RESEARCH ARTICLE

Serum MMP-9 and IL-1β levels in acute ischemic stroke and their association with initial neurological severity: a case-control study

Haider Adnan Rahman[1*], Kadhem Muhammed Sabae[1]

1. Department of Pathological Analysis, College of Health and Medical Technology, Al-Furat Al-Awsat Technical University, Kufa, Iraq

Abstract

Background: Ischemic stroke (IS) is a leading cause of global mortality and long-term disability. The acute inflammatory response is a critical element in the early pathophysiology and contributes to neuronal damage. Although matrix metalloproteinase-9 (MMP-9) and interleukin-1 beta (IL-1β) have been implicated in early ischemic brain injury, their combined prognostic value in the acute phase remains unclear.

Objective: This study aimed to evaluate the association between serum MMP-9 and IL-1β concentrations within the first 24 h of ischemic stroke onset and initial severity of neurological deficits.

Materials and Methods: A case-control study was conducted with 60 patients diagnosed with acute ischemic stroke and 60 age- and sex-matched healthy controls. Serum levels of MMP-9 and IL-1β were quantified using enzyme-linked immunosorbent assay (ELISA). The National Institutes of Health Stroke Scale (NIHSS) was used to assess stroke severity at admission.

Results: Serum levels of MMP-9 and IL-1β were significantly elevated in ischemic stroke patients compared to those in the control group ($p < 0.001$). Both biomarkers demonstrated a significant positive correlation with the NIHSS scores, indicating an association with greater neurological impairment. Furthermore, a strong positive correlation was observed between MMP-9 and IL-1β levels ($r = 0.929$, $p = 0.022$).

Conclusion: Elevated serum concentrations of MMP-9 and IL-1β within the first 24 h of ischemic stroke are strongly correlated with the severity of the condition, supporting their potential application as acute inflammatory and prognostic biomarkers.

Keywords: Acute Ischemic Stroke; MMP-9; IL-1β; NIHSS; Inflammation.

Received: 28.01.2026 / Accepted: 25.05.2026

Introduction

Stroke remains a major global public health challenge and is one of the leading causes of death and long-term disability worldwide. According to the latest Global Burden of Disease (GBD) study for 2021, stroke causes approximately 7 million deaths per year and more than 160 million disability-adjusted life years (DALYs) lost [1]. Ischemic stroke, the most common subtype, results from the occlusion of a cerebral artery and accounts for a substantial proportion of this global burden [2]. Acute ischemic stroke (AIS) represents a major clinical emergency. The resulting interruption of cerebral blood flow triggers a complex cascade of pathophysiological events characterized by energy failure, excitotoxicity, oxidative stress, and an intense inflammatory response, leading to irreversible neuronal injury and neurological impairment [3,4].

A substantial and early part of the AIS cascade involves a neuroinflammatory response that begins within minutes of stroke onset and may persist for several days [5]. This response is initiated by the release of damage-associated molecular patterns (DAMPs) from necrotic brain tissue, which activates resident microglia and astrocytes. This activation triggers a strong inflammatory reaction, culminating in the production of pro-inflammatory cytokines, chemokines, and other mediators that promote peripheral immune cell infiltration [6]. One of the most clinically relevant consequences of acute inflammation is the disruption of the blood-brain barrier (BBB), a selective interface that separates the central nervous system (CNS) from systemic circulation. This derangement is mediated by metabolic stress, oxidative damage, and inflammatory signaling, with subsequent vasogenic edema, neuronal injury, and an increased risk of hemorrhagic transformation [7,8].

Among numerous inflammatory mediators, MMP-9 and IL-1β have emerged as key players in the hyperacute stage of AIS. MMP-9, a zinc-dependent endopeptidase, increases markedly after ischemia, with maximal expression reported approximately 24 h after the insult [3]. It can directly contribute to BBB disruption by degrading extracellular matrix components and tight junction proteins, and it may aggravate neuroinflammation and brain edema. [9] At the same time, IL-1β, a potent pro-inflammatory cytokine produced early by activated microglia and oth-

* Correspondence to: Haider Adnan Rhman
E-mail: haider.rahmanlapmsc.chm@student.atu.edu.iq

er inflammatory cells, increases rapidly after stroke onset and contributes to the propagation of the inflammatory cascade [10]. IL-1β is involved in leukocyte adhesion, enhancement of inflammatory signaling and neuronal apoptosis [11].

