DOI: 10.37990/medr.1498380 Med Records 2024;6(3):396-400

MEDICAL RECORDS-International Medical Journal

Research Article

# The Role of Laboratory Parameters in the Differentiation of Stroke Cases

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**Abstract**

**Aim:** Globally, stroke is considered as one of the most important causes of mortality and morbidity. The most important steps for the diagnosis of stroke include rapid and focused physical examination followed by determination of the stroke's type. The study was conducted to determine the relationship between laboratory parameters frequently requested in the emergency department and stroke type.

**Material and Method:** The study is a retrospective cross-sectional study. Patients' age, gender, comorbidities, stroke type, hospitalization, in-hospital mortality and laboratory parameters were recorded and compared. p value of <0.05 was considered statistically significant.

**Results:** 251 patients were included in the study. The median age of the patients included in the study was 74 [64-81]. 137 (54.6%) of the patients were women. The most common comorbidity in the patients included in the study was hypertension. Ischemic stroke was seen in 236 (94%) patients and 236 (94%) were hospitalized. the platelet count in the hemorrhagic stroke and ischemic stroke group was 173 (153–204) $10^9$/L and 218 (180–2262) $10^9$/L, respectively. Platelet count in patients in the hemorrhagic stroke group was found to be significantly lower than in the ischemic stroke group (p=0.013). There was no significant difference in white blood cell, lymphocyte, sodium, potassium, C-reactive protein levels between both groups (p=0.318, 0.245, 0.461, 0.202, 0.322; respectively).

**Conclusion:** Platelet count may be used as a biomarker to differentiate between ischemic and hemorrhagic stroke in patients who are examined for stroke.

**Keywords:** Differentiation, hemorrhagic, ischemic, platelet, stroke

## INTRODUCTION

Globally, stroke is considered as one of the most important causes of mortality and morbidity (1). Although the incidence and prevalence of hemorrhagic stroke has gradually decreased compared to ischemic stroke, both rank among the major causes of disability and long-term hospitalization (2). After 25 years of age, for all people, the lifetime risk of having a stroke is accepted as 25% (3).

The most important steps for the diagnosis of stroke include rapid and focused physical examination and exclusion of stroke mimics, followed by determination of the stroke's type (3). Neuroimaging is an important technique that determines stroke type; however, there are certain challenges in early diagnosis and treatment including the difficulty associated with detecting early and small infarct areas via computed tomography (CT) and the availability of neuroimaging means at healthcare facilities (4). Furthermore, it is well-established that non-contrast CT, as diagnostic tool, may have reduced accuracy in patients with subarachnoid hemorrhage more than 6 hours after symptom onset (5). Thus, the availability of objective, simple, and inexpensive blood parameters for the diagnosis and prognosis of this patient group may facilitate the management of patients.

Ionic imbalance, electrical disturbances, and thrombotic events caused by ischemia and associated damage begin within minutes following ischemic stroke. This pathophysiologic cascade results in necrosis or apoptosis after a certain time period (6). In hemorrhagic stroke,

CITATION
Bildik B, Bulak D, Eroglu BS, et al. The Role of Laboratory Parameters in the Differentiation of Stroke Cases. Med Records. 2024;6(3):396-400. DOI:1037990/medr.1498380

**Received:** 09.06.2024 **Accepted:** 27.08.2024 **Published:** 12.09.2024
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proinflammatory and anti-inflammatory pathways are simultaneously activated following the hemorrhage (3). These pathophysiologic changes may influence changes in biomarkers. The present study assesses the efficacy of low-cost and easy-to-access laboratory parameters, which are frequently used in emergency departments to determine stroke type.

## MATERIAL AND METHOD

### Study Design

The study is a retrospective cross-sectional study that includes patients >18 years of age who were presented to the emergency department between January 02, 2023–January 02,2024 and diagnosed with stroke. This study adhered to the principles of the Declaration of Helsinki. The study was conducted after the approval of the Institutional Ethics Committee (2024/1782). All data was carefully anonymized to ensure confidentiality, and thorough statistical analyses were conducted following this meticulous process.

