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Original article

Endothelial adhesion molecules in acute ischemic stroke: A cross-sectional evaluation of VCAM-1 and ICAM-1 as potential biomarkers of severity

Haris Nur[1], Muhammad Yunus Amran[2,3,4], Muhammad Akbar[1,3,4], Rusdina Bte Ladju[5], Jumraini Tammasse[1,3,4], Anastasi Juliana[1]

[1]Department of Neurology, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia; [2]Division of Interventional Neurology and Neuroendovascular Therapy, Department of Neurology, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia; [3]Brain Centre, Dr. Wahidin Sudirohusodo General Hospital, Makassar, Indonesia; [4]Hasanuddin University Teaching Hospital, Makassar, Indonesia; [5]Department of Pharmacology, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia.

Abstract. *Background and aim:* Stroke is a leading cause of death and disability worldwide, with ischemic stroke being the most common type. Neuroinflammation plays a pivotal role in ischemic brain injury, where endothelial adhesion molecules such as vascular cell adhesion molecule-1 (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1) mediate leukocyte recruitment and blood–brain barrier disruption. This study aimed to investigate the association between circulating VCAM-1 and ICAM-1 levels and stroke severity in patients with acute ischemic stroke. *Methods:* An analytical observational study with a cross-sectional design was conducted at Dr. Wahidin Sudirohusodo Central General Hospital and affiliated facilities in Makassar, Indonesia, from June 2025 to August 2025. Fifty-eight first-ever acute ischemic stroke patients aged 18–70 years were consecutively recruited. Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS) within 1–7 days of onset. Venous blood samples were collected and analyzed for VCAM-1 and ICAM-1 levels. Statistical analyses included Spearman correlation and comparative tests, with $p < 0.05$ considered significant. *Results:* The mean age of patients was 58.2 years, with a male predominance (53.4%). Hypertension (58.6%) was the most common risk factor. Most patients presented with minor (44.8%) or moderate (48.3%) severity. Mean VCAM-1 and ICAM-1 levels were 38.62 ng/mL and 18.16 ng/mL, respectively. No significant correlation was observed between VCAM-1 ($r = 0.098$, $p = 0.462$) or ICAM-1 ($r = -0.050$, $p = 0.708$) and NIHSS scores. However, a significant association was found between VCAM-1 levels and stroke severity in non-hypertensive patients ($r = 0.420$, $p = 0.041$). *Conclusions:* Circulating VCAM-1 and ICAM-1 levels were not significantly associated with overall stroke severity in acute ischemic stroke. VCAM-1 may have prognostic relevance in specific subgroups, but larger longitudinal studies are warranted to clarify their biomarker potential. (www.actabiomedica.it)

Key words: Acute Ischemic Stroke, VCAM-1, ICAM-1, Stroke Severity, Biomarkers

Introduction

Stroke remains one of the leading causes of mortality and long-term disability worldwide, representing a major global health and socioeconomic challenge. According to the Global Burden of Disease (GBD) 2019 report, stroke is the second leading cause of death and the third leading cause of disability globally.