Although the individual roles of these biomarkers have been widely investigated, their concurrent relationship with initial stroke severity, particularly within the first 24 h after symptom onset, remains insufficiently characterized. Previous studies have reported that elevated MMP-9 or IL-1β levels are associated with greater stroke severity and poorer outcomes [11,12].

However, the potential complementary value of these biomarkers in reflecting early neurological impairment has not been fully established yet. The identification of readily measurable and reliable inflammatory biomarkers during the hyperacute phase remains an important clinical need, as such markers may improve early severity assessment and provide further insights into the pathophysiology of AIS. Accordingly, the present study aimed to evaluate the association between serum MMP-9 and IL-1β levels and the initial neurological severity in patients with AIS.

Materials and Methods

Study Design

This case-control study was conducted from October 2025 to January 2026 and enrolled 120 participants. The patient group comprised 60 individuals with AIS (41 men and 19 women) diagnosed by a specialist neurologist. Patients were consecutively recruited from the inpatient neurology departments of Al-Furat Al-Awsat Neuroscience Center and Al-Najaf Teaching Hospital in Najaf City, Iraq. The control group comprised 60 age- and sex-matched apparently healthy volunteers (40 males and 20 females) with no history of cerebrovascular disease, chronic inflammatory disorders, autoimmune disease, malignancy, or other major systemic illness. This study protocol was approved by the Scientific Research Committee of the Najaf Health Directorate, Training and Human Development Center, Ministry of Health, Najaf, Iraq (Approval No. 35005, dated September 28, 2025). Institutional permission to conduct the study was obtained from the Al-Furat Al-Awsat Neuroscience Center and Al-Najaf Teaching Hospital. All study procedures were performed in accordance with the ethical principles of the Declaration of Helsinki and its amendments. Written informed consent was obtained from all participants or their legally authorized representatives before enrollment and before any study-related procedures.

The inclusion criteria for patients were as follows: (1) age between 30 and 80 years; (2) definitive diagnosis of AIS by a specialist neurologist based on clinical evaluation and neuroimaging findings; and (3) presentation to the hospital within 24 h of symptom onset, with intracerebral hemorrhage excluded by initial non-contrast computed tomography (CT) and cerebral ischemia confirmed by magnetic resonance imaging (MRI) showing an ischemic lesion.

The exclusion criteria for patients were as follows: (1) final diagnosis of hemorrhagic stroke or transient ischemic attack (TIA); (2) known chronic inflammatory disease or autoimmune disease, such as rheumatoid arthritis or systemic lupus erythematosus; (3) active malignancy or major surgery within three months before acute cerebral ischemia; (4) severe renal failure or severe hepatic failure; (5) clinical or laboratory evidence of acute infection at admission; and (6) chronic use of anticoagulants or systemic anti-inflammatory drugs.

Clinical Assessment and Data Collection

Baseline demographic and clinical data, including age, sex, nationality, body mass index (BMI), and relevant medical history, were recorded at the study entry using a standardized data collection form. Body weight was measured in kilograms using a calibrated scale, and height was measured in meters. BMI was calculated as weight divided by height squared (kg/m^2) and categorized as normal weight, overweight, or obese according to standard adult BMI cut-off values. Information on vascular risk factors, including hypertension and diabetes mellitus, was obtained from the medical history and hospital records. Stroke severity at admission was assessed by a certified neurologist using the National Institutes of Health Stroke Scale (NIHSS) before the laboratory biomarker analysis.

Blood Sample Collection and Processing

Venous blood samples (5 mL) were collected from all participants in appropriate vacuum tubes during enrollment. Blood samples were collected within 24 h of stroke onset for patients with AIS. The collected samples included 2 mL in a citrate tube containing 3.2% sodium citrate for D-dimer determination, 2 mL in an ethylenediaminetetraacetic acid (EDTA) tube for glycated hemoglobin (HbA1c) determination, and the remaining blood volume in a serum separator tube (SST). The SST samples were allowed to clot at room temperature for 30 min and then centrifuged at 3000 rpm for 5 min to obtain serum. Serum samples were aliquoted into sterile cryovials and stored at -20°C until analysis.