### Patient Selection

The study encompassed patients who had been diagnosed with stroke in the emergency department of our hospital. Exclusions comprised patients under 18 years of age, pregnant women, individuals diagnosed with transient ischemic attack, those with a history of head trauma, patients for whom complete data could not be retrieved from the hospital information system, and those who received a different diagnosis after being hospitalized following a stroke diagnosis in the emergency department.

### Data Collection

Patients' age, gender, comorbidities (cardiac disease, diabetes mellitus, hypertension, previous cerebrovascular disease, chronic obstructive pulmonary disease, chronic renal failure, and malignancy), hospitalization, stroke type, and mortality were recorded. Laboratory parameters, including platelet, white blood count (WBC), hemoglobin, lymphocyte, C-reactive protein (CRP), albumin, urea, creatinine, AST, ALT,sodium, potassium, and international normalized ratio levels were recorded. The data were taken from the institutional automation system.

### Outcome

To determine the relationship between laboratory parameters frequently requested in the emergency department and stroke type.

### Statistical Analysis

For the purpose of conducting statistical analyses, we utilized IBM SPSS version 22.0. The normal distribution hypothesis for the continuous variables was tested using the Shapiro-Wilks and Kolmogorov-Smirnov tests. We presented data with normal distribution as mean ± standard deviation, and data without normal distribution as median (1st and 3rd quartile values). Group differences were assessed using Student's t-test or Mann-Whitney U-test as appropriate, while Pearson's chi-squared test was employed to compare categorical data. To illustrate the sensitivity and specificity of the platelet count, Receiver Operating Characteristic (ROC) analysis was conducted, and specific values were calculated to depict sensitivity and specificity. We considered a p-value of <0.05 to be indicative of statistical significance.

## RESULTS

251 patients were included in the study. The median age of the patients included in the study was 74 [64-81]. 137 (54.6%) of the patients were women. The most common comorbidity in the patients included was hypertension. Of the 185 patients (73.7%), hypertension was an additional disease. Regarding other comorbidities, 121 (48.2%) of the patients had coronary artery disease, 89 (35.5%) had diabetes mellitus, and 66 (26.3) had a history of cerebrovascular disease. Ischemic stroke was seen in 236 (94%) patients and 236 (94%) were hospitalized. The number of mortalities was 13 (5.2%). The demographic data for the patients is conveniently available in Table 1.

Table 1 . Demographic data of the patients

| Variable | Overall (n=251) |
|---|---|
| Age (year) median [Q1-Q3] | 74 [64-81] |
| Gender n (%) | |
| Female | 137 (54.6) |
| Male | 114 (45.4) |
| Comorbidities n (%) | |
| Hypertension | 185 (73.7) |
| Coronary artery disease | 121 (48.2) |
| Diabetes mellitus | 89 (35.5) |
| Past cerebrovascular event | 66 (26.3) |
| Chronic obstructive pulmonary disease | 25 (10.0) |
| Chronic renal failure | 19 (7.6) |
| Malignancy | 11 (4.4) |
| Stroke type n (%) | |
| Hemorrhagic | 15 (6.0) |
| Ischemic | 236 (94.0) |
| Hospital admission n (%) | |
| Yes | 236 (94.0) |
| No | 15 (6.0) |
| Mortality n (%) | |
| Yes | 13 (5.2) |
| No | 238 (94.8) |