Between 1990 and 2019, the global incidence of stroke increased by 70%, mortality by 43%, prevalence by 102%, and disability-adjusted life years (DALYs) by 143% (1). This rising trend underscores the persistent and growing burden of stroke, particularly in low- and lower-middle-income countries, where access to preventive care, acute management, and rehabilitation services remains limited (2). The highest burden has been observed in regions such as Eastern Europe, Sub-Saharan Africa, and Asia, reflecting disparities in health systems and stroke care infrastructure. In Indonesia, stroke represents a critical public health concern. The Basic Health Research reported a prevalence of 10.9 per 1,000 population, making it the most common cause of neurological morbidity. Stroke also accounts for 21.1% of all deaths nationwide, positioning it as the leading cause of mortality in the country (3). Beyond mortality, stroke contributes substantially to long-term disability, reduced quality of life, and increased economic burden due to prolonged hospitalization, rehabilitation needs, and loss of productivity. The growing prevalence of vascular risk factors such as hypertension, diabetes, dyslipidemia, and smoking in the Indonesian population is expected to further increase the burden of stroke in the coming years (4). The majority of strokes are ischemic, resulting from reduced cerebral blood flow, usually caused by arterial occlusion, while 10-40% are hemorrhagic, due to rupture of cerebral vessels. Ischemic stroke may be caused by embolism or thrombosis secondary to intracranial atherosclerosis, leading to impaired cerebral perfusion. Cerebral ischemia triggers neuronal injury through excitotoxicity, oxidative stress, and inflammation, ultimately resulting in apoptosis and necrosis of brain cells. The inflammatory cascade involves activation of resident and peripheral immune cells, which stimulate endothelial cells to express adhesion molecules such as vascular cell adhesion molecule-1 (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1) (5). VCAM-1 and ICAM-1 are endothelial adhesion molecules that play a central role in the inflammatory response following acute ischemic stroke (AIS). These molecules mediate the adhesion of leukocytes to activated endothelium and facilitate their transmigration across the blood-brain barrier (BBB) into ischemic brain tissue. The infiltration of leukocytes further amplifies neuroinflammation by releasing pro-inflammatory cytokines, reactive oxygen species, and proteolytic enzymes, thereby exacerbating neuronal injury and contributing to secondary brain damage. Disruption of the BBB integrity through this process not only worsens cerebral edema but also perpetuates a cycle of inflammation and tissue injury (6). Elevated circulating levels of VCAM-1 and ICAM-1 have been consistently reported in patients with AIS, and these elevations are hypothesized to reflect the extent of endothelial activation and systemic inflammation. Because of their role in leukocyte-endothelial interactions, these adhesion molecules are increasingly being investigated as potential biomarkers of stroke severity and prognosis (7). Several studies have demonstrated associations between higher serum levels of VCAM-1 or ICAM-1 and greater neurological impairment, while others have suggested a link with worse functional outcomes or mortality. However, findings remain inconsistent, with some studies reporting no significant correlation, raising questions about whether these molecules act merely as bystanders of inflammation or have a causal role in worsening ischemic injury. Stroke severity in clinical practice is most reliably assessed using the National Institutes of Health Stroke Scale (NIHSS), a standardized and validated tool widely applied in both clinical and research settings (8). The NIHSS provides a quantitative measure of neurological deficits and has been shown to correlate strongly with infarct volume, functional outcomes, and mortality. Investigating the relationship between circulating levels of VCAM-1 and ICAM-1 with NIHSS scores may therefore provide valuable insights into the pathophysiological role of these molecules and their potential utility as biomarkers for assessing stroke severity. Clarifying this relationship is crucial not only for understanding the mechanisms of neuroinflammation in stroke but also for exploring novel prognostic tools and therapeutic targets in the management of AIS (1). Evidence regarding the association of VCAM-1 and ICAM-1 with stroke severity remains inconsistent. Elevated ICAM-1 levels were significantly associated with poor prognosis in ischemic stroke patients. Correlation between increased VCAM-1 levels and stroke severity. Observed no association between serum VCAM-1 levels and stroke

severity reported no significant correlation between VCAM-1 and ICAM-1 levels with ischemic stroke severity (9). Given these conflicting findings, it remains unclear whether increased levels of VCAM-1 and ICAM-1 are merely markers of the inflammatory response or play a causal role in worsening clinical outcomes. Therefore, this study aims to investigate the relationship between VCAM-1 and ICAM-1 levels and stroke severity in patients with AIS.

Material and Methods

Study design

This study employed an analytical observational approach with a cross-sectional design. Patients with AIS who fulfilled the predetermined inclusion and exclusion criteria were consecutively recruited as study subjects. The inclusion criteria comprised adult patients diagnosed with AIS confirmed by clinical examination and neuroimaging within the eligible study period. Patients with hemorrhagic stroke, concomitant systemic inflammatory or infectious diseases, autoimmune disorders, malignancy, or incomplete clinical and laboratory data were excluded from the analysis. All eligible participants provided informed consent prior to inclusion in the study. The research was conducted at Dr. Wahidin Sudirohusodo Central General Hospital, a tertiary referral and teaching hospital in Makassar, Indonesia, as well as at affiliated hospitals and health facilities within Makassar City. Data collection and sample analysis were carried out over a three-month period, from June 2025 to August 2025.

Sample criteria

The study population consisted of patients diagnosed with AIS who were admitted to Dr. Wahidin Sudirohusodo Central General Hospital and affiliated health facilities in Makassar during the study period. Participants were recruited consecutively according to predefined eligibility criteria. The inclusion criteria were as follows: (1) patients with AIS confirmed by clinical examination and neuroimaging, with symptom onset between one to seven days; (2) adults aged 18-70 years experiencing their first ischemic stroke episode; and (3) patients or their legal representatives who provided written informed consent to participate in the study. Patients were excluded if they had comorbid conditions that could potentially influence biomarker levels or clinical outcomes, including chronic kidney disease, chronic heart failure, severe liver disease, autoimmune disorders, active infectious diseases, malignant diseases, or a history of myocardial infarction. These exclusion criteria were applied to minimize potential confounding factors and to ensure the reliability of biomarker measurements in the context of AIS. In addition, patients who initially consented but subsequently withdrew their participation during the study were categorized as drop-outs and excluded from the final analysis.

