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Effects of Albumin, Uric Acid, Hemoglobin, and C-Reactive Protein Levels on Rehabilitation Outcomes in Stroke: A Retrospective Clinical Study

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ABSTRACT

Objective: The aim was to explain the relationship between recovery in motor functions and ambulation skills after stroke and albumin, uric acid, C-reactive protein (CRP), and hemoglobin levels.

Materials and Methods: Patients who received inpatient rehabilitation in the physical medicine and rehabilitation (PM&R) clinic within the past 2 years were included in the study. Patients' discharge report, albumin, CRP, uric acid, and hemoglobin levels were obtained from the blood tests taken during hospitalization through the hospital system. The relationship between Brunnstrom staging (BS) and functional ambulation category (FAC) assessments before treatment and on the 15th day of rehabilitation, and the initial albumin, CRP, uric acid, and hemoglobin levels was investigated.

Results: The files of 135 patients were accessed. Six patients were excluded because they did not meet the inclusion criteria, and 4 patients were excluded because their data were incomplete. The study was completed with 125 patients. Albumin levels were low in 22 (17.6%) patients, and hemoglobin levels were low in 75 (60%) patients. CRP levels were above normal in 53 (42.4%) patients. When uric acid levels were examined, 1 (0.8%) patient was below normal, and 15 (12%) patients were above normal. There was no significant relationship between BS and albumin, CRP, uric acid, and hemoglobin levels ($p>0.05$). There was a significant positive relationship between improvements in FAC and albumin and hemoglobin levels ($p<0.05$).

Conclusion: Post-stroke FAC recovery is associated with albumin and hemoglobin levels.

Keywords: Albumin, C-reactive protein, Hemoglobin, Stroke, Uric acid

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INTRODUCTION

Stroke is a cerebrovascular disease (CVD) that causes loss of brain function due to interruption of blood flow to the brain or bleeding.[1] It is a significant health problem worldwide. It is a significant cause of morbidity and mortality acquired in adulthood.[2] Most patients develop hemiplegia, affecting upper extremity functions and ambulation skills.[3] Stroke rehabilitation is the primary treatment option recommended for functional limitations and disabilities that occur after a stroke.[4]

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The success of stroke rehabilitation depends on many factors, including the severity of the stroke, emotional reasons, social aspects, early initiation of rehabilitation, and the experience of the stroke rehabilitation team.[5] Several blood biomarkers have been used to provide prognostic information after ischemic stroke. Thirty-four different blood biomarkers are associated with physical outcomes after ischemic stroke. Increased C-reactive protein (CRP) is one of the early poor prognostic factors.[6] Hypoalbuminemia is a strong, independent prognostic indicator of mortality and poorer functional outcomes in long-term follow-up.[7] Serum uric acid levels are nonlinearly associated with the risk of poor functional outcome (U-shaped). This may be due to both the antioxidant and prooxidant nature of uric acid.[8] It is known that low baseline hemoglobin levels are negatively associated with functional recovery.[9]

This study aimed to demonstrate the relationship between albumin, CRP, uric acid, and hemoglobin levels and improvement in motor functions and ambulation skills in early stroke rehabilitation. Since stroke results are usually compared with a single blood parameter in the literature, our study makes a difference by examining the relationship with more parameters.

MATERIALS AND METHODS

Study Design

This study was designed as a retrospective clinical study. It was conducted in the Physical Medicine and Rehabilitation (PM&R) clinic between April and May 2025. Approval was obtained from the Şişli Hamidiye Etfal Training and Research Hospital Clinical Research Ethics Committee (April 22, 2025/approval no:4838). The study was conducted according to the STROBE checklist recommendations. Informed consent was obtained from the patients. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Participants

Stroke patients aged 18 years and older who were admitted to the inpatient physical therapy and rehabilitation program in our PM&R department within the last 2 years were included in the study. Patients with a history of traumatic stroke, those whose rehabilitation program could not be optimally performed due to cognitive impairment, and those whose hospitalization or rehabilitation period was shorter than 15 days were not included in the study. All patients received a similar stroke rehabilitation protocol.