Laboratory Analyses

All biochemical and inflammatory markers were measured according to standard laboratory procedures, using commercially available assay kits. All blood parameters reported in this study were measured as quantitative variables, and no qualitative or semi-quantitative assays were performed. Serum MMP-9 and IL-1β levels were quantitatively measured using the sandwich ELISA technique with commercial ELISA kits (BT LAB, Shanghai, China), according to the manufacturer's instructions. Optical density was measured at 450 nm using an ELISA microplate read-

er, and biomarker concentrations were calculated from the standard curves supplied with the kits. Routine biochemical parameters, including total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), random blood sugar (RBS), and HbA1c levels, were quantitatively determined using automated clinical chemistry methods on a Mindray BS-240 Pro automated chemistry analyzer (Mindray Ltd., Shenzhen, China). Plasma D-dimer levels were quantitatively measured using an immunoassay-based concentration assay kit (Randox Laboratories Ltd., United Kingdom). Serum C-reactive protein (CRP) concentrations were quantitatively determined using a fluorescence immunoassay method on an i-Chroma device (Boditech Med Inc., Chuncheon, Republic of Korea).

Statistical Analysis

Statistical calculations were performed using IBM SPSS Statistics, Version 26.0. Continuous variables were assessed for normality using the Shapiro-Wilk test. Normally distributed variables are presented as mean ± standard deviation (SD), and categorical variables are presented as frequencies and percentages. Comparisons between categorical variables were performed using the chi-square test, whereas comparisons between normally distributed continuous variables were performed using the independent samples t-test. The relationships between biomarker concentrations and other continuous variables, including the NIHSS score, were estimated using Pearson's correlation coefficient (r). The threshold for statistical significance was set at $p < 0.05$ for all tests. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of MMP-9 and IL-1β in differentiating patients with AIS from healthy controls. The area under the curve (AUC), sensitivity, specificity, and optimal cut-off values were calculated.

Results

Table 1 summarizes the demographic and clinical characteristics of the 60 patients with AIS and 60 healthy controls included in the study. There were no significant differences between the two groups in terms of mean age (57.83 ± 10.78 vs. 57.70 ± 10.26 years; $p = 0.945$) or sex distribution ($p = 0.845$), confirming successful age and sex matching. In contrast, BMI was significantly higher in patients with AIS than in healthy controls (30.41 ± 3.47 vs. 22.50 ± 1.65 kg/m², $p < 0.0001$). In BMI categories, 26 patients with AIS (43.3%) were overweight and 33 (55.0%) were obese, whereas 59 healthy controls (98.3%) had a normal BMI. The NIHSS severity categorization showed that most patients had moderate stroke severity at admission.

Table 2 presents a comparative analysis of the metabolic and inflammatory biomarkers between patients with AIS and healthy controls. The AIS group demonstrated significantly elevated levels of nearly all the measured parameters. Specifically, the mean concentrations of RBS (147.6 ± 8.117 mg/dL), HbA1c (6.53 ± 0.267%), TC (212.7 ± 7.58 mg/dL), TG (203.8 ± 12.72 mg/dL), and LDL-C (143.3 ± 4.751 mg/dL) were significantly higher in patients than in controls ($p \leq 0.011$ for all). Similarly, CRP (14.22 ± 1.52

Table I. – Comparative Analysis of Demographic and Clinical Profiles between AIS Patients and Healthy Controls

Characteristic	AIS Patients (n = 60)	Healthy Controls (n = 60)	P-value
Age (years), mean ± SD	57.83 ± 10.78	57.70 ± 10.26	0.945
Age group, n (%)			0.952
< 40 years	3 (5.0%)	3 (5.0%)	
40-49 years	11 (18.3%)	11 (18.3%)	
50-59 years	16 (26.7%)	15 (25.0%)	
≥ 60 years	30 (50.0%)	31 (51.7%)	
Sex, n (%)			0.845
Male	41 (68.3%)	40 (66.7%)	
Female	19 (31.7%)	20 (33.3%)	
M:F ratio	2.16:1	2.00:1	
BMI (kg/m²), mean ± SD	30.41 ± 3.47	22.50 ± 1.65	<0.0001
BMI category, n (%)			<0.0001
Normal weight	1 (1.7%)	59 (98.3%)	
Overweight	26 (43.3%)	1 (1.7%)	
Obese	33 (55.0%)	0 (0.0%)	
NIHSS severity category, n (%)			<0.0001
No stroke (0)	0 (0.0%)	60 (100%)	
Minor stroke (1-4)	7 (11.7%)	0 (0.0%)	
Moderate stroke (5-15)	39 (65.0%)	0 (0.0%)	
Moderate-to-severe stroke (16-20)	14 (23.3%)	0 (0.0%)	
Severe stroke (21-42)	0 (0.0%)	0 (0.0%)	