Research procedure

Patients diagnosed with AIS were admitted to the treatment wards of Dr. Wahidin Sudirohusodo Central General Hospital Makassar and its affiliated hospitals. The diagnosis of AIS was established based on clinical history, neurological examination, and supporting investigations, including non-contrast head computed tomography (CT) scans to exclude hemorrhagic stroke. All patients fulfilling the inclusion criteria and none of the exclusion criteria were consecutively enrolled in the study. Prior to participation, the research team provided a thorough explanation of the study objectives and procedures to the patients or their families, and written informed consent was obtained. The severity of ischemic stroke was assessed using the NIHSS in patients with symptom onset ranging from one to seven days. Following clinical assessment, venous blood samples were collected for biomarker analysis. A total of 3 mL of venous blood was drawn into plain tubes for the measurement of circulating VCAM-1 and ICAM-1 levels. To ensure sample integrity, blood obtained via syringe was carefully transferred into plain tubes under aseptic conditions. The collected samples were immediately placed in a cool box maintained at a temperature of approximately 4°C during transport to the Hasanuddin University Medical Research Center (HUMRC) laboratory at Hasanuddin University Hospital. Upon arrival, samples were stored at -20°C until

further analysis. Laboratory procedures for biomarker measurement were performed according to standardized protocols to ensure reliability and reproducibility. All clinical, laboratory, and demographic data were recorded in a structured case report form. The compiled dataset was subsequently processed and subjected to statistical analysis to examine the relationship between VCAM-1 and ICAM-1 levels and the severity of AIS.

Data and statistical analysis

The data obtained was processed through statistical analysis using SPSS version 27. The data normality test used Kolmogorov Smirnov because the sample size was ≥ 50. The data analysis aims to assess the relationship between these variables with a p value < 0.05 is considered meaningful. Determine the correlation between the ratio of VCAM-1 and ICAM-1 levels to severity with Spearman (non-parametric data distribution). To compare the values of VCAM-1 and ICAM-1 levels in the group of acute ischemic stroke of minor, moderate, moderate and severe severity with Anova or Kruskal Wallis.

Results

This study was conducted to study the relationship between VCAM-1 and ICAM-1 levels on the severity of patients with AIS. Data were collected from blood samples of first-time acute ischemic stroke patients who were hospitalized at the Dr. Wahidin Sudirohusodo Makassar Central General Hospital and affiliate hospital from June 2025 to August 2025. There were 58 patients with AIS who met the criteria. By gender, men outnumbered women (53.4% vs 46.6%). The average age in this study was 58.24 years. The severity categories examined with NIHSS were minor 44.8%, moderate 48.3%, moderatetly severe 5.2% and severe 1.7%. The most risk factors in this study were hypertension 58.6%, diabetes mellitus 29.3% and smoking 25.9%. This data can be seen in table 1 about the basic characteristics of the research subjects (Table 1).

VCAM-1 levels in acute ischemic stroke patients were obtained with a mean value of 38.62 ng/mL, a median of 38.53 ng/mL, a minimum of 20.85 ng/mL and a maximum of 56.23 ng/mL (Table 2). ICAM-1 levels in patients with AIS were obtained with a mean value of 18.16 ng/mL, a median of 15.34 ng/mL, a minimum of 6.48 ng/mL and a maximum of 20.18ngmL. This study showed no statistical significance between VCAM-1 (p = 0.341) and ICAM-1 (p = 0.470) levels on severity assessed using NIHSS at day 1-7 onset in acute ischemic stroke patients (Table 3).

Based on the spearman correlation normality test, a weak, positive, and insignificant correlation was found in VCAM-1 (r = 0.098, p = 0.462). A weak, negative, and insignificant correlation of ICAM-1 (r = - 0.050, p = 0.708) was found to be the severity assessed using NIHSS in patients with AIS on days 1-7 (Table 4). In the scatterplot graph (Figure 1), graph (a) shows VCAM-1 tends to rise when NIHSS values are high while graph (b) shows ICAM-1 tends to decrease when NIHSS values are high. Other results were that in VCAM-1 and ICAM-1 levels associated with stroke risk factors, there was a weak and significant correlation between VCAM-1 levels in non-hypertensive patients (r = 0.420, p = 0.041) (Table 5).

