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Prognostic significance of whole blood parameters in patients with spontaneous subarachnoid hemorrhage

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Abstract

Subarachnoid hemorrhage (SAH) is an emergency requiring rapid diagnosis and treatment. No marker has yet to be determined, demonstrating the diagnosis and prognosis of SAH. The aim of this study was to retrospectively evaluate the patients diagnosed with subarahcnoid hemorrhage and aneurysms in the emergency room of our hospital. Those (43 male and 62 female) admitted to the emergency room and diagnosed with SAH through angiography were included into the study. The study was retrospectively designed by investigating the patients hospital records. On admission, all blood parameters of the patients were evaluated. The parameters of surviving and dying patients, such as neutrophils, lymphocyte, mean platelet volume, erythrocyte distribution width, platelet and neutrophil ratio to lymphocytes, were compared on admission. One hundred and five patients were included into the study, and 40 patients died due to SAH. Lymphocyte count, neutrophil count and neutrophil/lymphocyte ratio (NLR) were found to be higher among the dying patients. Lymphocyte count, neutrophil count and NLR may be significant markers in terms of survival in the patients with SAH.

Keywords: Subarachnoid hemorrhage, aneurysm, whole blood, emergency room cerebral angiography

Introduction

Subarachnoid hemorrhage (SAH) is the bleeding seen in the subarachnoid region of the brain, cerebellum and spinal cord that are usually arterial, but rarely venous type. SAH is an acute hemorrhagic cerebrovascular event that can be seen as life-threatening at any age level. SAH has a high mortality and morbidity rate and can occur as traumas, aneurysms, vascular malformations, bleeding disorders, brain tumors and anticoagulant treatment complications. No cause can be explained or found in 15-30% of cases [1,2]. SAH usually occurs after intracranial aneurysm ruptures, has poor prognosis and leads to serious socio-economic problems [3]. Hemorrhages due to aneurysm rupture or arteriovenous malformation are the most common causes of spontaneous SAHs [4].

Although SAHs are more commonly encountered among women, the difference between both genders varies with age. While the incidence is high among men at young age, SAHs are more frequently seen within women over 55 years of age. The formation of SAHs shows seasonal (winter and spring) and diurinal patterns (late hours in the morning) [5]

As the first diagnostic method, computed tomography (CT) should be considered in a patient suspected with SAH. In SAH, blood can characteristically be accumulated focally around the ruptured aneurysm or may fill the cisterns in a diffused way. Non-ruptured aneurysms of >5mm may be seen in contrast-enhanced CT. Calcified walls of the large aneurysms can also be observed on CT. In addition, cranial CT also provides information about the size of the ventricles, hematomas, infarction, cisterns, the amount of blood in the fissures, place of aneurysm and which aneurysm bleeds in those with multiple aneurysms, and [6].

Digital subtraction angiography (DSA) is the gold standard for imaging aneurysms. The presence of aneurysm, the number of aneurysms if more than one, the width of the neck, the shape of the aneurysm wall, the size, direction and relationship of the those with other vascular structures can be evaluated on DSA [7].

Although SAH constitutes a small proportion of all cerebrovascular hemorrhages (5-7%), the potential of SAH is high when it comes to mortality and morbidity. Nevertheless, there is no specific laboratory sign used in the diagnosis or prognosis of intracerebral hemorrhages.

Whole blood count is a frequently used test as the part of patients' assessment. Hemoglobin (Hg), hematocrit value (Hct), mean corpuscular volume (MCV) (fl), mean corpuscular hemoglobin (MCH) (pg), mean corpuscular hemoglobin concentration (MCHC) (gr/dL), red cell distribution width (RDW) give information about platelet indices (Mean Platelet Volume: MPV), PDW (Platelet Distrubition Width), and leukocyte count (monocyte count,

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neutrophil count, eosinophil count, lymphocyte count) [8].

In the present study, we aimed at investigating the association of hematological parameters with the mortality in the patients diagnosed with SAH in our emergency department.