Note: n = number of cases; SD = standard deviation; BMI = body mass index; NIHSS = National Institutes of Health Stroke Scale. Continuous variables were compared using the independent-samples t-test, and categorical variables were compared using the chi-square test.

mg/L), D-dimer (0.854 ± 0.079 μg/mL), MMP-9 (612.4 ± 115 ng/L), and IL-1β (824.5 ± 175.8 pg/mL) levels were significantly elevated in the AIS group (p = 0.001 for all). In contrast, HDL-C levels did not differ significantly between the two groups (52.05 ± 1.860 vs. 51.70 ± 0.7622 mg/dL; p = 0.863).

Correlation analysis was performed to investigate the interrelationships between key inflammatory markers and other measured variables among patients with AIS, and the results are presented in Table 3. A strong, statistically significant positive correlation was identified between MMP-9 and IL-1β levels (r = 0.929, p < 0.001). Furthermore, both MMP-9 and IL-1β levels showed significant positive correlations with CRP levels (r = 0.340, p = 0.008 and r = 0.425, p = 0.001, respectively). NIHSS scores were positively correlated with MMP-9 (r = 0.877, p < 0.001) and IL-1β (r = 0.925, p < 0.001). A significant negative correlation was observed between IL-1β and HDL-C levels (r = -0.296, p = 0.022). No other statistically significant correlations were observed with the remaining parameters.

Receiver operating characteristic (ROC) curve analysis of MMP-9 and IL-1β for the discrimination between patients with AIS and healthy controls is presented in Table 4. For MMP-9, the AUC was 0.89 (95% CI: 0.83-0.96), with an optimal cut-off value of 513.8 ng/L, yielding a sensitivity of 88.5% and a specificity of 80.9% (p < 0.0001). Similarly, IL-1β showed good discriminatory performance, with an AUC of 0.88 (95% CI: 0.82–0.94). At a cut-off value of 641.6 pg/ml, IL-1β yielded a sensitivity of 88.6% and a specificity of 70.2% (p < 0.0001). These findings indicate good discriminatory performance in this study population; however, further validation in clinically relevant comparator groups is required.

Table 4: Diagnostic Performance of MMP-9 and IL-1β as Biomarkers for AIS

Discussion

The present study demonstrated that serum levels of both MMP-9 and IL-1β were significantly elevated in patients within the first 24 h of AIS and were strongly correlated with the initial severity of neurological deficit, as measured by the NIHSS. These findings align with and extend the

Table II. – Comparative Analysis of Biochemical and Inflammatory Biomarkers in AIS Patients and Healthy Controls

Biomarker	AIS Patients (n = 60)	Healthy Controls (n = 60)	P-value
Metabolic Factors			
Random blood sugar (RBS), mg/dL Mean ± SD	147.6 ± 8.117	99.14 ± 1.413	0.001
HbA1c, % Mean ± SD	6.53 ± 0.267	5.26 ± 0.043	0.011
Lipid Profile			
Total cholesterol (TC), mg/dL Mean ± SD	212.7 ± 7.58	168.9 ± 1.448	0.001
Triglycerides (TG), mg/dL Mean ± SD	203.8 ± 12.72	96.05 ± 2.67	0.001
LDL-C, mg/dL Mean ± SD	143.3 ± 4.751	99.43 ± 2.324	0.001
HDL-C, mg/dL Mean ± SD	52.05 ± 1.860	51.70 ± 0.7622	0.863
Inflammatory Parameters			
C-reactive protein (CRP), mg/L Mean ± SD	14.22 ± 1.52	1.34 ± 0.11	0.001
D-dimer, μg/mL Mean ± SD	0.854 ± 0.079	0.249 ± 0.012	0.001
MMP-9, ng/L Mean ± SD	612.4 ± 115	417.4 ± 108.4	0.001
IL-1β, pg/mL Mean ± SD	824.5 ± 175.8	593.6 ± 117.7	0.001

Note: Values are expressed as mean ± SD. AIS = acute ischemic stroke; RBS = random blood sugar; TC = total cholesterol; TG = triglycerides; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; CRP = C-reactive protein. n = number of cases; SD = standard deviation; NS = not significant at P > 0.05; S = significant at P < 0.05.