On examining the relationship between laboratory parameters and hemorrhagic and ischemic stroke subgroups, the platelet count in the hemorrhagic stroke and ischemic stroke group was 173 (153–204) $10^9$/L and 218 (180–2262) $10^9$/L, respectively. Platelet count in patients in the hemorrhagic stroke group was found to be significantly lower than in the ischemic stroke group (p=0.013). The median WBC count in the hemorrhagic stroke group was 9.4 [6.7–10.6] $10^9$/L, while in the ischemic group it was 7.7 [6.2–9.7] $10^9$/L. There was not any

significant difference in WBC count between both groups (p=0.318). Similarly, while the median CRP level in the hemorrhagic stroke group was 5.5 [3.8-9.8] mg/L, it was 8.8 [4.0-17.4] mg/L in the ischemic stroke group, and no significant difference was found between the two groups (p=0.322). While lymphocyte, sodium and potassium in the hemorrhagic stroke group were 1.30 [1.1–2.1], 139 [139-140] and 4.6 [4.2–5.1], significant difference was not detected between the hemorrhagic and ischemic stroke groups (p values=0.245, 0.461, 0.202; respectively). Data on the relationship between parameters and subgroups are given in Table 2.

**Table 2. Relationship between laboratory parameters and hemorrhagic/ischemic subgroups**

| Variable | Hemorrhagic | Ischemic | p |
|---|---|---|---|
| **Hgb (mg/dl) mean±SD** | 13.4±1.4 | 12.7±1.9 | 0.187 |
| **WBC ($10^9$/L) median [Q1-Q3]** | 9.4 [6.7-10.6] | 7.7 [6.2-9.7] | 0.318 |
| **Lymphocyte ($10^9$/L) median [Q1-Q3]** | 1.30 [1.1-2.1] | 1.8 [1.3-2.3] | 0.245 |
| **Platelet ($10^9$/L) median [Q1-Q3]** | 173 [153-204] | 218 [180-262] | 0.013* |
| **Urea (mg/dl) median [Q1-Q3]** | 46 [36-51] | 51.4 [34-57] | 0.999 |
| **Creatinine (mg/dl) median [Q1-Q3]** | 0.8 [0.7-1.2] | 0.9 [0.7-1.2] | 0.484 |
| **AST (U/L) median [Q1-Q3]** | 27 [19-35] | 23 [18-28] | 0.229 |
| **ALT (U/L) median [Q1-Q3]** | 15 [11-23] | 16 [11-23] | 0.982 |
| **Albumin median [Q1-Q3]** | 4.3 [4.0-4.6] | 4.1 [3.9-4.4] | 0.413 |
| **Na mEq/L median [Q1-Q3]** | 139 [139-140] | 139 [137-141] | 0.461 |
| **K mEq/L median [Q1-Q3]** | 4.6 [4.2-5.1] | 4.4 [4.0-4.8] | 0.202 |
| **CRP mg/L median [Q1-Q3]** | 5.5 [3.8-9.8] | 8.8 [4.0-17.4] | 0.322 |
| **INR median [Q1-Q3]** | 1.0 [0.9-1.2] | 1.0 [0.9-1.1] | 0.905 |

Hgb: hemoglobin, WBC: white blood cell, AST: aspartate aminotransferase, ALT: alanine transaminase, Na: sodium, K: potassium, CRP: C-reactive protein, INR: international normalized ratio

Sensitivity, specificity, positive predictive value, and negative predictive values were 64.83%, 73.33%, 97.45%, and 11.7%, respectively, for the ROC analysis to test the effectiveness of platelet count for determining ischemic stroke, (area under the curve=0.692) (Figure 1) when the platelet count was set to 196×$10^9$/L.

