THE IMPORTANCE OF CELL ADHESION MOLECULE LEVELS IN THE COURSE AND PROGNOSIS OF HEMORRHAGIC STROKE

Gulchekhra E. Usmanova - Ph.D. doctoral student
Gulnora S. Rakhimbaeva - D.M.Sc., professor
Tashkent State Medical University (Tashkent, Uzbekistan)
Guli.uzb1@gmail.com

Abstract. *This study investigates the role of intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) as biomarkers in hemorrhagic stroke prognosis. Analyzing 83 patients, researchers found that ICAM- 1 levels increased 2.5-fold within 48 hours and continued rising, while VCAM-1 levels increased 1.5-fold before slightly decreasing. Both correlated with stroke severity and mortality. The study highlights the Full Outline of Unresponsiveness (FOUR) scale as a superior tool for assessing critically ill patients and suggests that ICAM-1 and VCAM-1 could aid in predicting stroke outcomes and guiding treatment strategies.*

Keywords *— hemorrhagic stroke, Glasgow Coma Scale (GCS), FOUR, ICAM-1, VCAM-1*

Introduction. Hemorrhagic strokes are among the most severe forms of cerebrovascular disease, often leading to high rates of premature death, disability, and complications. These strokes impose significant economic burdens on society, requiring long-term treatment and rehabilitation. According to international data, intracerebral hemorrhages account for 3.7% to 38.5% of all stroke cases, with an incidence rate of 1.9 per 100,000 people [1]. In the United States, the mortality rate from hemorrhagic strokes in 2020 ranged from 39% to 50%, with half of these deaths occurring within the first 48 hours [3]. Additionally, the one-month mortality rate for intracerebral hematomas (ICH) is approximately 40%, increasing to 54% within a year [4-5].

Arterial hypertension is the leading cause of primary intracerebral hemorrhage, responsible for over 50% of cases. In Uzbekistan, more than 60,000 cases of acute cerebrovascular accidents are recorded annually. The disability rate following stroke is 83.8%, while the mortality rate stands at 17.3%, with over 160 new cases occurring daily. Given the diverse clinical presentations of hemorrhagic stroke, there is an urgent need to develop new prognostic criteria to assess disease severity, predict outcomes, and evaluate the risk of recurrence [2].

Despite extensive research efforts, the prognosis of hemorrhagic stroke remains a critical issue. The identification of reliable blood biomarkers for diagnosis and outcome prediction is an area of growing interest. Neuroinflammation markers in peripheral blood reflect the body's response to acute cerebrovascular events, offering potential insights into disease progression.

Aim of the Study. This study aims to evaluate the role of inflammatory biomarkers intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) in the pathogenesis of hemorrhagic stroke.

Materials and Methods. A total of 83 patients with hemorrhagic stroke were examined at the intensive care and neurology departments of the Tashkent Medical Academy Clinic. All patients were in the acute stage of the disease, diagnosed with hemorrhagic stroke. Comprehensive assessments included clinical- neurological examinations, neuroimaging, and laboratory analyses, following modern clinical guidelines. The GCS and the Full Outline of UnResponsiveness (FOUR) scale were used to assess consciousness levels upon admission.

ICAM-1 and VCAM-1 levels were determined by quantitative enzyme immunoassay. Statistical processing of the results was carried out using Statistica 6.0.

Results and Discussion. Of the 83 patients, 46 (55.4%) were men and 37 (44.6%) were women, with an age range of 36–84 years (mean age: 63.2 years).

Table 1.

Distribution of patients by age

Age	Number of patients	Percentage (%) of total
30-39	4	4.8%
40-49	16	19.3%
50-59	25	30.1%
60-69	29	34.9%
70-79	6	7.2%
80-90	3	3.6%

By hemorrhage localization: parenchymal – 50.6% (n=42), subarachnoid – 12% (n=10), parenchymal- subarachnoid – 8.4% (n=7), brainstem – 3.6% (n=3), ventricular – 7.2% (n=6), parenchymal-ventricular – 8.4% (n=7), subarachnoid-ventricular – 4.8% (n=4), subarachnoid-parenchymatous-ventricular – 2.4% (n=2) and hemorrhage into the cerebellum – 2.4% (n=2).