Table III. – Correlation Matrix of MMP-9 and IL-1β with Metabolic and Inflammatory Markers in AIS Patients

Characteristic	MMP-9		IL-1β	
	r	p-value	r	p-value
MMP-9	1			
IL-1β	0.929	<0.001	1	
Glucose	0.234	0.109	0.205	0.116
HbA1c	0.214	0.118	0.221	0.090
Total cholesterol	0.181	0.166	0.215	0.099
Triglycerides	0.207	0.127	0.172	0.237
LDL-C	0.189	0.148	0.197	0.131
HDL-C	-0.173	0.186	-0.296	0.022
CRP	0.340	0.008	0.425	0.001
D-dimer	0.215	0.087	0.209	0.094
NIHSS	0.877	<0.001	0.925	<0.001

Note: r = Pearson's correlation coefficient; p = p-value; NIHSS = National Institutes of Health Stroke Scale..

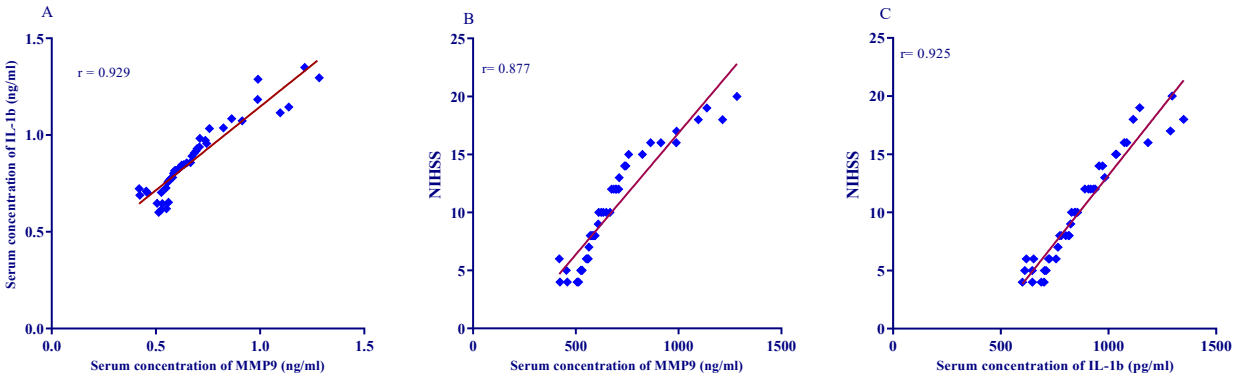


Figure 1: The correlations panel for (A) MMP-9 and IL-1β levels among IS patients (r = 0.929, p < 0.001). (B) NIHSS and MMP-9 levels among IS patients (r = 0.877, p < 0.001). (C) NIHSS and IL-1β levels among IS patients (r = 0.925, p < 0.001).

Table IV. – Diagnostic Performance of MMP-9 and IL-1β as Biomarkers for AIS

Marker	AUC (95% CI)	Cut-off value	Sensitivity	Specificity	P-value
MMP-9 (ng/L)	0.89 (0.83-0.96)	513.8	88.5%	80.9%	<0.0001
IL-1β (pg/mL)	0.88 (0.82-0.94)	641.6	88.6%	70.2%	<0.0001

AUC: Area under the curve

existing body of evidence implicating these two molecules as key mediators in the acute neuroinflammatory cascade that drives early brain injuries. These results support the potential utility of these metabolites as accessible biomarkers associated with early inflammatory activity and initial neurological severity in AIS.

The significant elevation of MMP-9 in our patient cohort is consistent with the large body of recent literature. Numerous studies have established that MMP-9 levels rise rapidly following an ischemic event, typically peaking within the first 24 hours, which corresponds to the sampling window of our study [13–15]. This temporal profile is critical because MMP-9 is a major enzymatic mediator of the blood-brain barrier (BBB) breakdown, acting through degradation of extracellular matrix components and tight-junction proteins after AIS.[16] Our finding of a strong positive correlation between MMP-9 levels and NIHSS scores is supported by several recent studies. For instance, Pacinella et al. (2025) and Xiao et al. (2025) reported that elevated MMP-9 concentrations were associated with greater neurological severity and poorer functional outcomes [17,18]. Furthermore, Liang et al. (2025) proposed that MMP-9 might be a promising biomarker capable of predicting the final infarct volume, providing a mechanistic link between its enzymatic activity, extent of tissue damage, and the resulting clinical deficits observed in our study [19].