Table 1. Basic Characteristics of Research Subjects

Characteristic	Total (n= 58) N (%)
Gender (n)	
• Man	**31 (53.4 %)**
• Woman	**27 (44.6 %)**
Age	
• < 60 years old	**35 (60.35 %)**
• > 60 years old	**23 (39.65 %)**
Severity	
• Minor	**26 (44.8 %)**
• Moderate	**28 (48.3 %)**
• Moderate severe	**3 (5.2 %)**
• Severe	**1 (1.7 %)**
Risk factors	
• Hypertension	**34 (58.6 %)**
• Diabetes mellitus	**17 (29.3 %)**
• Smoke	**15 (25.9 %)**

Discussion

This study investigated the relationship between circulating VCAM-1 and ICAM-1 levels and stroke severity in patients with AIS. Among 58 patients included, the majority were male, with an average age of 58 years, and the most common risk factors were hypertension, diabetes mellitus, and smoking consistent with known epidemiological trends of stroke worldwide. The severity of stroke, as measured by the NIHSS, was predominantly in the minor to moderate range. Our findings demonstrated that although VCAM-1 levels tended to increase with higher NIHSS scores and ICAM-1 levels tended to decrease, neither association reached statistical significance. Specifically, VCAM-1 showed a weak, positive but insignificant correlation with stroke severity, while ICAM-1 showed a weak, negative and insignificant correlation. This study provides insights into the potential role of circulating VCAM-1 and ICAM-1 as biomarkers of stroke severity in patients with AIS. These results suggest that circulating levels of VCAM-1 and ICAM-1 within the first seven days of stroke onset may not reliably reflect the clinical severity of ischemic stroke. Several studies have reported findings consistent with our results. Significant correlation between VCAM-1 or ICAM-1 levels and stroke severity assessed by NIHSS, suggesting that the role of these adhesion molecules may be limited to the early inflammatory cascade without directly determining the extent of clinical deficits (10). Similarly, serum VCAM-1 levels were not associated with stroke severity in acute ischemic stroke patients, further supporting the notion that circulating adhesion molecules may serve as markers of endothelial activation but not as predictors of neurological severity. The findings of this study suggest that circulating VCAM-1 levels may have clinical significance in acute ischemic stroke (AIS), particularly among patients without a history of hypertension. While the overall correlation between adhesion molecules and stroke severity did not reach statistical significance across the entire cohort, the observed association of VCAM-1 with stroke severity in the non-hypertensive subgroup highlights a potentially important pathophysiological mechanism. VCAM-1 is an endothelial adhesion molecule that plays a central role in leukocyte recruitment and transmigration during vascular inflammation. In the context of AIS, increased expression of VCAM-1 may reflect acute endothelial activation in response to ischemic injury. In patients with chronic hypertension, however, the endothelium is often already subjected to long-standing inflammatory and structural changes, including arterial stiffness, microvascular remodeling, and persistent upregulation of adhesion molecules. These baseline alterations may obscure the acute dynamic changes in VCAM-1 during ischemic events. Conversely, in non-hypertensive patients, the absence of chronic vascular injury may allow VCAM-1 to more accurately reflect the acute endothelial response to ischemia, thereby providing a more reliable marker of stroke severity. Clinically, this finding could have implications for the use of VCAM-1 as a biomarker to stratify AIS severity or predict outcomes in selected

Table 2. Comparison of VCAM-1 and ICAM-1 levels in patients with AIS

	Mean	Median	Minimum	Maximum
VCAM-1 (ng/ml)	38.62	38.53	20.85	56.23
ICAM-1 (ng/ml)	18.16	15.34	6.48	20.18

Table 3. Comparison of VCAM-1 and ICAM-1 levels to the severity of patients with AIS

	Minor (median ± [min,max]) n = 26	Moderate (median ± [min,max]) n = 28	Moderate-severe (median ± [min,max]) n = 3	Severe n = 1	Value *p*
VCAM-1 (ng/ml)	39.11 ± [20.85, 56.23]	36.34 ± [22.56, 50.18]	45.20 ± [38.05, 51.04]	44.78	0.341*
ICAM-1 (ng/ml)	17.84 ± [6.48, 47.93]	15.16 ± [10.74, 56.90]	10.45 ± [9.50, 19.46]	20.18	0.470**

*Anova Test, ** Kruskal Wallis Test.