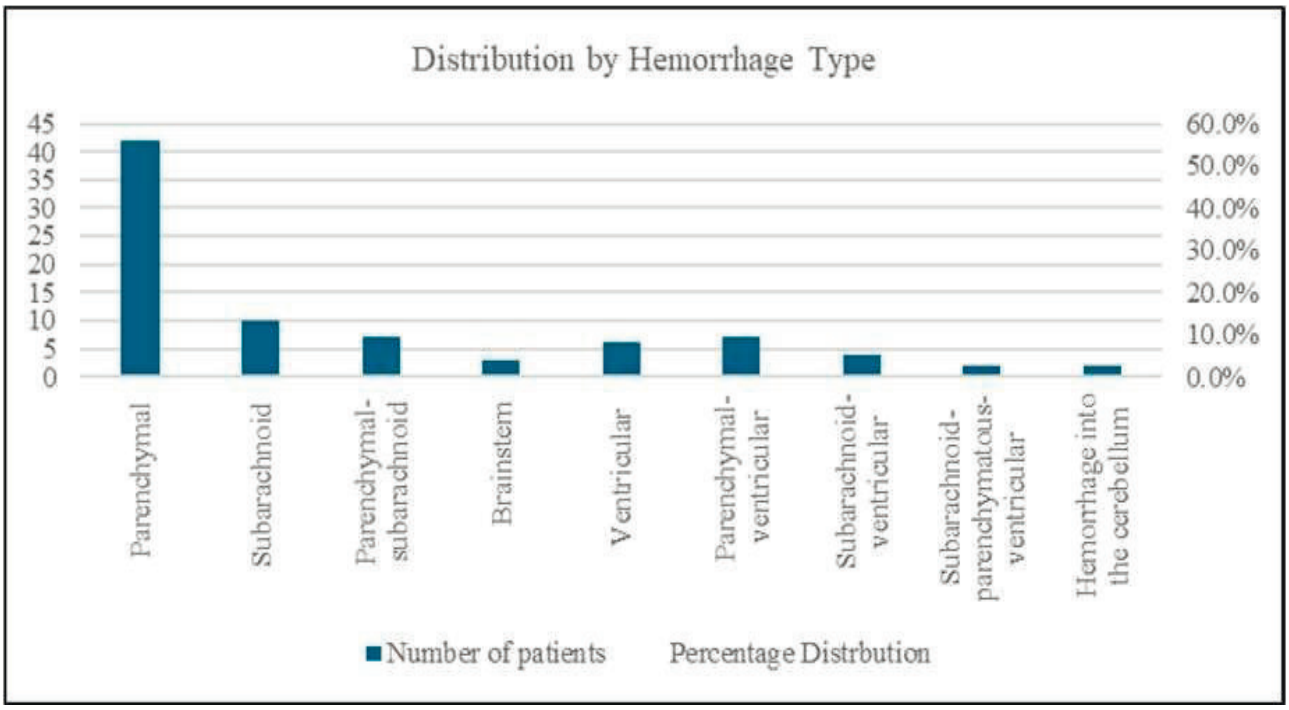


Fig. 1. Distribution by Hemorrhage Type

The GCS, FOUR Scale, and Hemphill Scale were used to assess neurological impairment and predict 30-day survival in hemorrhagic stroke patients. The Hemphill Scale evaluates five key factors: patient age (<80 or >80 years), GCS score, hematoma location and volume, and the presence of intraventricular hemorrhage. According to the GCS, 54.2% (n=45) of patients exhibited moderate obtundation, 16.9% (n=14) had profound obtundation, 10.8% (n=9) were in stupor, 9.6% (n=8) had grade I coma, and 8.4% (n=7) had grade II coma. No fatalities occurred among patients scoring 1-2 points, while one death was recorded at 3 points, and seven deaths at 4 points.

The FOUR scale is a comprehensive tool used to assess neurological status, focusing on eye responses, brainstem reflexes, motor responses, and respiratory patterns. Unlike the GCS, it provides a more detailed evaluation of brainstem function, making it especially valuable for intubated patients

and those in deep coma states. The FOUR scale ranges from 0 (deep coma, cortical death) to 16 points (clear consciousness), allowing for a nuanced assessment of neurological impairment [6].

In this study, patients were categorized based on their FOUR scale scores 58% (n=14) had a severe condition with moderate stupor (15 points), 17% (n=7) exhibited a severe course with deep stupor (13–14 points), 12% (n=5) had stupor (9–12 points), 7% (n=4) were in a comatose state (7–8 points), and 6% (n=2) had grade II coma (1–6 points).

Table 2.

Distribution of Patients By Four Scale

FOUR Scale	Points	Number of patients	Percentage (%) of total
Moderate stupor	15	48	57.8%
Deep stupor	13-14	14	16.9%
Stupor	9-12	10	12.0%
Coma I	7-8	6	7.2%
Coma II	1-6	5	6.0%

The FOUR scale's advantages lie in its ability to differentiate between varying levels of impaired consciousness and to predict early mortality, making it particularly useful in critical care and stroke management. It is also superior to GCS for assessing brainstem reflexes and respiratory function, crucial in determining the severity and prognosis of hemorrhagic stroke.

Neurological Symptoms and Biomarker Analysis

Hemorrhagic stroke patients exhibited severe neurological deficits, including motor disturbances (hemiparesis/ hemiplegia) in 95%, oculomotor nerve paresis in 27%, dysphagia in 31%, dysarthria in 52%, aphasia in 49%, hemianopsia in 24%, facial muscle weakness on the opposite side in 95%, and impaired sensation in 69% of the cases.

Additionally, ICAM-1 and VCAM-1 levels were significantly elevated, reflecting the body's inflammatory response to acute cerebrovascular injury.

