

C-Reactive Protein at Admission as a Prognostic Marker of Severity and Mortality in Acute Ischemic Stroke: A Cross-Sectional Study**M. Saurav¹, Sneha R.², Rashmi G. K.³**¹Senior Resident, MBBS, MD (General Medicine)²Assistant Professor, MBBS, MD (General Medicine), DNB (General Medicine)³Assistant Professor, Department of Microbiology, Subbaiah Institute of Medical Sciences

Received: 01-03-2026 / Revised: 15-04-2026 / Accepted: 21-05-2026

Corresponding author: Dr. Sneha R

Conflict of interest: Nil

Abstract

Background: Acute ischemic stroke (AIS) is an important cause of mortality and long-term neurological disability. Inflammation plays an integral role in the pathophysiology of cerebral ischemia, and C-reactive protein (CRP), an acute-phase reactant, may reflect the magnitude of systemic inflammatory activation and tissue injury following stroke. The identification of readily available biochemical markers capable of predicting neurological severity and mortality may facilitate early risk stratification.

Aim: To evaluate admission serum CRP as a prognostic marker of neurological severity and mortality among patients with acute ischemic stroke.

Materials and Methods: This cross-sectional study included 115 adult patients with symptomatic acute ischemic stroke admitted to the Department of General Medicine, McGann District Hospital, Shivamogga, between June 2023 and June 2024. Patients with hemorrhagic stroke, pregnancy or lactation, anemia, and inflammatory or neoplastic conditions capable of increasing CRP and ferritin were excluded. Venous blood samples were obtained at admission, and CRP was measured by turbidimetry. Stroke severity at discharge was assessed using the National Institutes of Health Stroke Scale (NIHSS). Data were analyzed using SPSS version 26.

Results: The mean age was 49.39 ± 14.10 years, and 63.48% of participants were male. At discharge, 67.83% had moderate stroke (NIHSS 5–15), 21.74% had moderate-to-severe stroke, and 5.22% each had mild and severe stroke. Mean admission CRP increased progressively with neurological severity: 42.30 ± 14.06 mg/L in minor, 80.39 ± 27.24 mg/L in moderate, 192.67 ± 35.16 mg/L in moderate-to-severe, and 351.77 ± 97.83 mg/L in severe stroke ($p < 0.0001$). CRP showed a strong positive correlation with NIHSS ($r = 0.99$, $p = 0.01$). Mortality increased with increasing CRP, reaching 66.67% among patients in the highest CRP/severity group.

Conclusion: Elevated CRP at admission was strongly associated with greater neurological severity and mortality in acute ischemic stroke. Admission CRP may therefore serve as a simple and clinically useful adjunct for early prognostic stratification.

Keywords: Acute ischemic stroke; C-reactive protein; CRP; NIHSS; mortality; prognosis; inflammation.

DOI: 10.25258/ijcpr.18.6.434

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Stroke remains one of the major causes of death and disability worldwide and imposes substantial clinical, social, and economic burdens.[1] It is characterized by the sudden onset of neurological dysfunction resulting from a vascular cause.[2] Ischemic stroke accounts for the majority of acute stroke events and occurs when cerebral blood flow is interrupted because of arterial thrombosis, embolism, or other mechanisms that compromise cerebral perfusion.[3] The pathological consequences of cerebral ischemia extend beyond the initial interruption of blood supply. Energy failure, excitotoxicity, intracellular calcium

accumulation, oxidative stress, disruption of the blood-brain barrier, activation of glial cells, leukocyte infiltration, and inflammatory signaling contribute to progressive neuronal injury.[4,5] The ischemic core undergoes rapid and largely irreversible cellular injury, whereas the surrounding penumbra contains potentially viable tissue that may be rescued if perfusion is restored promptly.[5] Inflammation is particularly important in determining the progression and clinical consequences of ischemic brain injury. Ischemia induces the release of inflammatory cytokines and acute-phase proteins and promotes leukocyte

recruitment and endothelial activation.[6] Consequently, circulating inflammatory biomarkers have been investigated for their potential ability to supplement clinical assessment and predict stroke outcomes.