Table 4. The relationship between VCAM-1 and ICAM-1 levels on the severity of patients with AIS

	NIHSS	
	Value *r*	**Value p**
VCAM-1	0,098	0,462
ICAM-1	-0,050	0,708

patient populations. If validated in larger cohorts, VCAM-1 measurement may support more individualized risk assessment, particularly for patients without traditional vascular comorbidities such as hypertension. Moreover, given its mechanistic role in leukocyte–endothelial interactions, VCAM-1 could represent not only a biomarker but also a potential therapeutic target to modulate post-ischemic inflammatory injury (11). This study explored the potential role of circulating VCAM-1 and ICAM-1 as biomarkers of stroke severity in patients with AIS. Our findings add to the growing body of evidence linking endothelial dysfunction with stroke pathophysiology. However, several important considerations should be highlighted. From a methodological standpoint, we implemented strict laboratory quality control procedures to ensure the reliability of biomarker measurements. Internal calibration was performed regularly, and duplicate testing of samples was conducted to minimize technical variability. These measures enhance the credibility of our findings by reducing potential measurement error and ensuring consistency across assays. On the other hand, other studies have reported contrasting results. Significant association between elevated VCAM-1 levels and greater stroke severity, proposing that increased VCAM-1 expression reflects enhanced leukocyte adhesion and migration into ischemic brain tissue, thereby amplifying neuroinflammation and clinical deficits. Likewise, the higher ICAM-1 levels were significantly associated with poor prognosis in ischemic stroke, indicating that ICAM-1 may contribute to persistent neuroinflammation and blood brain barrier disruption (12). These differences across studies may be attributable to variations in study design, timing of blood sample collection, patient characteristics, and laboratory methods used for biomarker measurement. Interestingly, our study also found a weak but significant correlation between VCAM-1 levels and stroke severity in non-hypertensive patients, suggesting that comorbid vascular risk factors may influence the expression and circulating levels of adhesion molecules (13,14).

Several studies support our findings reported no significant correlation between VCAM-1 or ICAM-1 and stroke severity, concluding that adhesion molecule levels reflect systemic inflammation rather than directly determining clinical deficits. Similarly, found no association between serum VCAM-1 and NIHSS severity in patients with AIS. These studies, like ours, suggest that VCAM-1 and ICAM-1 may function as markers of endothelial activation but do not necessarily reflect the clinical neurological outcome during the acute phase (5,15). Conversely, other studies have reported contrasting results found that elevated VCAM-1 levels correlated with more severe strokes, proposing that VCAM-1 contributes to enhanced leukocyte adhesion and transmigration, thereby amplifying ischemic injury. The higher ICAM-1 levels were associated with poor prognosis and higher stroke severity, suggesting that ICAM-1-mediated leukocyte infiltration contributes to blood brain barrier disruption and prolonged neuroinflammation. These discrepancies highlight the ongoing debate about whether adhesion molecules are merely byproducts of inflammation or actively contribute to ischemic injury progression (16,17). Although this study supports the relevance of VCAM-1 and ICAM-1 in AIS, the variability in sampling times represents a critical limitation that may have attenuated the observed associations. We recommend that future research implement standardized sampling intervals to more accurately capture biomarker dynamics and strengthen the evidence for their prognostic utility in acute ischemic stroke. Hypertension, in particular, is known to induce chronic endothelial dysfunction, which may confound the interpretation of VCAM-1 and ICAM-1 levels in acute ischemic stroke. The absence of a significant association in our study could also be explained by several biological and methodological factors. First, adhesion molecule expression is dynamic and may fluctuate depending on the timing of measurement. Samples collected within 1-7 days after stroke onset may capture heterogeneous stages of the inflammatory process, potentially masking

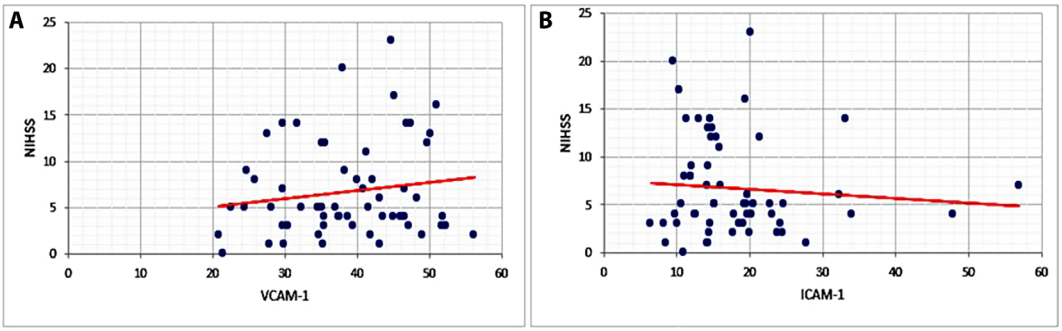

Figure 1. Graph of the relationship between VCAM-1 and ICAM-1 levels on the severity of patients with AIS.