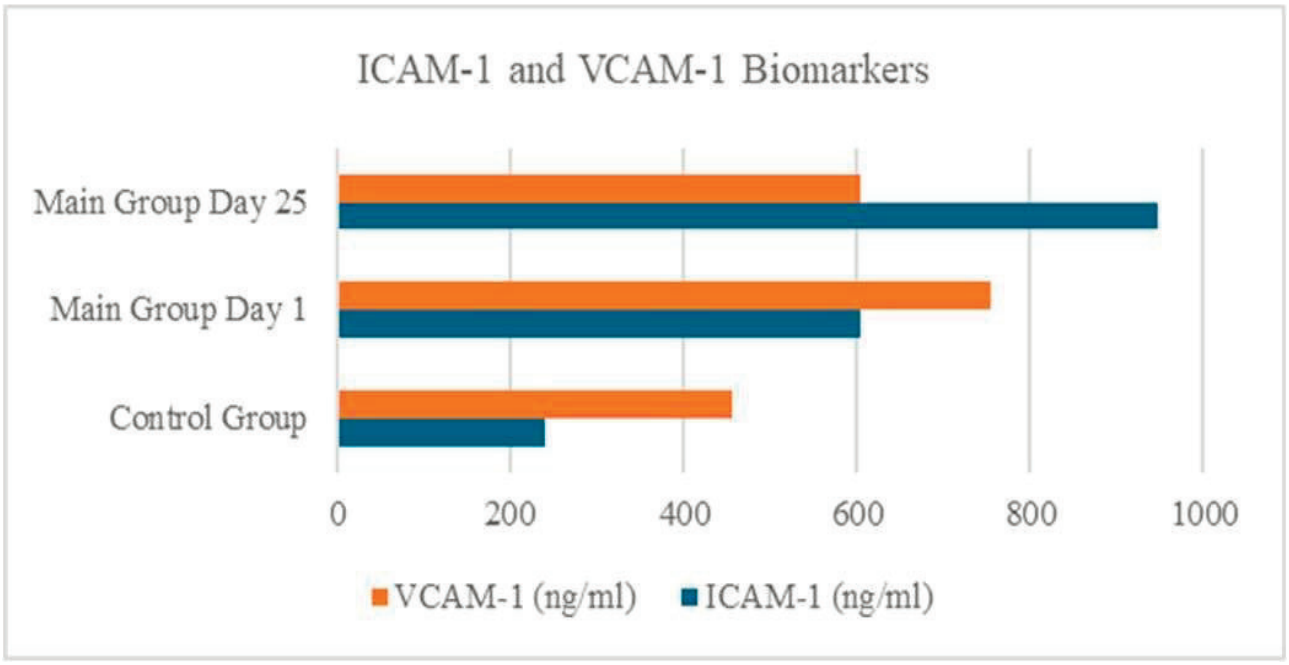


Fig. 2. ICAM-1 and VCAM-1 Biomarker Levels

ICAM-1 levels increased 2.5-fold within the first 48 hours compared to the control group and continued rising by day 25. A significant positive correlation was found between ICAM- 1 levels and NIH stroke severity scores at day 25. VCAM-1 levels increased 1.5-fold within the first 48 hours and showed a slight decline by day 25. Higher VCAM-1 levels correlated with more severe neurological deficits. Consequently, both ICAM-1 and VCAM-1 levels were notably elevated in patients with fatal outcomes.

These findings highlight the critical role of inflammatory processes in stroke progression and underscore the potential of ICAM-1 and VCAM-1 as prognostic biomarkers.

ICAM-1 and VCAM-1 are cell adhesion molecules involved in inflammatory responses and are regulated by pro- inflammatory cytokines and cellular stress. VCAM-1, primarily expressed by endothelial cells, is released into the bloodstream, and its levels have been shown to correlate with stroke severity in ischemic events [7-8].

Hemorrhagic strokes most commonly affect individuals of working age and are frequently associated with intracerebral hematomas. Prognosis is influenced by factors such as age, consciousness level (as assessed by the GCS and FOUR scales), hematoma localization, and volume.

Understanding the pathophysiological mechanisms underlying hemorrhagic stroke can enhance early treatment strategies and improve patient outcomes. Rapid correction of hemodynamic, metabolic, and electrolyte imbalances in the acute phase is critical in determining neurological recovery.

The integration of neurological scales in clinical practice is essential for accurate diagnosis, therapeutic decision- making, and prognosis estimation. The development of combinatory prognostic scales remains a promising area in neurology. The FOUR scale, in particular, offers advantages over the GCS by providing a more comprehensive assessment of neurological function, particularly in intubated patients.

Conclusion. VCAM-1 plays a crucial role in inflammatory processes and is a key factor in the development of cardiovascular diseases, including hypertension, ischemic heart disease, and stroke. Cell adhesion molecules such as ICAM-1 and VCAM1 hold promise for further research in stroke prognosis and therapeutic strategies.

The use of these biomarkers could enhance cardiovascular risk assessment, while the FOUR scale remains a valuable tool for evaluating neurological function and predicting mortality in critically ill patients. Additionally, the FOUR scale is effective in distinguishing coma-mimicking conditions and has significant utility in clinical trials assessing treatment outcomes in hemorrhagic stroke.

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