Clinical and Laboratory Assessments

Patients' demographic data, hospitalization, and 15th day of hospitalization were evaluated through the discharge report. Motor evaluations were evaluated with Brunnstrom staging (BS), and ambulation levels were evaluated with functional ambulation category (FAC). Brunnstrom recovery staging evaluates motor recovery for 3 different regions: as upper extremity, the hand, and the lower extremity. Staging is done from 1 to 6 for each subheading. Higher levels indicate a better motor level.[10] FAC scores ambulation from 0 to 5. While there is no functional ambulation in Stage 0, the person can ambulate independently in Stage 5.[11]

Albumin, uric acid, hemoglobin, and CRP levels included in routine laboratory checks taken during hospitalization were obtained through the hospital system. Normal values were accepted as 35–52 g/L for albumin, 0–5 mg/L for CRP, 3.5–7.2 mg/dL for uric acid, and 130–175 g/L for hemoglobin. Patients were divided into 3 groups as those with no improvement, those with improvement, and those at the maximum stage from the beginning, in both Brunnstrom motor recovery staging and FAC. These groups were compared according to whether the albumin, CRP, uric acid, and hemoglobin levels were within the normal range. Thus, the effect of whether the laboratory values was normal or not on recovery was examined. In addition, the recovery and non-recovery groups were compared to show the effect of gender and aphasia on recovery in stroke.

Statistical Analysis

Descriptive statistics were given as numbers and percentages for categorical variables, and as mean, standard deviation or median, and interquartile range for numerical variables. In independent groups, non-parametric tests such as Mann–Whitney U and Kruskal–Wallis tests were used for numerical variables that did not conform to normal distribution. Student's T-test was applied for numerical data that conformed to normal distribution. Chi-square test was used for categorical data. In analyses where Kruskal–Wallis test was used, Dwass, Steel, Critchlow–Fligner analysis was used for post-hoc pairwise comparisons. Statistical analysis of the study was performed using "The jamovi project (2024)" jamovi (Version 2.5) [Computer Software] (Retrieved from https://www.jamovi.org).

RESULTS

The discharge report of 135 patients was examined. For various reasons, 6 patients whose treatment lasted <15 days and 4 patients with incomplete data were excluded from the study. A total of 125 patients were included in the study. The median age of the patients was 64 (interquartile range [IQR]=25) years. The median time since stroke was 3 (IQR=3) months. 65 (52%) of the patients were male. 93 (74.4%) of the patients had essential hypertension, 47 (37.6%) had diabetes mellitus, 21 (16.8%) had dyslipidemia, 28 (22.4%) had coronary artery disease, and 49 (39.2%) had other systemic diseases. Albumin levels were low in 22 (17.6%) of the patients, and hemoglobin levels were low in 75 (60%). CRP values were above normal in 53 (42.4%) patients. When uric acid levels were examined, 1 (0.8%) patient was below normal, 15 (12%) patients were above normal, and 109 (87.2%) were within normal limits (Table 1).

Table 1. Demographic variables of the patients and pre-treatment laboratory values

	Median (IQR)/n (%)
Age (year)	64 (25)
Gender	
Female	60 (48)
Male	65 (52)
Duration of cerebrovascular accident (month)	3 (3)
Additional diseases	
Essential hypertension	93 (74.4)
Diabetes mellitus	47 (37.6)
Dyslipidemia	21 (16.2)
Coronary artery disease	28 (22.4)
Other system diseases	49 (39.2)
Albumin	
Low	22 (17.7)
Normal	103 (82.3)
Hemoglobin	
Low	75 (60)
Normal	50 (40)
CRP	
High	53 (42.4)
Normal	72 (57.6)
Uric acid	
Low	1 (0.8)
Normal	15 (12)
High	109 (87.2)
Cerebrovascular accident etiology	
Ischemic	93 (74.4)
Hemorrhagic	30 (24)
Other	2 (16)
Number of cerebrovascular accident	
First	102 (81.6)
≥2	23 (18.4)
Clinical presentation	
Right hemiplegia	61 (48.8)
Left hemiplegia	56 (44.8)
Bilateral weakness	3 (2.4)
Loss of balance	5 (4)
Aphasia	
Motor	22 (17.6)
Sensory	2 (1.6)
Global	1 (0.8)
Dysarthria	43 (34.4)

IQR: Interquartile range.