Table 5. Relationship of VCAM-1 and ICAM-1 levels to AIS severity by risk factors

Risk factors		Molecular Adhesion	NIHSS	
			Value *r*	Value *p*
DM	Yes	VCAM-1	0,180	0,490
		ICAM-1	-0,117	0,655
	Not	VCAM-1	0,018	0,911
		ICAM-1	-0,019	0,906
HT	Yes	VCAM-1	-0,098	0,582
		ICAM-1	-0,052	0,768
	Not	VCAM-1	0,420	0,041
		ICAM-1	0,023	0,916
Smoke	Yes	VCAM-1	-0,031	0,914
		ICAM-1	-0,384	0,158
	Not	VCAM-1	0,159	0,309
		ICAM-1	0,131	0,403

stronger associations at earlier or later phases. In addition, it is critical to recognize that VCAM-1 and ICAM-1 exhibit distinct temporal expression profiles after cerebral ischemia, so that a single measurement within the 1–7-day window may capture only part of their dynamic response. Within 1–7 days after AIS, the dominant process occurring in the brain is inflammation. This inflammatory process leads to increased expression of the adhesion molecules VCAM-1 and ICAM-1 (18). Both preclinical and clinical data show that soluble ICAM-1 begins to rise within 6–24 hours of stroke onset, peaks at approximately 24–48 hours, and then gradually declines toward baseline by day 7. Soluble VCAM-1, by contrast, is detectable within the first 12–24 hours, reaches maximum levels between 48–72 hours, and remains significantly elevated throughout the first post-stroke week before descending as recovery enters the subacute–chronic transition (18,19). Because our protocol involved only one blood draw per patient during days 1–7, we likely measured each patient's adhesion-molecule level at differing points on these curves, which may have attenuated any correlation with NIHSS score. To overcome this limitation and to determine which time points best reflect BBB integrity and neurological severity, future studies should incorporate serial sampling—ideally at 1, 3, and 7 days post-onset—as recommended for stroke-recovery trials and biomarker studies (20). Second,

the relatively small sample size (n = 58) may limit the statistical power to detect modest associations (7, 21). Despite the lack of significant correlations in our cohort, VCAM-1 and ICAM-1 assays remain rapid, minimally invasive, and may hold promise as adjuncts to neuroimaging or composite biomarker panels for clinical risk stratification—provided that optimal sampling windows and clinically meaningful threshold values can be established. Third, circulating levels of adhesion molecules may not fully represent local endothelial activation at the site of ischemia, where the inflammatory response is most pronounced. Significant correlation between VCAM-1 and ICAM-1 levels and stroke severity, they add to the growing body of evidence suggesting variability in the role of adhesion molecules as biomarkers in acute ischemic stroke. Further large-scale, multicenter studies with serial measurements at multiple time points are needed to better clarify their prognostic value and pathophysiological significance (22,23). While the overall findings contribute to the understanding of endothelial adhesion molecules in stroke pathophysiology, certain limitations must be considered when interpreting the results. First, the relatively small sample size represents a major limitation. With a limited number of participants, the statistical power to detect subtle but clinically relevant associations is reduced. This may have contributed to the lack of significance in some of the correlations observed in our analysis. Furthermore, the predominance of patients with minor to moderate stroke severity in our cohort further restricts the generalizability of the findings. The underrepresentation of severe AIS cases means that the relationship between adhesion molecules and the full spectrum of stroke severity could not be comprehensively evaluated. In addition, this study was not supported by external grant funding, which may have limited the availability of resources, and the relatively short study period further constrained patient recruitment and longitudinal follow-up. These limitations highlight the need for validation in larger and more diverse study populations. Future research should focus on multi-center studies with larger sample sizes that adequately represent the full range of AIS severity. Such studies would not only enhance the statistical robustness of the findings but also improve their external validity, allowing for broader clinical application. Additionally, standardized and repeated measurements at multiple time points after stroke onset may better capture the dynamic changes in endothelial biomarkers and their prognostic implications.

Conclusions

This study highlights the potential role of circulating VCAM-1 and ICAM-1 as biomarkers of stroke severity in AIS, reflecting endothelial activation and vascular inflammation. While our findings provide valuable preliminary insights, the limited sample size, predominance of mild until moderate cases, and variability in sampling times restrict their generalizability. Future studies with larger, multicenter cohorts and longitudinal biomarker sampling at multiple time points are warranted to validate these associations and clarify their temporal dynamics, thereby strengthening their potential application in the clinical management of AIS. These findings are consistent with previous reports showing inconsistent associations between adhesion molecules and stroke severity, highlighting the complexity of post-stroke inflammatory processes. While VCAM-1 and ICAM-1 may reflect systemic endothelial activation, their role as independent biomarkers of stroke severity remains uncertain.