C-reactive protein (CRP) is an acute-phase protein synthesized predominantly by hepatocytes in response to inflammatory stimuli, particularly cytokine-mediated stimulation.[7] Although CRP is a nonspecific inflammatory biomarker, elevated concentrations have been associated with cardiovascular and cerebrovascular disease. In ischemic stroke, CRP may reflect both the systemic inflammatory response and the magnitude of tissue injury. Previous investigations have demonstrated relationships between elevated CRP and greater stroke severity, larger infarct volume, adverse functional outcomes, and mortality.[8-10] Den Hertog et al. reported that CRP measured during the early phase of acute ischemic stroke was associated with poor outcome and death.[9] Bian et al. similarly demonstrated that CRP may have prognostic value for clinical outcomes following acute ischemic stroke.[8]

The National Institutes of Health Stroke Scale (NIHSS) provides a standardized quantitative assessment of neurological impairment and is widely employed to classify stroke severity and assist prognostication. Nevertheless, combining clinical severity scores with accessible biochemical markers may potentially strengthen early risk stratification. There remains a relative paucity of regional Indian data evaluating CRP as a prognostic marker in acute ischemic stroke. The present study therefore evaluated the relationship between serum CRP measured at hospital admission, NIHSS-defined neurological severity at discharge, and mortality among patients with acute ischemic stroke.

Materials and Methods

Study design and setting: A hospital-based cross-sectional study was conducted in the Department of General Medicine, McGann District Hospital, Shivamogga, Karnataka, over one year from June 2023 to June 2024.

Study population: The study included 115 patients diagnosed with symptomatic acute ischemic stroke and admitted during the study period. The minimum sample size was calculated using parameters derived from previous studies, including a standard deviation of 2.8, relative precision of 0.40, and alpha error of 5%.

Inclusion criteria: Adult patients presenting with symptomatic acute ischemic stroke during the study period and providing informed written consent were included.

Exclusion criteria: Patients younger than 18 years, pregnant or lactating women, and patients with hemorrhagic stroke were excluded. Patients with inflammatory or neoplastic disorders capable of independently elevating CRP or serum ferritin were also excluded. Anemic patients, defined as hemoglobin <13 g/dL in males and <12 g/dL in females, were excluded.

Clinical evaluation: After enrollment, demographic characteristics and relevant clinical information were documented using a standardized proforma. A detailed history and neurological examination were undertaken. Information regarding established vascular risk factors, including hypertension, diabetes mellitus, ischemic heart disease, smoking, and alcohol consumption, was recorded. Routine investigations included complete blood count, renal and liver function tests, fasting lipid profile, random blood glucose, electrocardiography, two-dimensional echocardiography, serum CRP, and serum ferritin. Neuroimaging included non-contrast computed tomography of the brain. Magnetic resonance imaging with magnetic resonance angiography and carotid Doppler examinations were performed when clinically indicated.

CRP measurement: Venous blood was obtained at admission. Serum CRP was measured using an instrument based on the principle of turbidimetry.

Assessment of stroke severity: Neurological impairment was evaluated using the National Institutes of Health Stroke Scale at discharge. NIHSS scores were classified as minor (1–4), moderate (5–15), moderate-to-severe (16–20), and severe (21–42).

Outcome measures: The principal outcome was the relationship between admission CRP and NIHSS-defined stroke severity at discharge. Mortality during the study period was additionally examined in relation to admission CRP.

Statistical analysis: Data were entered into Microsoft Excel and analyzed using SPSS version 26. Percentages and proportions were calculated for categorical variables. Appropriate inferential statistical tests were applied to evaluate relationships between CRP, stroke severity, and clinical outcome. A p-value <0.05 was considered statistically significant.

Ethical considerations: The study was undertaken after approval from the Institutional Ethics Committee. Written informed consent was obtained from enrolled participants.

Results

A total of 115 patients with acute ischemic stroke were evaluated.

Table 1: Baseline characteristics of the study population

Characteristic	Number	Percentage
Age 18–30 years	18	15.65
Age 31–40 years	10	8.70
Age 41–50 years	24	20.87
Age 51–60 years	31	26.96
Age >60 years	32	27.83
Male	73	63.48
Female	42	36.52
Hypertension	52	45.22
Diabetes mellitus	34	29.57
Ischemic heart disease	25	21.74
Smoking	40	34.78
Alcohol addiction	12	10.43

The mean age was 49.39 ± 14.10 years. Patients older than 60 years constituted the largest age group (27.83%). Males represented 63.48% of the study population. Hypertension was the most frequent associated risk factor, occurring in 45.22%, followed by smoking (34.78%) and diabetes mellitus (29.57%).