The etiology was ischemic in 93 (74.4%) patients, hemorrhagic in 30 (24%) patients, and CVD due to other causes in 2 (1.6%) patients. While it was the first stroke in 102 (81.6%) patients, 23 (18.4%) patients had more than one stroke history. The hemiplegic side was the right in 61 (48.8%) patients, and the left in 56 (44.8%) patients. Bilateral weakness was present in 3 (2.4%) patients, and balance loss due to cerebellar stroke was present in 5 (4%) patients. Aphasia was present in 25 (20%) patients. Of these, 22 (88%) were motor, 2 (8%) were sensory, and 1 (4%) was global aphasia. In addition, 43 (34.4%) patients without aphasia had dysarthria (Table 1). The distribution of BS and FAC of the patients before treatment is shown in Table 2.

Table 2. Brunnstrom staging and FAC levels of patients before treatment

	n (%)
BS upper extremity	
Stage 1	30 (24)
Stage 2	20 (16)
Stage 3	13 (10.4)
Stage 4	12 (9.6)
Stage 5	25 (20)
Stage 6	25 (20)
BS hand	
Stage 1	42 (33.6)
Stage 2	14 (11.2)
Stage 3	15 (12)
Stage 4	7 (5.6)
Stage 5	18 (14.4)
Stage 6	29 (23.2)
BS Lower extremity	
Stage 1	9 (7.2)
Stage 2	13 (10.4)
Stage 3	30 (24)
Stage 4	16 (12.8)
Stage 5	21 (16.8)
Stage 6	36 (28.8)
FAC	
Stage 0	36 (28.8)
Stage 1	18 (14.4)
Stage 2	11 (8.8)
Stage 3	16 (12.8)
Stage 4	35 (28)
Stage 5	9 (7.2)

BS: Brunnstrom staging, FAC: Functional ambulation category.

The initial data and changes in functionality of the patients were also compared between males and females. While the mean age of female patients was significantly higher than male patients, hemoglobin and uric acid values were significantly lower than male patients (p=0.001, p<0.001, p=0.008, respectively). No significant difference was found in the presence of essential hypertension, presence of diabetes mellitus, CVD etiology, hospital stay, CRP, albumin pre-treatment and post-treatment BS and FAC evaluations according to gender (p>0.05) (Table 3). In addition, since the presence of aphasia is also important in rehabilitation, the improvements of patients with and without aphasia were also compared. When the improvements in FAC were compared between the aphasic and non-aphasic groups, no significant difference was found between them (p=0.321). When the improvements in BS were compared in the aphasic and non-aphasic groups, a significant difference was found between the groups (p=0.007). In pairwise comparisons between the groups, no difference was found in terms of aphasia between the group with improvement and the group that was at maximum BS from the beginning (p=0.774), while the rate of aphasia in the group without improvement was significantly higher than in the groups with improvement and those at maximum BS from the beginning (p=0.045, p=0.033, respectively) (Table 4).

When patients with no improvement in BS, with improvement in BS, and those who were at the highest BS from the beginning were compared, no significant difference was found between the groups in terms of albumin, CRP, uric acid, and hemoglobin values (p>0.05). When the groups consisting of patients with no improvement in FAC, with improvement in FAC, and those who were at FAC level 5 from the beginning were compared, no significant difference was found between the groups in terms of CRP and uric acid (p>0.05). There was a significant difference between the groups in terms of albumin values (p=0.027). In post hoc pairwise comparisons, albumin values

Table 3. Pre- and post-treatment changes according to gender

	Female (n=60)	Male (n=65)	p
Age (year)	69 (IQR=16)	58 (IQR=17)	0.001m
Duration of CVE (ay)	3 (IQR=6.25)	4 (IQR=5)	0.630m
Duration of hospital stay (day)	20 (IQR=11)	22 (IQR=12)	0.462m
Presence of essential hypertension	42	51	0.279x
Presence of diabetes mellitus	23	24	0.871x
CVE etiology			
Ischemic	47	46	0.139x
Hemorrhagic	11	19	
Others	2	0	
Albumin (g/L)	37.90 (IQR=5.67)	40 (IQR=5.20)	0.116m
CRP (mg/L)	3.23 (IQR=5.67)	4.5 (IQR=6.63)	0.976m
Uric acid (mg/dL)	4.70 (IQR=1.80)	5.50 (IQR=1.60)	0.008t
Hemoglobin (g/L)	117 (IQR=16.75)	133 (IQR=20.0)	<0.001m
Pre-treatment BS			
Upper extremity	4.0 (IQR=3.25)	3.0 (IQR=4.0)	0.226m
Hand	3.5 (IQR=4.25)	3.0 (IQR=4.0)	0.597m
Low extremity	5.0 (IQR=3.0)	4.0 (IQR=2.0)	0.134m
Pre-treatment FAC	3.0 (IQR=3.0)	2.0 (IQR=4.0)	0.995m
Post-treatment BS			
Upper extremity	5.0 (IQR=4)	4.0 (IQR=4.0)	0.335m
Hand	5.0 (IQR=5)	3.0 (IQR=4.0)	0.677m
Low extremity	6.0 (IQR=2.0)	4.0 (IQR=3.0)	0.202m
Post-treatment FAC	3.0 (IQR=4.0)	4.0 (IQR=4.0)	0.462m

