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Correlation between High-Sensitivity C-Reactive Protein Levels with Cognitive Function and Clinical Outcome in Acute Ischemic Stroke Patients

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KEYWORDS

Ischemic stroke; hs-CRP; inflammation; cognitive impairment; MoCA-INA; biomarker

ABSTRACT:

Introduction: Inflammation plays a critical role in the pathophysiology of ischemic stroke. High-sensitivity C-reactive protein (hs-CRP) is a biomarker of systemic inflammation that may reflect neuronal injury and predict neurological outcomes. However, the relationship between hs-CRP levels, cognitive impairment, and functional outcomes in acute ischemic stroke remains unclear.

Objectives: To evaluate the correlation between serum hs-CRP levels, cognitive function, and clinical outcomes in patients with acute ischemic stroke.

Methods: This observational cross-sectional study was conducted at Dr. Wahidin Sudirohusodo Hospital and affiliated hospitals in Makassar between December 2025 and February 2026. Sixty-four patients with acute ischemic stroke (onset 1–7 days) were recruited using consecutive sampling. Serum hs-CRP levels were measured using enzyme-linked immunosorbent assay (ELISA). Cognitive function was assessed using the Montreal Cognitive Assessment Indonesian version (MoCA-INA), and functional outcomes were evaluated using the modified Rankin Scale (mRS). Correlation analysis between hs-CRP levels and clinical parameters was performed using Spearman correlation.

Results: The mean age of participants was 57.91 ± 9.41 years, and 54.7% were male. The median hs-CRP level was 166.99 pg/mL, and the median mRS score was 2 (range 1–5 Spearman correlation analysis demonstrated a strong negative correlation between hs-CRP levels and MoCA-INA scores ($r = -0.638$; $p < 0.001$). However, no significant correlation was observed between hs-CRP levels and mRS scores ($p = 0.817$).

Conclusions: Elevated hs-CRP levels were significantly associated with poorer cognitive function in patients with acute ischemic stroke but were not associated with functional outcomes measured by the modified Rankin Scale.

1. Introduction

Stroke remains one of the leading causes of mortality and long-term disability worldwide. Approximately 15 million individuals experience stroke each year. with stroke deemed the second-leading cause of death globally [1,2]. The burden of stroke has increased substantially over the last three decades, particularly in low- and middle-income countries [1].

Ischemic stroke accounts for approximately 70–85% of all stroke cases and results from occlusion of cerebral arteries, leading to reduced cerebral blood flow and neuronal injury [3]. The resulting ischemia initiates a cascade of pathophysiological processes, including

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excitotoxicity, oxidative stress, apoptosis, and inflammatory responses [4]. Inflammation has been recognized as a key contributor to secondary neuronal injury following ischemic stroke. Cerebral ischemia triggers activation of microglia and astrocytes, which release pro-inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and interleukin-1β (IL-1β). These cytokines stimulate hepatic synthesis of acute-phase proteins, including C-reactive protein (CRP) [5]. High-sensitivity C-reactive protein (hs-CRP) is a sensitive biomarker used to detect low-grade systemic inflammation. Elevated hs-CRP levels have been associated with increased risk of cardiovascular and cerebrovascular diseases and may serve as a prognostic marker in ischemic stroke [6,7].

Post-stroke cognitive impairment is a frequent complication affecting approximately 30–60% of stroke survivors [8]. Cognitive deficits may involve attention, executive function, memory, language, and visuospatial abilities, which significantly affect quality of life and functional independence.

Although several studies have suggested that inflammatory processes contribute to cognitive impairment following stroke, the relationship between hs-CRP levels, cognitive function, and clinical outcomes in acute ischemic stroke patients remains inconsistent. Therefore, this study aimed to evaluate the association between hs-CRP levels, cognitive function assessed using MoCA-INA, and functional outcomes assessed using the modified Rankin Scale.

2. Objectives

This study aimed to determine the association between high-sensitivity C-reactive protein (hs-CRP) levels and cognitive function, as assessed by the Montreal Cognitive Assessment Indonesian version (MoCA-Ina), as well as clinical outcomes, measured by the Modified Rankin Scale (mRS), in patients with acute ischemic stroke.

3. Methods

Study Design and Setting

This study was an observational analytic study using a cross-sectional design. The study was conducted at Dr. Wahidin Sudirohusodo Hospital, a tertiary referral center in Makassar, Indonesia, and at several affiliated teaching hospitals within the Hasanuddin University medical network. Data collection was conducted between December 2025 and February 2026.