Table 2: NIHSS severity at discharge

NIHSS category	Number	Percentage
Mild (<5)	6	5.22
Moderate (5–15)	78	67.83
Moderate-to-severe (16–20)	25	21.74
Severe (21–42)	6	5.22
Mean $\pm$ SD	11.87 $\pm$ 2.13	—

Moderate neurological impairment was the predominant category, accounting for 67.83% of participants. The mean discharge NIHSS was 11.87 ± 2.13 .

Table 3: Admission CRP according to NIHSS severity

NIHSS severity	Admission CRP, mean $\pm$ SD
Minor (1–4)	42.30 $\pm$ 14.06 mg/L
Moderate (5–15)	80.39 $\pm$ 27.24 mg/L
Moderate-to-severe (16–20)	192.67 $\pm$ 35.16 mg/L
Severe (21–42)	351.77 $\pm$ 97.83 mg/L
p-value	<0.0001

A pronounced stepwise increase in CRP was observed with increasing stroke severity. Severe strokes demonstrated approximately eight times the mean CRP observed in minor stroke. The relationship between CRP concentration and NIHSS severity was statistically significant ($p < 0.0001$).

Table 4: Admission CRP and mortality

CRP level, mean $\pm$ SD	Survived n (%)	Death n (%)
42.30 $\pm$ 14.06	6 (100%)	0
80.39 $\pm$ 27.24	78 (100%)	0
192.67 $\pm$ 35.16	23 (92%)	2 (8%)
351.77 $\pm$ 97.83	2 (33.33%)	4 (66.67%)

No deaths occurred among patients belonging to the two lower CRP/severity categories. Mortality was 8% in the 192.67 $\pm$ 35.16 mg/L group and increased to 66.67% in patients with the highest CRP levels. Overall, 109 patients (94.78%) survived and 6 (5.22%) died.

Table 5: Correlation between NIHSS and CRP

Parameter	Value
Correlation coefficient (r)	0.99
p-value	0.01

A very strong positive correlation was reported between CRP and NIHSS score ($r = 0.99$, $p = 0.01$), indicating increasing CRP concentrations with increasing neurological severity.

Discussion

The present study demonstrated a strong relationship between admission CRP concentration

and subsequent neurological severity in patients with acute ischemic stroke. CRP progressively increased from 42.30 ± 14.06 mg/L among patients with minor stroke to 351.77 ± 97.83 mg/L among those classified as severe. The difference across severity groups was statistically significant ($p < 0.0001$), and CRP showed a strong positive correlation with NIHSS score. These observations support the concept that inflammation constitutes an important component of ischemic brain injury. Cerebral ischemia initiates a complex inflammatory cascade characterized by endothelial activation, cytokine release, leukocyte recruitment, oxidative stress, and blood-brain barrier dysfunction.[4-6] CRP is synthesized predominantly in response to inflammatory cytokine stimulation and may consequently provide an indirect measure of the magnitude of this inflammatory response.

Bian et al. evaluated CRP as a potential predictor of outcome following acute ischemic stroke and reported that elevated CRP within the early period after stroke was associated with unfavorable functional outcomes.[8] Their observations support the present finding that higher CRP concentrations are associated with greater neurological impairment. Den Hertog et al. similarly demonstrated an association between CRP measured during the very early phase of acute ischemic stroke and both poor outcome and death.[9] This is clinically relevant because CRP is readily measurable, inexpensive, and routinely available in most hospital laboratories.

The findings are also consistent with the observations of Shoaeb et al., who reported a positive relationship between CRP and NIHSS. Their study demonstrated significantly greater CRP concentrations among patients with severe stroke compared with patients with mild-to-moderate neurological impairment.[10] The direction of association is therefore consistent with the marked stepwise rise in CRP observed across NIHSS categories in the present study.