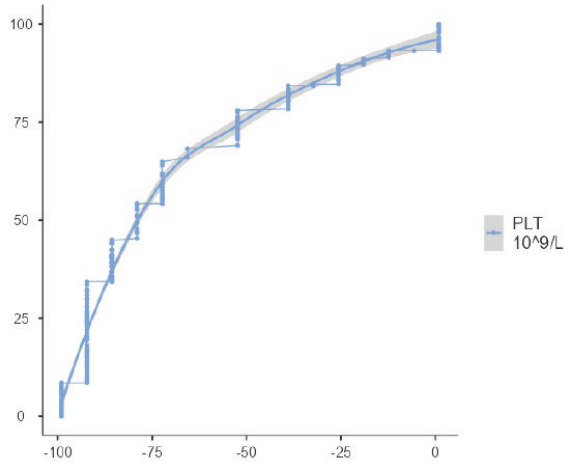


**Figure 1.** The ROC analysis to test the effectiveness of platelet count for determining ischemic stroke

## DISCUSSION

Our study showed a significant difference in platelet count between hemorrhagic and ischemic stroke patients. Specifically, patients with hemorrhagic strokes exhibited a notably lower platelet count in comparison to those with ischemic strokes. Previous studies focusing on the role of platelets in atherosclerotic events (7) reported elevated platelet counts in isolated thrombotic events, including pulmonary embolism (8). Other studies suggested that mean platelet volume, i.e., a biomarker of platelet turnover, was increased in patients with deep vein thrombosis (8,9). Prodan et al. reported that coated platelets, a platelet subgroup, were lower in patients with spontaneous intracerebral hemorrhage than in the control group (10). In the same study, high levels of coated platelets were observed in patients with non-lacunar ischemic infarction with even lower levels of coated platelets in patients with non-lacunar ischemic stroke and early hemorrhagic transformation (10). A retrospective study of 455 cases reported that elevated platelet count and low platelet count were risk factors for ischemic and hemorrhagic stroke, respectively (11). This suggests that our study findings are consistent with some studies in the literature.

Kakhki et al., in a 2020 study, reported that the lymphocytes percentage and WBC were higher in patients with ischemic stroke than in patients with hemorrhagic stroke (12). In a particular study, no significant difference was found between the hemorrhagic and ischemic stroke subgroups based on lymphocyte values (13). In one study, there was no significant difference in leukocyte values between hemorrhagic and ischemic stroke groups (14), however, Kaya et al. reported a significant increase in WBC levels within the hemorrhagic stroke group (15). In the relevant literature, the use of these biomarkers, which contribute to inflammation, for the purposes of hemorrhagic–ischemic differentiation is under debate. In the study of ours, there was no significant difference between ischemic and

hemorrhagic stroke groups based on WBC and lymphocyte counts.

Certain studies in the literature report that CRP levels were significantly higher in patients with ischemic stroke than in patients with hemorrhagic stroke (12,16,17). In our study, CRP levels were slightly higher in patients with ischemic stroke, but there was no statistically significant difference. This can be explained by the differing number of cases included in the literature. Furthermore, the time of hemorrhage and ischemia onset was not recorded as a parameter in the present study, which may have an effect on the CRP levels, an inflammatory biomarker.

A 2018 study reported that there was no significant difference between patients with hemorrhagic and ischemic stroke based on sodium and potassium levels (18), while another reported that sodium levels were significantly lower in the hemorrhagic stroke group (12). The study by Mansoor et al. revealed that sodium levels were notably lower in the ischemic stroke group, while potassium levels were significantly higher in the hemorrhagic stroke group (19). Setyawati et al. found no significant difference in sodium levels, yet they reported that potassium levels were higher in patients with ischemic stroke (20). However, in the study of ours, there was no significant intergroup difference based on sodium and potassium levels consistent with some previous studies in the literature.

### Limitation

Our study is a single-center study with a relatively smaller sample size. In addition, the time between the evaluated parameters and the onset of the patient's symptoms could not be determined exactly. It is not known whether the patients had inflammatory processes that were not present in their records before the application process.

## CONCLUSION

Laboratory parameters are tests that might be important in distinguishing between ischemic and hemorrhagic stroke because they are easily accessible and cost-effective. Platelet count may be considered as a biomarker to differentiate between ischemic and hemorrhagic stroke in patients who are examined for stroke in the emergency department.

***Financial disclosures:*** *The authors declared that this study has received no financial support.*

***Conflict of interest:*** *The authors have no conflicts of interest to declare.*

***Ethical approval:*** *The study was conducted after the approval of the Karabük University Non-Interventional Clinical Research Ethics Committee (2024/1782).*

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