Materials and Methods

One hundred and five patients referred from other medical centers were admitted to the emergency department of Konya Application and Research Hospital of Baskent University between January 2014 and December 2017. The hospital records of all patients, diagnosed with SAHs and in whom aneuryms were determined on DSA, were retrospectively investigated in the present study. The patients with spontaneous SAH over the age of 18 years, and those undergoing DSA and diagnosed with an aneurysm after DSA assessment were included into the study; in addition, the findings of non-traumatic patients whose outcomes were finalized by the relevant department as good health after the admission, and the results of the dying patients were also evaluated in the study.

The patients at the age of ≤18 years and developing SAH due to trauma, those not diagnosed with aneurysm on DSA, and the cases with thrombocytopenia, thrombocytosis and malignancies were excluded out of the study. Forty-three patients meeting the exclusion criteria were ruled out of the assessment. We first obtained the related data from the hospital records of the patients diagnosed with SAHs or admitted to our emergency department via the referrals from other medical centers due to the diagnosis of SAHs, and then evaluated the patients hospital records including systemic and neurological findings, white blood cellcount (WBC), cranial CT and DSA results. A questionnaire prepared previously by the authors in order to evaluate the radiological and laboratory test results were filled in for each patient diagnosed with SAH. Such features as the name, age, gender, citizenship identity number, blood parameters, admission time, complaints on admission to the emergency department, medications taken and history of each patient were recorded onto the questionnaire. WBC results of all patients were also evaluated. Cranial CT and DSA findings performed in our emergency department were also evaluated and documented by a radiologist.

In evaluating blood test findings, the levels of Hg, (Hct, WBC count, neutrophil, lymphocyte, neutrophil lymphocyte ratio (NLR), platelet (Plt), MPV and RDW were recorded. The outcomes related to the patients hospitalization due to SAH were also recorded. The epidemiological values of the dying patients from SAH were compared with Whole blood count test results of the surviving patients.

Laboratory Assessment

A routine electronic blood count device was used to measure Whole blood count parameters (Cell-Dyne 3700, Abbott, Abbott Park, IL, USA).

Statistical Analysis

The accumulated data were recorded into the questionnaires prepared by the researchers. All statistical analyses were performed using a statistical software package (SPSS Version 15.0, SPSS Inc., Chicago, USA). Conformity analyses were performed to test the appropriateness for normal distribution. The student's tand and the paired t tests were performed for the comparisons in dependent groups. The numerical values were expressed as mean ± standard deviation (SD). P value of <0.05 was considered to be significant. In our study, we compared the findings of the dying patients from SAH and those of the surviving patients diagnosed with SAH in our emergency room.

Results

This study was carried out with the patients diagnosed with SAH in the emergency department of Konya Application and Research Hospital of Baskent University, and those referred from other medical centers to our emergency between January 2014 and December 2017. In the present study, 105 patients diagnosed with aneurysm on DSA were retrospectively evaluated. Forty percent (n=43) of the patients were male, while 59% (n=62) were female. The mean age of the patients was found as 56.4±11.6 years. Eleven patients (10.47%) were over 70 years of age, and 38% (n=40) of the patients died from SAH. Among the patients dying from SAH, 55% (n=22) and 45% (n=18) were women and men, respectively (Table 1).

Table 1. Age and gender distribution of patients who died (exitus) and lived

	Live (n=65)	Exitus (n=40)	P<0.05
Gender	F=40 M=25	F=22 M=18	
Age*	54±11.7	60.2±10.6	p=0.008

*Mean±standard deviation values

While the mean age of the dying patients was 60.2±10.6 years, the survivors mean age rate was found to be 54±11.7. The difference between age levels was considered to be statistically significant (p=0.008).