Participants

Patients diagnosed with acute ischemic stroke who were admitted to the neurology wards during the study period were screened for eligibility. Participants were recruited using a consecutive sampling method, in which all eligible patients who met the inclusion criteria were included until the required sample size was achieved.

Eligible participants were patients aged between 18 and 70 years who were diagnosed with a first-ever acute ischemic stroke with symptom onset between 1 and 7 days prior to hospital admission. The diagnosis of ischemic stroke was established based on clinical neurological examination and confirmed through neuroimaging studies, including non-contrast computed tomography (CT) scan or magnetic resonance imaging (MRI).

Patients were excluded if they had conditions that could influence systemic inflammatory markers or interfere with cognitive assessment. Exclusion criteria included chronic heart failure, malignancy, active infection, severe liver disease, and autoimmune disorders. Patients who declined participation or withdrew consent during the study were also excluded.

hs-CRP measurement

After informed consent was obtained, venous blood samples were collected for measurement of hs-CRP levels. Approximately 5 mL of venous blood was collected, centrifuged, and analyzed using a commercially available ELISA kit (Elabscience®, USA. Catalog No: E-EL-H5134) according to the manufacturer's protocol. Laboratory analysis was performed at the Hasanuddin University Medical Research Center (HUMRC) laboratory.

Cognitive and Functional Outcome Assessment

Cognitive function was evaluated using the Montreal Cognitive Assessment Indonesian version (MoCA-INA). The MoCA-INA is a validated cognitive screening tool designed to detect mild cognitive impairment across multiple cognitive domains, including executive function, memory, attention, language, visuospatial ability, abstraction, and orientation[9]. The MoCA-INA assessment was administered by trained physicians during the acute phase of stroke admission. Scores

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ranged from 0 to 30, with higher scores indicating better cognitive performance[10,11].

Functional outcomes were assessed on the 7th day after onset using the modified Rankin Scale (mRS), which is widely used to measure disability and functional independence in stroke patients. The mRS scale ranges from 0 to 6, where 0 indicates no symptoms, and 6 represents death [12]. Additional demographic and clinical variables were also collected, including age, sex, hypertension, diabetes mellitus, smoking history, lesion location, and hemispheric involvement based on neuroimaging findings.

Statistical Analysis

All data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 25. Continuous variables were presented as medians with interquartile ranges, depending on the distribution of the data. Categorical variables were presented as frequencies and percentages.The Kolmogorov–Smirnov test was used to assess the normality of data distribution. The relationship between hs-CRP levels and clinical outcomes was analyzed using Spearman's rank correlation analysis. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations

This study was approved by the Biomedical Research Ethics Committee of the Faculty of Medicine, Hasanuddin University (Ethical Approval No. 213/UN.4.6.4.5.31/PP36/2026). All participants or their legal guardians provided written informed consent before participation. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.

4. Results

A total of 64 patients with acute ischemic stroke were included in this study (Table 1). The mean age of participants was 57.91 ± 9.41 years, indicating that most patients were in the middle-aged to older adult group. Male patients slightly predominated, accounting for 35 individuals (54.7%), while female patients accounted for 29 individuals (45.3%). Regarding vascular risk factors, hypertension was the most common comorbidity observed in this population, present in 38 patients (59.4%). Diabetes mellitus was reported in 13 patients (20.3%), and a history of smoking was identified in 18 patients (28.1%). These findings are consistent with established epidemiological data identifying hypertension and metabolic disorders as major contributors to ischemic stroke.

Table 1Demographic and Clinical Characteristics of Research Subjects

Variables	Category	Total (n=64)	Percentage (%)
Gender	Male	35	54.7
	Female	29	45.3
History of hypertension	Yes	38	59.4
	No	26	40.6
History of diabetes mellitus	Yes	13	20.3
	No	51	79.7
Medical history heart	Yes	7	10.9
	No	57	89.1
Smoking history	Yes	18	28.1
	No	46	71.9
Involvement Hemisphere cerebral	Right	26	43.8
	Left	28	40.6
	Bilateral	10	15.6
Location of lesion	Cortical	20	31.3
	Subcortical	34	53.1
	Mixed	10	15.6

Based on neuroimaging findings, the majority (n = 34, 53.1%) of lesions were located in the subcortical region. Cortical lesions were identified in 20 patients (31.3%), while mixed cortical–subcortical lesions were found in 10 patients (15.6%). In terms of hemispheric involvement, the left hemisphere was affected in 28 patients (43.8%), the right hemisphere in 26 patients (40.6%), and bilateral involvement was observed in 10 patients (15.6%).