Concurrently, our results showed a profound increase in serum IL-1β levels, a pivotal proinflammatory cytokine, in patients with AIS. This is in agreement with the established understanding that IL-1β is one of the earliest and most critical initiators of the post-stroke inflammatory cascade and is produced within hours by activated microglia [15,20]. The significant association between IL-1β levels and NIHSS scores is also consistent with the study of Catană et al. (2023) and the review by Iordache et al. (2025), which indicate that elevated IL-1β levels are associated with greater neurological severity and poorer outcomes after AIS [11,15]. Mechanistically, IL-1β contributes to the amplification of the inflammatory response by inducing other cytokines, promoting leukocyte adhesion and infiltration, and contributing to neuronal apoptosis, thereby potentially exacerbating the initial ischemic injury [15].

A novel aspect of our study is the concurrent measurement and analysis of MMP-9 and IL-1β levels, which revealed a significant positive correlation (r = 0.929). This strong correlation is consistent with the previously described experimental link between IL-1β signaling and MMP-9 expression.[21,22] This finding suggests that the early increase in IL-1β levels may contribute to the subsequent upregulation of MMP-9, thereby promoting a synergistic inflammatory mechanism of injury. IL-1β-driven inflammation initiates this cascade, and the resulting MMP-9 expression perpetuates it by disrupting the BBB, facilitating the infiltration of additional inflammatory cells and creating a vicious cycle of neuroinflammation and tissue damage [23,24]. Therefore, the combined measurement of these two biomarkers may provide complementary information regarding the inflammatory response and initial stroke severity.

Furthermore, our study identified significant correlations with other key biomarkers, shedding light on the interplay between inflammation, vascular injury, and lipid metabolism. Positive correlations between MMP-9, IL-1β, and CRP levels in AIS have been previously reported. Surjawan et al. (2012) and Cimmino et al. (2013) described a significant relationship between MMP-9 and CRP, suggesting that CRP-related inflammatory activity may pro-

mote MMP-9 expression and may be associated with AIS outcomes. Similarly, Sarafaniuk and Klymenko (2022) reported a positive association between IL-1β and CRP, supporting the view that pro-inflammatory cytokines and acute-phase proteins may serve as markers of inflammation in AIS [25–27].

Finally, the negative association between IL-1β and HDL in the present study is noteworthy. HDL exerts anti-inflammatory and immunomodulatory effects [28], and experimental evidence has shown that HDL can suppress inflammasome activation and reduce IL-1β secretion [29]. Therefore, the negative association observed in the present study may reflect increased inflammatory activity accompanied by a reduced HDL-associated protective capacity. This interaction highlights the close interplay between the inflammatory and metabolic pathways in AIS.

Limitations

This study had several limitations. First, its case-control design precludes causal inference and limits the interpretation of biomarkers as prognostic indicators. Second, the sample size was relatively modest, and the study was conducted at two hospitals within a single geographic region, which may limit generalizability. Third, biomarker levels were measured at a single time point within 24 h of stroke onset, and no longitudinal follow-up or functional outcome assessment was performed. Finally, the observed differences in BMI and metabolic parameters between patients and controls may have confounded the results.

Future Research Directions

Future studies should include larger multicenter cohorts and clinically relevant comparator groups, such as those with transient ischemic attack, hemorrhagic stroke, and stroke mimics. In addition, patients with AIS should be stratified according to NIHSS severity categories and followed longitudinally using functional outcome measures, such as the modified Rankin Scale, at 30 or 90 days. Serial measurements of MMP-9 and IL-1β would help clarify their temporal profiles, whereas multivariable models should be adjusted for BMI, diabetes mellitus, dyslipidemia, CRP, D-dimer, infection status, and reperfusion therapy.

Conclusion

In conclusion, this study demonstrated that serum MMP-9 and IL-1β levels measured within 24 h of AIS were significantly associated with initial neurological severity. The close correlation among these markers, as well as their associations with CRP and HDL-C, highlights the interplay between inflammation and metabolic dysregulation during the acute phase of AIS. These findings suggest that the combined assessment of MMP-9 and IL-1β may provide additional insight into early inflammatory activity in AIS; however, larger prospective studies with longitudinal follow-up are needed to validate their clinical utility.

Declarations

Funding:

This research received no external funding.