An important observation was the relationship between CRP and mortality. No deaths occurred in the two lowest CRP/severity categories, whereas mortality reached 8% among patients with CRP of 192.67 ± 35.16 mg/L and 66.67% among those with CRP of 351.77 ± 97.83 mg/L. Ghabaee et al. previously evaluated CRP for prediction of early mortality after ischemic stroke and demonstrated its prognostic relevance alongside the NIHSS.[11] CRP should nevertheless not be interpreted as a stroke-specific biomarker. Infection, inflammatory disease, malignancy, tissue injury, and several other disorders may elevate its concentration. The exclusion of patients with recognized inflammatory and neoplastic disorders in the present study helped reduce some potential confounding.

The study has limitations. It was conducted at a single tertiary-care institution with a relatively modest sample of 115 patients. Its cross-sectional design restricts causal interpretation, and longer-term functional outcomes were not assessed. Furthermore, CRP is a nonspecific inflammatory marker, and residual confounding cannot be completely excluded. Despite these limitations, the consistent increase in CRP across NIHSS categories and its association with mortality indicate that admission CRP could provide useful supplementary prognostic information alongside conventional neurological assessment.

Conclusion

Admission C-reactive protein was significantly associated with neurological severity and mortality among patients with acute ischemic stroke. CRP concentrations increased progressively from minor to severe stroke and demonstrated a strong positive relationship with NIHSS scores. Patients with markedly elevated CRP also experienced substantially greater mortality. CRP is inexpensive, widely available, and rapidly measurable and may therefore serve as a useful adjunct to clinical severity assessment for early risk stratification of acute ischemic stroke. Larger prospective multicenter studies with serial CRP measurements and long-term functional outcome assessment are required to establish its independent prognostic value.

References

1. Donkor ES. Stroke in the 21st century: a snapshot of the burden, epidemiology, and quality of life. *Stroke Res Treat.* 2018;2018:3238165. doi:10.1155/2018/3238165.
2. Sacco RL, Kasner SE, Broderick JP, et al. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2013;44(7):2064-2089. doi:10.1161/STROKE.0b013e318296aeca.
3. Bamford J, Sandercock P, Dennis M, Burn J, Warlow C. Classification and natural history of clinically identifiable subtypes of cerebral infarction. *Lancet.* 1991;337(8756):1521-1526.
4. Smith CJ, Emsley HC, Gavin CM, et al. Peak plasma interleukin-6 and other peripheral markers of inflammation in the first week of ischaemic stroke correlate with brain infarct volume, stroke severity and long-term outcome. *BMC Neurol.* 2004;4:2. doi:10.1186/1471-2377-4-2.
5. Donkor ES. Stroke in the 21st century: a snapshot of the burden, epidemiology, and quality of life. *Stroke Res Treat.* 2018;2018:3238165.

6. Tohgi H, Konno S, Takahashi S, Koizumi D, Kondo R, Takahashi H. Activated coagulation/fibrinolysis system and platelet function in acute thrombotic stroke patients with increased C-reactive protein levels. *Thromb Res.* 2000;100:373-379. doi:10.1016/S0049-3848(00)00356-X.
7. Bian J, Guo S, Huang T, Li X, Zhao S, Chu Z, Li Z. CRP as a potential predictor of outcome in acute ischemic stroke. *Biomed Rep.* 2023;18(2):17. doi:10.3892/br.2023.1599.
8. Bian J, Guo S, Huang T, Li X, Zhao S, Chu Z, Li Z. CRP as a potential predictor of outcome in acute ischemic stroke. *Biomed Rep.* 2023;18(2):17. doi:10.3892/br.2023.1599.
9. den Hertog HM, van Rossum JA, van der Worp HB, van Gemert HM, de Jonge R, Koudstaal PJ, Dippel DW. C-reactive protein in the very early phase of acute ischemic stroke: association with poor outcome and death. *J Neurol.* 2009;256(12):2003-2008. doi:10.1007/s00415-009-5228-x.
10. Shoaeb MA, Shehata MA, Taema KM, Hammouda MA. CRP in cerebrovascular stroke: prognostic implications. *Egypt J Crit Care Med.* 2014;2(1):43-52.
11. Ghabaee M, Zandieh A, Mohebbi S, Fakhri M, Sadeghian H, Divani F, et al. Predictive ability of C-reactive protein for early mortality after ischemic stroke: comparison with NIHSS score. *Acta Neurol Belg.* 2014;114:41-45. doi: 10.1007/s13760-013-0238-y.