Table 2. The hs -CRP Level Among Ischemic Stroke Subjects

	N	Median	Min	Max

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hs -CRP (pg /ml)	64	166.9	7.72	606.5

The distribution of serum hs-CRP levels among patients with acute ischemic stroke showed considerable variability. The median value of the hs-CRP level was 166.9 pg/mL, with a range of 7.72–606.5 pg/mL, indicating heterogeneity in inflammatory responses among patients (Table 2). These findings suggest that systemic inflammatory activity varies substantially in the acute phase of ischemic stroke.

In this study, the median Modified Rankin Scale (mRS) score in the ischaemic stroke group was 2, with a range of 1 to 5. The MoCA-INA score, as a parameter of cognitive function, showed a median value of 22.5, with a range of 8 to 30, in the ischemic stroke group. Correlation analysis using Spearman's test demonstrated a significant relationship between hs-CRP levels and cognitive function. A strong negative correlation was observed between hs-CRP levels and MoCA-INA scores ($r = -0.638$; $p < 0.001$). This finding indicates that higher levels of systemic inflammation, as reflected by increased hs-CRP concentrations, were associated with lower cognitive performance among patients with acute ischemic stroke (Table 3). In contrast, no statistically significant association was observed between hs-CRP levels and functional outcomes measured using the modified Rankin Scale. The correlation coefficient between hs-CRP levels and mRS scores was −0.029 with a p-value of 0.817, indicating that systemic inflammatory activity measured by hs-CRP was not associated with functional disability in this study (Table 3).

Table 3. The Relationship Between Serum hs-CRP Levels and Cognitive Function and Clinical Outcomes in Patients with Acute Ischemic Stroke

	mRS		**MoCA-INA**	
Characteristics	**r value**	**p-value**	**r value**	**p-value**
hs-CRP	-0.029	0.817	-0.638	<0.001

5. Discussion

This study investigated the relationship between systemic inflammatory activity as measured by high-sensitivity C-reactive protein (hs-CRP), with cognitive function and functional outcomes in patients with acute ischemic stroke. The main findings demonstrated that elevated high-sensitivity C-reactive protein (hs-CRP) levels were significantly correlated with poorer cognitive function, indicating that higher levels of systemic inflammation are associated with lower cognitive performance in patients with acute ischemic stroke. However, no significant association was observed between hs-CRP levels and functional outcomes measured using the modified Rankin Scale (mRS).

These findings support the growing body of evidence indicating that inflammatory processes play an important role in the pathophysiology of post-stroke cognitive impairment. Inflammation is widely recognized as a key mechanism involved in secondary brain injury following ischemic stroke. Cerebral ischemia initiates a cascade of cellular and molecular events that activate microglia and astrocytes within the central nervous system. These activated cells release pro-inflammatory cytokines, including interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and interleukin-1β (IL-1β), which amplify inflammatory signaling within ischemic brain tissue [3,4]. These cytokines also stimulate hepatic synthesis of acute-phase proteins such as C-reactive protein. Consequently, elevated hs-CRP levels reflect systemic inflammatory responses following ischemic stroke [13,14]. Previous studies have demonstrated that hs-CRP levels increase within the first 24–48 hours after stroke onset and may remain elevated during the acute and subacute phases of the disease [15].

Inflammatory responses may exacerbate neuronal injury through several mechanisms, including endothelial dysfunction, disruption of the blood–brain barrier, leukocyte infiltration, and oxidative stress [16,17]. These processes contribute to neuronal damage and impaired neurovascular function, which may influence neurological recovery following stroke.

Several biological mechanisms may explain this association. First, systemic inflammation may impair cerebral microcirculation and promote cerebral small-vessel disease. These vascular abnormalities may disrupt white matter tracts essential for cognitive processing, particularly within frontal-subcortical networks responsible for executive function and attention [14]. Second, inflammatory mediators may directly affect neuronal survival and synaptic plasticity. Elevated cytokine levels have been associated with hippocampal

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dysfunction, which plays a critical role in memory formation and learning processes [18]. Third, chronic inflammation may contribute to structural brain changes, including white matter hyperintensities, cortical thinning, and hippocampal atrophy. These structural alterations have been strongly linked to cognitive impairment in both vascular dementia and post-stroke cognitive decline [14,18].