Author Contributions

Conceptualization: HAR KMS; methodology: HAR KMS; validation: HAR KMS; formal analysis: HAR KMS; investigation: HAR KMS; resources: HAR KMS; data curation: HAR KMS; writing – original draft preparation: HAR KMS; writing – review and editing: all authors; visualization: HAR KMS; supervision: HAR KMS; project administration: HAR KMS; funding acquisition: HAR KMS. All authors have read and agreed to the published version of this manuscript.

Conflict of Interest:

The authors declare no conflict of interest.

Availability of data and material

The datasets used and/or analyzed in the current study are available from the corresponding author upon reasonable request.

Ethical Approval

This study was approved by the Scientific Research Committee of the Najaf Health Directorate, Training and Human Development Center, Ministry of Health, Najaf, Iraq (Approval No. 35005, dated September 28, 2025). The study was conducted at the Al-Furat Al-Awsat Neuroscience Center and Al-Najaf Teaching Hospital in Najaf, Iraq. Written informed consent was obtained from all participants or their legally authorized representatives prior to enrollment. All procedures were performed in accordance with the Declaration of the Helsinki.

Use of Artificial Intelligence:

Used artificial intelligence to improve sentence structure and clarity.

References

1. Feigin VL, Brainin M, Norrving B, Martins SO, Pandian J, Lindsay P, et al. World Stroke Organization: Global Stroke Fact Sheet 2025. Int J stroke Off J Int Stroke Soc. 2025 Feb;20(2):132–44.
2. Majumder D. Ischemic Stroke: Pathophysiology and Evolving Treatment Approaches. Neurosci insights. 2024;19:26331055241292600.
3. Yang Y, Zhu H, Xiong T, Li S. Inflammatory Biomarkers in Ischemic Stroke: Mechanisms, Clinical Applications, and Future Directions. Neurosurg Subspecialties [Internet]. 2025;1(4):188–96. Available from: https://www.xiahepublishing.com/3067-6150/NSSS-2025-00029
4. Iadecola C, Anrather J. The immunology of stroke: from mechanisms to translation. Nat Med. 2011 Jul;17(7):796–808.
5. Alsbrook DL, Di Napoli M, Bhatia K, Biller J, Andalib S, Hinduja A, et al. Neuroinflammation in Acute Ischemic and Hemorrhagic Stroke. Curr Neurol Neurosci Rep. 2023 Aug;23(8):407–31.
6. Sun B, Zhang J, Li Z, Wang J, Zhao C, Xu X. Role of damage-associated molecular patterns in the pathogenesis and therapeutics of traumatic brain injury. Burn Trauma [Internet]. 2025 Jan 3;13:tkaf043. Available from: https://doi.org/10.1093/burnst/tkaf043
7. Blase A, di Girasole CG, Benjamin L, Turowski P. Phased blood-brain barrier disruption in ischaemic stroke: implications for therapy? Fluids