Ethic Approval: All research designs were reviewed and approved by the Health Research Ethics Committee of Dr Wahidin Sudirohusodo Hospital, Faculty of Medicine, Hasanuddin University (493/UN4.6.4.5.31/PP36/2025) on July 14, 2025.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Authors Contribution: HN, MYA, AJ (Concept, Design, Supervision, Resources, Materials, Data Collection and Processing, Analysis and Interpretation, Literature Search, Writing Manuscript), MYA, MA (Concept, Design, Analysis and Interpretation, Literature Search, Writing Manuscript), MA and RBL, JT (Concept, Design, Analysis and Interpretation, Literature Search). All authors read and approved the final version of the manuscript.

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Data Availability Statement: All the data are available from the corresponding author upon a reasonable request (HN).

Abbreviations

GBD: Global burden of disease
DALYs: Disability-adjusted life years
VCAM-1: Vascular cell adhesion molecule-1
ICAM-1: Intercellular adhesion molecule-1
AIS: Acute ischemic stroke
BBB: Blood-brain barrier
NIHSS: National Institutes of Health Stroke Scale
CT: Computed tomography
HUMRC: Hasanuddin University Medical Research Centre

References

1. Navi BB, Sherman CP, Genova R, et al. Mechanisms of Ischemic Stroke in Patients with Cancer: A Prospective Study. Ann Neurol. 2021;90(1):159-69. doi:10.1002/ana.26129
2. Moazzen S, Janke J, Slooter AJC, et al. The association of pre-operative biomarkers of endothelial dysfunction with the risk of post-operative neurocognitive disorders: results from the BioCog study. BMC Anesthesiol. 2024;24(1):358. Published 2024 Oct 8. doi:10.1186/s12871-024-02722-3
3. Li L, Huang M, Shen J, et al. Serum Levels of Soluble Platelet Endothelial Cell Adhesion Molecule 1 in COVID-19 Patients Are Associated With Disease Severity. J Infect Dis. 2021;223(1):178-79. doi:10.1093/infdis/jiaa642
4. Wang L, Chen Y, Feng D, Wang X. Serum ICAM-1 as a Predictor of Prognosis in Patients with Acute Ischemic Stroke. Biomed Res Int. 2021;2021:5539304. Published 2021 Mar 18. doi:10.1155/2021/5539304
5. Sibiya S, Mlambo ZP, Mthembu MH, Mkhwanazi NP, Naicker T. Analysis of ICAM-1 rs3093030, VCAM-1 rs3783605, and E-Selectin rs1805193 Polymorphisms in African Women Living with HIV and Preeclampsia. Int J Mol Sci. 2024;25(19):10860. Published 2024 Oct 9. doi:10.3390/ijms251910860
6. Puig N, Camps-Renom P, Camacho M, et al. Plasma sICAM-1 as a Biomarker of Carotid Plaque Inflammation in Patients with a Recent Ischemic Stroke. Transl Stroke Res.2022;13(5):745-756.doi:10.1007/s12975-022-01002-x
7. Chetan IM, Vesa ŞC, Domokos Gergely B, et al. Increased Levels of VCAM-1 in Patients with High Cardiovascular Risk and Obstructive Sleep Apnea Syndrome. Biomedicines. 2023;12(1):48. Published 2023 Dec 24. doi:10.3390/biomedicines12010048
8. Li H, Chen M, Feng Q, et al. MicroRNA-34a in coronary heart disease: Correlation with disease risk, blood lipid, stenosis degree, inflammatory cytokines, and cell adhesion molecules. J Clin Lab Anal. 2022;36(1):e24138. doi:10.1002/jcla.24138
9. Greenwood JC, Talebi FM, Jang DH, et al. Low postoperative perfused vessel density is associated with increased soluble endothelial cell adhesion molecules during circulatory shock after cardiac surgery. Microvasc Res. 2023;150:104595. doi:10.1016/j.mvr.2023.104595
10. Ren B, Song Z, Chen L, Niu X, Feng Q. Long non-coding RNA UCA1 correlates with elevated disease severity, Th17 cell proportion, inflammatory cytokines, and worse prognosis in acute ischemic stroke patients. J Clin Lab Anal. 2021;35(3):e23697. doi:10.1002/jcla.23697
11. Zhang X, Zhou F, Wang W, et al. Levels of adhesion molecules and clinical outcomes in patients with ischemic stroke after mechanical thrombectomy. Front Neurol. 2022;13:1024162. Published 2022 Sep 29. doi:10.3389/fneur.2022.1024162
12. Maglinger B, Sands M, Frank JA, et al. Intracranial VCAM1 at time of mechanical thrombectomy predicts ischemic stroke severity. J Neuroinflammation. 2021;18(1):109. Published 2021 May 11. doi:10.1186/s12974-021-02157-4
13. Takasawa S, Makino M, Yamauchi A, et al. Intermittent hypoxia increased the expression of ESM1 and ICAM-1 in vascular endothelial cells via the downregulation of microRNA-181a1. J Cell Mol Med. 2024;28(1):e18039. doi:10.1111/jcmm.18039
14. Sanip Z, Rasool AHG, Pahimi N, et al. Elevated Inflammation and Adhesion Molecule hsCRP, GDF-15 and VCAM-1 in Angina Patients with Non-obstructive Coronary Artery Disease. Malays J Med Sci. 2024;31(6):148-59. doi:10.21315/mjms2024.31.6.12
15. Miller MR, Landis HE, Miller RE, Tizabi Y. Intercellular Adhesion Molecule 1 (ICAM-1): An Inflammatory Regulator with Potential Implications in Ferroptosis and Parkinson's Disease. Cells. 2024;13(18):1554. Published 2024 Sep 15. doi:10.3390/cells13181554
16. Zhang DD, Cao Y, Mu JY, et al. Inflammatory biomarkers and cerebral small vessel disease: a community-based cohort