Previous studies have reported similar findings. Prabowo et al. demonstrated that elevated hs-CRP levels were associated with greater stroke severity and worse neurological outcomes [19]. In addition, several observational studies have reported that inflammatory biomarkers such as CRP and IL-6 are associated with an increased risk of post-stroke cognitive impairment [20].

In contrast to the findings regarding cognitive function, this study did not identify a significant association between hs-CRP levels and functional outcomes measured using the modified Rankin Scale. The absence of this relationship may be explained by several factors. Functional recovery after stroke is a complex process influenced by multiple determinants, including lesion location, infarct volume, neuroplasticity, rehabilitation intensity, and preexisting comorbidities [21]. While systemic inflammation may contribute to neuronal injury, it may not independently determine overall functional disability.

Furthermore, the modified Rankin Scale primarily measures physical disability and independence in daily activities. Cognitive impairment may therefore not be fully reflected in mRS scores, particularly in patients who experience mild motor deficits but significant cognitive dysfunction [21]. Another possible explanation relates to the relatively short follow-up period in this study. Functional outcomes were assessed at 30 days following stroke onset, whereas several studies suggest that the predictive value of inflammatory biomarkers may become more evident during longer follow-up periods, such as 90 days or 6 months.

The results of this study have several important clinical implications. First, hs-CRP may serve as a useful biomarker for identifying patients at risk of post-stroke cognitive impairment. Early identification of patients with elevated inflammatory markers may allow clinicians to implement targeted monitoring and early cognitive rehabilitation strategies.

Second, routine measurement of hs-CRP levels may help clinicians stratify patients according to inflammatory status. This information could support individualized treatment approaches including aggressive control of vascular risk factors, closer neurological monitoring, and early cognitive screening. Finally, the findings support the concept that neuroinflammation represents a potential therapeutic target in stroke management. Future therapeutic strategies aimed at modulating inflammatory pathways may help reduce secondary neuronal injury and improve cognitive outcomes following stroke.

This study has several strengths. First, it evaluates the relationship between systemic inflammatory biomarkers and both cognitive and functional outcomes in patients with acute ischemic stroke. Second, cognitive function was assessed using the MoCA-INA, which is a sensitive and validated tool for detecting mild cognitive impairment. Third, this study contributes important clinical data from Indonesia, where research on inflammatory biomarkers in stroke remains relatively limited.

Several limitations should be considered. First, the cross-sectional design limits the ability to establish causal relationships. Second, hs-CRP levels were measured at a single time point and may not reflect dynamic inflammatory changes over time. Third, the relatively small sample size may limit generalizability.

Future studies with larger sample sizes and longitudinal designs are needed to better understand the relationship between inflammatory biomarkers and long-term cognitive outcomes following stroke. Additionally, future studies should investigate the combined predictive value of multiple inflammatory biomarkers, such as IL-6, TNF-α, and matrix metalloproteinases. Integrating multiple biomarkers may improve the accuracy of prognostic models for stroke outcomes.

Conclusion

Elevated hs-CRP levels were significantly associated with poorer cognitive function in patients with acute ischemic stroke. However, hs-CRP levels were not significantly associated with functional outcomes measured using the modified Rankin Scale. These findings suggest that systemic inflammation may contribute to post-stroke cognitive impairment and that hs-CRP may serve as a potential biomarker for

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identifying patients at risk of cognitive decline following stroke.