mMann-Whitney U test, xChi-square test; tStudent-T test; CVD: Cerebrovascular disease; CRP: C-reactive protein; BS: Brunnstrom staging; FAC: Functional ambulation category; IQR: Interquartile range.

Table 4. The effect of aphasia on clinical recovery

	Aphasic (n=25)	Non-aphasic (n=100)	p
BS			
Group 1	15	28	0.007x
Group 2	9	53	
Group 3	1	19	
FAC			
Group 1	11	33	0.321x
Group 2	14	61	
Group 3	0	6	

xChi-square test; BS: Brunnstrom staging; FAC: Functional ambulation category; Group 1: No-recovery, Group 2: Recovery, Group 3: Best level since the beginning; IQR: Interquartile range.

were significantly lower in the group with no improvement in FAC compared to the group with improvement (p=0.022). No significant difference was observed in other pairwise comparisons (p>0.05). Similarly, a significant difference was observed between the groups in terms of hemoglobin values (p=0.042). In post hoc pairwise comparisons, the hemoglobin level of the group with improvement in FAC was found to be significantly higher than the group with no improvement (p=0.047). There was no significant difference in other pairwise comparisons (p>0.05) (Table 5).

DISCUSSION

In this study, the relationship between motor recovery and ambulation in the early period after stroke and albumin, CRP, uric acid, and hemoglobin values was tried to be explained. No relationship was found between recovery in BS and the laboratory values examined. In FAC recovery, it was seen that there was a relationship between albumin and hemoglobin levels. In addition, it was tried to show the relationship between gender and aphasia and recovery. It was seen that gender did not cause a difference in BS and FAC recovery. While aphasia did not cause a difference in FAC recovery, the aphasia rate was higher in the group without recovery in BS compared to the other groups.

It is of great importance to determine the prognostic factors of stroke, which is a significant cause of morbidity and mortality. Stroke is seen in female patients at older ages and is more mortal.[12] In our study, the mean age of female patients was significantly higher than male patients, and uric acid and hemoglobin levels were significantly lower. However, these differences did not create a significant difference in clinical recovery. Aphasia, as a different prognostic factor, is associated with longer hospital stays and complications. Aphasia, compared to hemiparesis, may lead to poor clinical outcomes.[13] In our study, the presence of aphasia was significantly higher in the group without recovery than in the group with recovery and in patients with maximum BS from the beginning. Perhaps these data will enable future studies to include applications for communication skills.

Low serum albumin levels are common in stroke patients[14] and are associated with poor clinical outcomes and increased mortality.[15] It also provides information about the premorbid nutritional status of stroke patients due to its long half-life.[16] Our study has also shown that albumin is associated with ambulation. Globulin is also an acute-phase protein measured in serum. It increases in inflammation and is associated with hemorrhagic transformation in patients undergoing intra-arterial thrombolysis.[17] A decrease in the albumin and globulin