The mean WBC values of the survivors were 12.2±4.35, whereas those of the dying patients were found as 15.9±5.9 years. A statistical difference was determined between WBC levels of the two groups (p=0.01). In terms of the neutrophil levels, the surviving and dying patients' values were determined to be 9.88±4.47 and 14.2±5.17, respectively. There was a significant difference between the two groups in terms of neutrophil levels (p=0.00). As to lymphocyte counts, the mean values of the surviving and dying patients were detected as 1.77±1.02 and 1.11±0.46 respectively, and a significant difference was present between the two groups (p=0.00). While the survivors' mean NLR values were found to be 7.93±5.89, the mean NLR values of dying patients were 13.56±5.24, and there was also a significant difference between the two groups (p=0.00) (Figure 1).

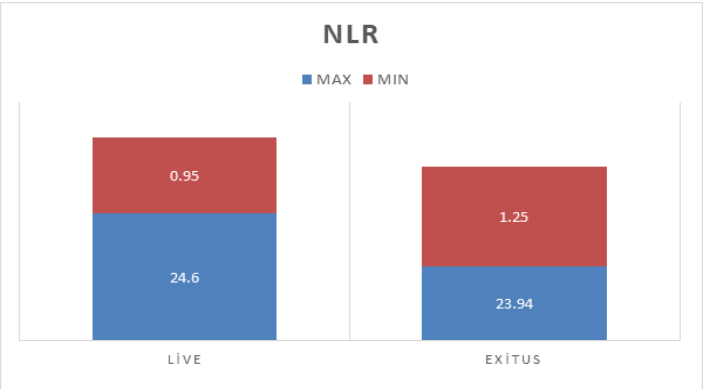

Figure1. Levels of NLR

As to the platelet counts and RDW values, no significant differences were detected between the survivors and the dying patients' values (p=0.1, p=0.2, respectively). The mean MPV values also showed no difference between the survivors and the dying patients (p=0.8) (Table 2)

Table 2. Statistical analysis of patients who died (exitus) and lived

	Live (n=65)	Died (n=40)	P<0.05
WBC*	12.2±4.3	15.9±5.4	0.01
Neutrophil*	9.88±4.47	14.2±5.17	0.00
Lympocyte*	1.77±1.02	1.11±0.46	0.00
NLR*	7.93±5.89	13.56±5.24	0.00
Thrombocyte*	254.5±85.2	283.3±90.3	0.1
RDW*	15.2±2.13	15.7±1.68	0.2
MPV*	7.79±1.74	7.71±1.02	0.8

*Mean±standard deviation values, NLR: Neutrophil/Lymphocyte Ratio, WBC: White Blood Count, RDW: Red Cell distribution width, MPV: Mean Platelet Volume

Discussion

SAH is the condition where blood suddenly leaks or mixes into cerebrospinal fluid, which can develop due to spontaneous and traumatic causes. SAH is an important emergency with high morbidity and mortality leading to serious complications and requiring early diagnosis and treatment. SAH is frequently seen after an aneurysm rupture (85%) [9].

The management of SAH should be performed quickly and accurately. The most common reason for admissions to the emergency department is headache [10]. Its mortality rate reaches 40% within the first week, and the SAH-induced deaths between 10 to 15% occur in the pre-hospitalization period, while 25% develop during 24 hours after the onset of hemorrhages [11].

In a patient suspected with SAH, as the first choice to diagnose SAH, CT should always be kept in mind. Blood can be accumulated or found focally around the characteristic ruptured aneurysm or may fill the cisterns in a diffused way. Non-ruptured aneurysms of >5 mm may be seen in contrast-enhanced CT. The calcified walls of large aneurysms can also be seen on CT [12].

DSA is the indispensable gold standard for imaging aneurysms. The presence of the aneurysm, the number of multiple aneurysms, the width of the neck, the shape of the aneurysm wall, the size, direction and relationship of the domes with other vascular structures can be evaluated on DSA [13]. In our study, DSA was performed for all patients diagnosed with SAH through CT. All patients were investigated in terms of the existence of aneurysms, and those diagnosed with aneurysms were evaluated.