Refrences

1. Feigin VL, Stark BA, Johnson CO, Roth GA, Bisignano C, Abady GG, et al. Global, regional, and national burden of stroke and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Neurol 2021;20:795–820. https://doi.org/10.1016/S1474-4422(21)00252-0.
2. Feigin VL, Brainin M, Norrving B, Martins S, Sacco RL, Hacke W, et al. World Stroke Organization (WSO): Global Stroke Fact Sheet 2022. International Journal of Stroke 2022;17:18–29. https://doi.org/10.1177/17474930211065917.
3. Campbell BCV, De Silva DA, Macleod MR, Coutts SB, Schwamm LH, Davis SM, et al. Ischaemic stroke. Nat Rev Dis Primers 2019;5. https://doi.org/10.1038/s41572-019-0118-8.
4. Qin C, Yang S, Chu YH, Zhang H, Pang XW, Chen L, et al. Signaling pathways involved in ischemic stroke: molecular mechanisms and therapeutic interventions. Signal Transduct Target Ther 2022;7. https://doi.org/10.1038/s41392-022-01064-1.
5. Rehman S, Nadeem A, Akram U, Sarwar A, Quraishi A, Siddiqui H, et al. Molecular Mechanisms of Ischemic Stroke: A Review Integrating Clinical Imaging and Therapeutic Perspectives. Biomedicines 2024;12. https://doi.org/10.3390/biomedicines12040812.
6. Yu H, Huang Y, Chen XY, Nie WB, Wang YJ, Jiao Y, et al. High-sensitivity C-reactive protein in stroke patients – The importance in consideration of influence of multiple factors in the predictability for disease severity and death. Journal of Clinical Neuroscience 2017;36:12–9. https://doi.org/10.1016/j.jocn.2016.10.020.
7. Mao L, Zhang X, Hu Y, Wang X, Song Y, He J, et al. Nomogram based on cytokines for cardiovascular diseases in Xinjiang Kazakhs. Mediators Inflamm 2019;2019. https://doi.org/10.1155/2019/4756295.
8. Huang H, Zhan Y, Yu L, Li S, Cai X. Association between Blood Pressure and Post-Stroke Cognitive Impairment: A Meta-Analysis. Rev Cardiovasc Med 2024;25. https://doi.org/10.31083/j.rcm2505174.
9. Husein N, Francina Lumempouw S, Ramli Y. Montreal Cognitive Assesment Versi Indonesia MoCAIna Untuk Skrining Gangguan Fungsi Kognitif. Neurona. 2010.
10. Afrashteh F, Almasi-Dooghaee M, Kamyari N, Rajabi R, Baradaran HR. Is Montreal Cognitive Assessment a valuable test for the differentiation of Alzheimer's disease, frontotemporal dementia, dementia with Lewy body, and vascular dementia? Dementia e Neuropsychologia 2024;18. https://doi.org/10.1590/1980-5764-DN-2023-0124.
11. Thomann AE, Berres M, Goettel N, Steiner LA, Monsch AU. Enhanced diagnostic accuracy for neurocognitive disorders: A revised cut-off approach for the Montreal Cognitive Assessment. Alzheimers Res Ther 2020;12. https://doi.org/10.1186/s13195-020-00603-8.
12. Delfino C, Cavada G, Hoffmeister L, Lavados P, Muñoz Venturelli P. Patient centered outcomes in stroke: utility-weighted modified Rankin Scale results in a community-based study. Front Neurol 2025;16. https://doi.org/10.3389/fneur.2025.1539107.
13. Karmakar P, Monir Hossain M. High Sensitivity C-Reactive Protein (hsCRP): A Predictive Inflammatory Biomarker of Vascular Diseases. vol. 6. 2021.
14. Mengozzi M, Kirkham FA, Girdwood EER, Bunting E, Drazich E, Timeyin J, et al. C-Reactive Protein Predicts Further Ischemic Events in Patients With Transient Ischemic Attack or Lacunar Stroke. Front Immunol 2020;11. https://doi.org/10.3389/fimmu.2020.01403.
15. Anwar R, Shaheer Haider S, Anwar S. Association between High sensitivity CRP and Ischaemic stroke-A case control study. vol. 12. 2018.
16. Mekhora C, Lamport DJ, Spencer JPE. An overview of the relationship between inflammation and cognitive function in humans, molecular pathways and the impact of nutraceuticals. Neurochem Int 2024;181. https://doi.org/10.1016/j.neuint.2024.105900.
17. Salaudeen MA, Bello N, Danraka RN, Ammani ML. Understanding the Pathophysiology of

Ischemic Stroke: The Basis of Current Therapies and Opportunity for New Ones. Biomolecules 2024;14. https://doi.org/10.3390/biom14030305.

18. Wang L, Yang L, Liu H, Pu J, Li Y, Tang L, et al. C-Reactive Protein Levels and Cognitive Decline following Acute Ischemic Stroke: A Systematic Review and Meta-Analysis. Brain Sci 2023;13. https://doi.org/10.3390/brainsci13071082.
19. Prabowo Fajar, Sutarni Sri, Astuti. Korelasi kadar high-sensitivity C-reactive protein dengan gangguan kognitif pada. Berkala Neurosains, Vol 19, No 1 2020.
20. Webb AJS, Werring DJ. New Insights into Cerebrovascular Pathophysiology and Hypertension. Stroke 2022;53:1054–64. https://doi.org/10.1161/STROKEAHA.121.035850.
21. Gardener H, Romano LA, Smith EE, Campo-Bustillo I, Khan Y, Tai S, et al. Functional status at 30 and 90 days after mild ischaemic stroke. Stroke Vasc Neurol 2022;7:375–80. https://doi.org/10.1136/svn-2021-001333.