Table 5. Relationship between laboratory values and clinical improvement

BS	Group 1 (n=43)	Group 2 (n=62)	Group 3 (n=20)	p
Albumin (g/L)	39.20 (IQR=4.9)	38.15 (IQR=6.08)	40.14 (IQR=5.0)	0.496†
CRP (mg/L)	2.82 (IQR=6.79)	6.82 (IQR=11.98)	2.90 (IQR=3.79)	0.074†
Uric acid (mg/dL)	4.70 (IQR=2.15)	5.30 (IQR=2.38)	5.50 (IQR=0.85)	0.117†
Hemoglobin (g/L)	118 (IQR=21.0)	128.50 (IQR=20.50)	127.0 (IQR=22.25)	0.062†
FAC	Group 1 (n=44)	Group 2 (n=75)	Group 3 (n=6)	p
Albumin (g/L)	37.10 (IQR=4.80)	40.0 (IQR=5.10)	38.0 (IQR=3.38)	0.027†
CRP (mg/L)	3.50 (IQR=13.80)	4.12 (IQR=6.35)	2.90 (IQR=1.35)	0.849†
Uric aside (mg/dL)	5.30 (IQR=1.73)	5.10 (IQR=2.0)	5.0 (IQR=1.13)	0.913†
Hemoglobin (g/L)	118.0 (IQR=25.50)	130 (IQR=25.50)	120.50 (IQR=8.0)	0.042†

†Kruskal–Wallis test; BS: Brunnstrom staging, FAC: Functional ambulation category, Group 1: No-recovery, Group 2: Recovery, Group 3: Best level since the beginning, IQR: Interquartile range, CRP: C-reactive protein.

ratio is associated with mortality.[18] In our study, this ratio was not reversed in any patient, so the relationship with clinical outcomes could not be compared.

CRP is an acute-phase reactant that increases due to acute inflammation and tissue damage.[19] CRP is associated with white matter lesions, stroke severity, and mortality.[20,21] High CRP levels have been shown to lead to poor outcomes in the modified Rankin score at 3 months.[22] However, in a study evaluating cases with intracerebral hemorrhage, it was determined that CRP was not associated with clinical and imaging results.[23] In our study, no association was observed between CRP and either Brunnstrom motor staging or FAC. The fact that CRP is affected by many clinical conditions, the fact that patients cannot be questioned for the presence of chronic infection due to the retrospective study design, or that it is not known whether they received antibiotics for acute infection, may affect the results.

Uric acid is a product of purine metabolism. It can act as both a pro-oxidant and an antioxidant.[24] The protection of vascular endothelial cell function and its neuroprotective effects are antioxidant effects.[25] It has been observed that it causes a decrease in serum uric acid levels in the early phase of acute stroke, and this decrease is associated with severe stroke, large infarct volume, and poor outcomes.[26,27] Hyperuricemia has also been reported to be associated with poor outcomes in stroke patients.[28,29] Again, publications are showing that there is no significant relationship between uric acid and outcomes.[24,30,31] In our study, there was no relationship between uric acid levels and clinical improvements. All these differences may be due to the bidirectional effect of uric acid, differences in study designs, or patients receiving drug therapy that affects uric acid levels. Future studies should take these differences into account and ensure that the results are more reliable.

Having abnormal hemoglobin levels increases the incidence of stroke.[32] Low hemoglobin levels lead to an increase in infarct volume and infarct growth rate.[33] In addition, anemia increases the risk of mortality after stroke.[34] Low hemoglobin levels are associated with the presence of premorbid sarcopenia, prolonged hospital stay, and failure to improve dysphagia and daily living activities.[35] Although studies generally focus on anemia, high hemoglobin levels are also associated with mortality and poor clinical outcomes. In addition, high hemoglobin levels may increase the risk of stroke recurrence and composite cardiovascular disease.[36] In our study, the fact that the group with no improvement in FAC had significantly lower hemoglobin levels than the group with improvement supports the literature.

There are some limitations to our study. First, the study is retrospective, and only the 15th day rehabilitation results were evaluated. Second, since the study was conducted in a single center, different results may be obtained in different locations and ethnic groups. Third, some clinical conditions, such as stroke localization, intensive care history, and recent antibiotic treatment history, were not evaluated. In addition, since the participants were only included in the inpatient rehabilitation program in the ward, the patient group consisted of those who had more severe strokes and therefore cannot be generalized to all stroke cases.

CONCLUSION

Albumin and hemoglobin levels are associated with improvements in FAC in early stroke rehabilitation. Multicenter studies with a larger number of patients and longer follow-up periods may more clearly show the relationship between laboratory parameters and clinical improvement in stroke.

DECLARATIONS

Ethics Committee Approval: The study was approved by Şişli Hamidiye Etfal Training and Research Hospital Clinical Research Ethics Committee (No: 4838, Date: 22/04/2025).

Informed Consent: Informed consent was obtained from the patients.

Conflict of Interest: The authors declare that there is no conflict of interest.

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