As age level increases, the incidence of SAH also increases. The fifth and sixth decades constitutes the periods, when SAH most commonlyoccurs in both genders. Advanced age is the sine qua non for SAH as an independent risk factor [14]. However, the age levels SAH was seen most commonly at were between 40 and 60 years of age in our study. In some studies, the prognosis of SAH was reported to be affected adversely with the advanced age level. In a study including 299 patients, while the mortality rate was reported as 29% under the age of 60, it was emphasized to be 33% between 60-70 years and 55% over the age of 70 years [15]. In our study, the mean age level of the dying patients was 60 years of age.

The difference between both genders is another important risk factor for SAH, however. The prevalence of SAH is higher among women than that seen in men. In a study, it was found that there was no significant difference between both genders under 50 years of age, although the prevalence of SAH was significantly higher among women over 50 years of age [16]. In our study, 59% of all cases and 55% of the dying patients were composed of women.

In order to diagnose SAH, a non-invasive laboratory method or marker unexists for the patients presenting to the emergency department with the complaint of headache.

Acute inflammation commences in the hemorrhagic site shortly after the developmentof bleeding. This inflammatory response is closely associated with the poor outcomes in the patients with SAH. Neutrophils are the first cells to invade the inflammatory site [17].

The increases developing in leukocyte and neutrophil levels are non-specific findings of infection, inflammation, tissue necrosis, hemorrhage and excessive stress [18]. In recent studies, it was shown that the an inflammatory response beginning after the development of an intracerebral hemorrhage also determines the prognosis by playing a key role in the progression of brain injury [19].

In literature, an increase in WBC count seen in the patients with intracranial hemorrhage and ischemic stroke was demonstrated to be as sociated with poor prognosis and increased mortality [20,21]. In a study, the increased neutrophils and leucocytes in SAH was reported to be proportionate to the degree of brain damage [22]. In also another study, it was concluded that neutrophil values developing after aneurysm rupture are high in SAC patients, and this may be beneficial in demonstrating the prognosis [23]. As consistent with these findings, mean neutrophil and leukocyte counts were found to be higher than normal values in the patients experiencing SAH in our study, as well. However, these two values were also higher among the dying patients, compared to the average values of the surviving patients. Recently, the increased neutrophil levels pointing to the acute state in inflammation was also started to be used as a parameter reflecting lymphopenia that occured after acute physiological stress. This parameter, obtained by the ratio of neutrophils and lymphocytes, was used along with other inflammatory markers in studies and found to be a good indicator of inflammatory status. Several studies investigating the diagnostic and therapeutic role of NLR in many inflammatory diseases were conducted [24,25]. The increase in NLR values that was accepted as a new indicator for systemic inflammation was shown to be related to acute coronary syndrome, heart valve diseases, extremity ischemia, acute ischemic stroke, transient ischemic attack and ISH in recent studies [26,27]. In our study, however, this value was found behigher amongthe dying patients, compared to the surviving patients. As an intriguing finding in our study, we consider NLR values may be useful in predicting prognosis.

In various studies investigating the sequential alterations between SAH and inflammation, RDW and MPV levels were found to

increase in SAH [28,29]. In another pilot study where RDW was quite high in the patients with SAH, the researchers declared that more controlled cohort studies are needed for the routine use of RDW [30]. In another study, however, RDW and MPV values were determined not to change during SAH [31]. In our study, no significant association was also detected between the patients' status, and RDW and MPV.

Conclusion

SAH is an emergency requiring early diagnosis due to its serious clinical spectrum and complications. There are no definite laboratory markers for the early diagnosis and prognosis of SAHs in the emergency department. The levels of leukocytes, neutrophils and NLR may be beneficial in the prognosis of the patients with SAHs. We consider that healthcare professionals keep in mind first assessing these parameters accurately and in detail in the individuals with SAHs, and that larger series of studies including larger populations should be carried out in order to support and elucidate the entity.

Limitations

Our study is composed of limited number of participants, and we could not reach sufficient number of patients in the study because our center is not large. In addition, the retrospective nature of our study led to various limitations in accessing to obtaining some information.

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Conflict of interest
The authors declare that they have no competing interest.

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Ethical approval
This is a retrospective study, no need to ethics committee approval. But, clinical research approval has been obtained.

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