Barriers CNS. 2025 Aug;22(1):90.
8. Sasannia S, Leigh R, Bastani PB, Shin HG, van Zijl P, Knutsson L, et al. Blood-brain barrier breakdown in brain ischemia: Insights from MRI perfusion imaging. Neurotherapeutics [Internet]. 2025;22(1):e00516. Available from: https://www.sciencedirect.com/science/article/pii/S1878747924002034
9. Huang X, Hussain B, Chang J. Peripheral inflammation and blood–brain barrier disruption: effects and mechanisms. CNS Neurosci Ther [Internet]. 2021 Jan 1;27(1):36–47. Available from: https://doi.org/10.1111/cns.13569
10. Rodríguez-Gómez JA, Kavanagh E, Engskog-Vlachos P, Engskog MKR, Herrera AJ, Espinosa-Oliva AM, et al. Microglia: Agents of the CNS Pro-Inflammatory Response. Vol. 9, Cells. 2020. p. 1717.
11. Catană MG, Popenţiu IA, Văleanu M, Roman-Filip C, Mihăilă RG. IL-1 Beta-A Biomarker for Ischemic Stroke Prognosis and Atherosclerotic Lesions of the Internal Carotid Artery. Medicina (Kaunas). 2023 Oct;59(10).
12. Montaner J, Alvarez-Sabín J, Molina C, Anglés A, Abilleira S, Arenillas J, et al. Matrix metalloproteinase expression after human cardioembolic stroke: temporal profile and relation to neurological impairment. Stroke. 2001 Aug;32(8):1759–66.
13. Emmerich J, Chanpura A, Lu T, Baird A, Barone F, Gustafson D, et al. Blood-based MMP-9 for the early differentiation of acute ischemic stroke: a systematic review and meta-analysis. J stroke Cerebrovasc Dis Off J Natl Stroke Assoc. 2025 Nov;34(11):108454.
14. Guo P, Li H, Zhang X, Liu Y, Xue S, Yong VW, et al. Matrix metalloproteinase-9 in hemorrhagic transformation after acute ischemic stroke (Review). Mol Med Rep. 2025 Aug;32(2).
15. Iordache MP, Buliman A, Costea-Firan C, Gligore TCI, Cazacu IS, Stoian M, et al. Immunological and Inflammatory Biomarkers in the Prognosis, Prevention, and Treatment of Ischemic Stroke: A Review of a Decade of Advancement. Int J Mol Sci. 2025 Aug;26(16).
16. Turner RJ, Sharp FR. Implications of MMP9 for Blood Brain Barrier Disruption and Hemorrhagic Transformation Following Ischemic Stroke. Front Cell Neurosci [Internet]. 2016;Volume 10. Available from: https://www.frontiersin.org/journals/cellular-neuroscience/articles/10.3389/fncel.2016.00056
17. Pacinella G, Bona MM, Todaro F, Ciaccio AM, Daidone M, Tuttolomondo A. Tracing Inflammation in Ischemic Stroke: Biomarkers and Clinical Insight. Int J Mol Sci. 2025 Oct;26(19).
18. Xiao L, Huang Y, Wu L, Zeng S, Qiu C, Li X, et al. The role of inflammation in Ischemic stroke: from biomarker to treatment. Front Immunol. 2025;16:1608353.
19. Liang Y, Chen J, Chen Y, Tong Y, Li L, Xu Y, et al. Advances in the detection of biomarkers for ischemic stroke. Front Neurol. 2025;16:1488726.
20. Matys P, Mirończuk A, Starosz A, Grubczak K, Kochanowicz J, Kułakowska A, et al. Expanding Role of Interleukin-1 Family Cytokines in Acute Ischemic Stroke. Int J Mol Sci. 2024 Sep;25(19).
21. Tsai MM, Chen JL, Lee TH, Liu H, Shanmugam V, Hsieh HL. Brain Protective Effect of Resveratrol via Ameliorating Interleukin-1β-Induced MMP-9-Mediated Disruption of ZO-1 Arranged Integrity. Biomedicines. 2022 May;10(6).
22. Zhu H, Hu S, Li Y, Sun Y, Xiong X, Hu X, et al. Interleukins and Ischemic Stroke. Front Immunol. 2022;13:828447.
23. Yang C, Hawkins KE, Doré S, Candelario-Jalil E. Neuroinflammatory mechanisms of blood-brain barrier damage in ischemic stroke. Am J Physiol Cell Physiol. 2019 Feb;316(2):C135–53.
24. Wang H, Yiqiang Z, Cai J, Guo J. Immune-mediated blood-brain barrier disruption after ischemic stroke: mechanisms and therapeutic targets. Front Immunol. 2025;16:1716041.
25. Cimmino G, Ragni M, Cirillo P, Petrillo G, Loffredo F, Chiariello M, et al. C-reactive protein induces expression of matrix metalloproteinase-9: a possible link between inflammation and plaque rupture. Int J Cardiol. 2013 Sep;168(2):981–6.
26. Surjawan Y, As' ad S, Ranakusuma TAS, Wijaya A. C-reactive protein and matrix metalloproteinase-9 are associated with outcome of ischemic stroke. Indones Biomed J. 2012;4(3):157–63.
27. Sarafaniuk N, Klymenko M. PRODUCTION OF INTERLEUKINS 1β, 2, 4, 10 AND C-REACTIVE PROTEIN IN ISCHEMIC STROKE. Wiad Lek. 2022;75(3):598–604.
28. Bonacina F, Pirillo A, Catapano AL, Norata GD. HDL in Immune-Inflammatory Responses: Implications beyond Cardiovascular Diseases. Cells. 2021 Apr;10(5).
29. Thacker SG, Zarzour A, Chen Y, Alcicek MS, Freeman LA, Sviridov DO, et al. High-density lipoprotein reduces inflammation from cholesterol crystals by inhibiting inflammasome activation. Immunology. 2016 Nov;149(3):306–19.