicator of cardiac involvement and potential risk for stroke. However, none of the cases had atrial fibrillation, which is known to be a major risk factor for stroke. The NIHSS and mRS were used to assess stroke severity and functional outcomes, respectively. The majority of patients had moderate to severe strokes, and a significant proportion had functional disabilities, indicating the impact of stroke on patients' daily living activities. CRP levels were measured as a marker of inflammation, and the study found that 57% of patients had CRP levels below 0.6 mg/L, while 43% had levels above 0.6 mg/L. The CRP levels were found to be positively correlated with stroke severity in the hemorrhagic stroke group, indicating a potential association between inflammation and stroke outcomes. The correlations between CRP levels and functional outcomes (mRS and BI) were not statistically significant, indicating that CRP alone may not be a strong predictor of functional recovery. However, the study observed a higher degree of correlation between CRP and stroke severity (NIHSS) in the hemorrhagic stroke group, suggesting that inflammation may play a more significant role in the pathophysiology of hemorrhagic strokes [10]. The findings of this study are consistent with previous research showing that CRP levels are elevated in the acute phase of stroke and may be associated with worse outcomes. CRP has been implicated in secondary brain damage after focal cerebral ischemia and may contribute to a complex cascade of cerebral and systemic inflammatory responses following intracerebral hemorrhage [5-7].

CONCLUSIONS

In conclusion, this study highlights the potential role of CRP as a biomarker for predicting stroke severity and short-term outcomes. Elevated CRP levels were associated with worse outcomes, particularly in hemorrhagic strokes. However, further research is needed to fully understand the relationship between CRP and stroke outcomes, and the utility of CRP as a predictive marker in clinical practice. Early identification of patients with elevated CRP levels may help in tailoring individualized treatment strategies and provide a valuable indicator for predicting future atherosclerotic events. Routine CRP screening, especially in high-risk populations, may aid in risk stratification and guide preventive measures to reduce the burden of stroke and other cardiovascular events. Overall, CRP measurements offer promise as a potential tool in stroke management, but additional studies with larger sample sizes and long-term follow-up are warranted to establish its clinical significance fully.

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