study. Stroke Vasc Neurol. 2022;7(4):302-09. doi:10.1136/svn-2021-001102
17. Oley MH, Oley MC, Langi FLFG, et al. Factors related to serum levels of intercellular adhesion molecule-1 in probable COVID-19 patients in surgical treatment: an observational study. Pan Afr Med J. 2023;46:117. Published 2023 Dec 27. doi:10.11604/pamj.2023.46.117.41690
18. Bernhardt J, Hayward KS, Kwakkel G, et al. Agreed definitions and a shared vision for new standards in stroke recovery research: The Stroke Recovery and Rehabilitation Roundtable taskforce. Int J Stroke. 2017;12(5):444-50. doi:10.1177/1747493017711816
19. Bai M, Sun R, Cao B, Feng J, Wang J. Monocyte-related cytokines/chemokines in cerebral ischemic stroke. CNS Neurosci Ther. 2023;29(12):3693-3712. doi:10.1111/cns.14368
20. Qiu YM, Zhang CL, Chen AQ, et al. Immune Cells in the BBB Disruption After Acute Ischemic Stroke: Targets for Immune Therapy?. Front Immunol. 2021;12:678744. Published 2021 Jun 23. doi:10.3389/fimmu.2021.678744
21. Libório AB, de Medeiros CMMF, Santos LL, de Andrade LS, Meneses GC, Martins AMC. Endothelium-related biomarkers and cognitive decline in prevalent hemodialysis patients: A prospective cohort study. Eur J Neurol. 2024;31(12):e16438. doi:10.1111/ene.16438
22. Lessieur EM, Liu H, Saadane A, Du Y, Kiser J, Kern TS. ICAM-1 on the luminal surface of endothelial cells is induced to a greater extent in mouse retina than in other tissues in diabetes. Diabetologia. 2022;65(10):1734-1744. doi:10.1007/s00125-022-05719-0
23. Wegeberg AM, Okdahl T, Riahi S, et al. Elevated levels of interleukin-12/23p40 may serve as a potential indicator of dysfunctional heart rate variability in type 2 diabetes. Cardiovasc Diabetol. 2022;21(1):5. Published 2022 Jan 6. doi:10.1186/s12933-021-01437-w

Correspondence:
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Muhammad Yunus Amran, M.D., Ph.D., FIPM, FINR, FINA
Division of Interventional Neurology and Neuroendovascular Therapy, Department of Neurology, Faculty of Medicine, Hasanuddin University, Brain Centre, Dr. Wahidin Sudirohusodo General Hospital, and Hasanuddin University Teaching Hospital, Jl. Perintis Kemerdekaan KM 11, 90245, Makassar, South Sulawesi, Indonesia.
E-mail: muhyunusamran@med.unhas.ac.id; yunusamran10@gmail.com
ORCID: 0000-0001-5079-7490