Comparison of Stroke Cases with Other Neurological Diseases on the Basis of Hemogram Parameters

Introduction

It is predicted that, in the near future, the elderly population will increase in parallel with the increase in the world population, which, according to the United Nations Population Expectations report, is expected to exceed 9 billion by 2050. It is also estimated that the population over 65 years of age will double by 2050. This situation poses a serious danger to sustainable health services. After ischemic heart diseases, stroke is the most common cause of morbidity and mortality related to disease, and it is known that the prevalence of stroke increases in parallel with an increase in age (1). For this reason, it is predicted that dealing with stroke will become more important in health systems in the near future (2). Consequently, it is clear that new approaches are needed in the diagnosis, follow-up and treatment of stroke. If these approaches are non-invasive, inexpensive, standardized and reproducible, they will be able to be used more in daily practice (3). However, there is no test employed in clinical practice at every stage of stroke (4-5).

Stroke is a heterogeneous disease that can occur for many reasons. It is separated into two subgroups, with 80% of victims constituting the ischemic stroke subgroup (6). In ischemic stroke, inflammation and oxidative stress occurrence, exotoxin and cytokine release, and blood-brain barrier damage develop as a result of focal hypoperfusion due to systemic hypoperfusion, thrombosis and embolism (7-8). Although subarachnoid hemorrhage and intracerebral hematoma, which are hemorrhagic stroke types, are less common than ischemic stroke, their mortality and morbidity rates are higher (9).

Changes in the neutrophil-lymphocyte ratio (NLR) indicate inflammation, and studies have shown that it increases in cardiovascular disease and hemorrhagic-ischemic stroke, as well as in cancer, and is a poor prognostic factor (10-13). While there are few studies showing that hemogram parameters are used in daily practice (14), many parameters obtained from routine hemogram examinations can give limited information about the patient's clinical course at the time of initial diagnosis. However, in cases where there is no infection, the NLR is affected by far fewer variables than other parameters (10-14). In light the above information, this study aimed to examine the hemogram parameters including the NLR, which is fast, easy and

practical to determine, in stroke patients who are thought to have more physiological stress and inflammatory response among neurological diseases.

Material and Methods

Patient Recruitment

In this study, the demographic, laboratory and imaging characteristics of all patients who were admitted to our neurology clinic during a three-year period covering January 1, 2015 to January 1, 2018, were retrospectively analyzed. All neurological patients over 18 years of age who were hospitalized to the neurology clinic due to neurological symptoms and patients who were initially hospitalized in the intensive care unit and then transferred to the neurology clinic (hemogram parameters at the time of admission were taken into account) were included in the study. If the same patient had repeated hospitalizations, each hospitalization was calculated separately and included. Those who did not have a hemogram examination during their hospitalization, those who were referred to another hospital within the first 24 hours of the onset of symptoms, patients with a diagnosis of stroke who could not undergo brain imaging despite being referred within the first 24 hours of their symptoms, and patients with a disease with the potential to change their hemogram parameters or who were using drugs were excluded from the study.

Study protocol

All patients admitted to our neurology clinic were examined by a single neurologist. In the neurology clinic, 3,252 patients were hospitalized and followed up; after being evaluated according to the exclusion criteria, 100 patients were excluded and the data of a total of 3,152 patients were recorded. The first blood samples taken from the peripheral vein of the patients who were hospitalized after being evaluated in the outpatient clinic were collected in a calcium ethylenediaminetetraacetic acid (EDTA) tube. If the first application was conducted in the emergency department, the blood samples collected there were taken into account. Hemogram analysis with 22 parameters was performed with a Sysmex XN-550 device, and the NLRs were recorded by calculating from the complete blood count determined from the peripheral vein.

The diagnosis of the disease was determined by examining the epicrisis of each patient in detail. Patients with multiple neurological diseases in their history had their diseases and reasons for their current admission to the neurology service recorded. Brain imaging (magnetic resonance imaging (MRI) and computed tomography (CT)) of the patients diagnosed with stroke was examined. The MRIs were performed with scanners of 1.5 T (Magnetom Avanto; Siemens, Erlangen, Germany) using a dedicated head coil. Patients were placed in the supine position. The scanning protocol included diffusion weighted imaging (DWI) and an apparent diffusion coefficient sequence with a 5 mm section. CT acquisitions were performed according to the standard departmental protocols (5 mm-thick) on 32-section General Electric helical CT scanners (BrightSpeed Edge; GE Healthcare, Milwaukee, WI).

Patients with a diagnosis of stroke were separated into two groups: ischemic and hemorrhagic. Patients who were admitted to the clinic presenting a transient ischemic attack (TIA) and had the presence of infarction found on brain imaging were recorded as ischemic stroke. A TIA was defined as a neurological dysfunction due to focal cerebral, spinal or retinal ischemia, with no signs of acute infarction on imaging and clinical symptoms lasting less than an hour (15). The study protocol was approved by the local ethics committee.

Statistical Analysis

Data were analyzed using SPSS software (version 22.0; SPSS Inc, Chicago, IL). The numerical variables were presented as mean ± standard deviation or median (min-max), and the categorical variables were presented as numbers with percentages. We determined the parametric test assumptions (normality and homogeneity of variances) for numerical variables using the Shapiro-Wilk test. A student t test was used when the parametric test assumptions were met, and a Mann-Whitney U test was used for analysis when the parametric assumptions were not met. The difference between the groups in terms of categorical variables was determined using a chi-squared test. A p value<0.05 was considered significant for all values.

Results

A total of 3,152 patients, 1,604 of whom were women (50.9%), with a mean age of 66.1 ± 14 (18-100) years who were hospitalized in the neurology clinic between January 1, 2015 and January 1, 2018, were included in the study. Of the patients, 51.4% were hospitalized after

applying to the emergency department. When the reasons for admission to the neurology clinic were examined, 46.5% of the patients had stroke (42.7% ischemic), 9.1% had multiple sclerosis, 8.0% had peripheral vertigo, 7.8% had epilepsy, 5.6% had TIA, 3.3% had headache, 3.2% had Parkinson's disease, 2.7% had polyneuropathy, 1.7% had myasthenia gravis and 1.6% had discopathy.

In stroke patients, mean age, the mean leukocyte-neutrophil count and NLR were significantly higher than in those without stroke ($p < 0.001$, $p < 0.001$ and $p < 0.001$, respectively); but mean red blood cell, platelet and lymphocyte counts, and hemoglobin and hematocrit values were found to be significantly lower ($p < 0.001$, $p < 0.001$, $p < 0.001$, $p < 0.001$ and $p < 0.001$ respectively) (Table 1). When the hemogram parameters were compared according to stroke type, the red blood cell, hemoglobin, hematocrit and NLR values in patients with hemorrhagic stroke ($p = 0.019$, $p = 0.002$, $p = 0.002$ and $p = 0.001$, respectively) and platelet and lymphocyte values in ischemic stroke patients were found to be significantly higher ($p = 0.002$ and $p < 0.001$, respectively) (Table 1).

There were more females without a stroke diagnosis, and more males in the stroke group ($p = 0.001$). The incidence of hemorrhagic stroke in men was higher than ischemic stroke ($p = 0.002$), and it was observed that the stroke group was hospitalized through the emergency department more than the group without stroke ($p < 0.001$). The rate of hemorrhagic stroke was found to be statistically higher in the stroke group who entered through the emergency department compared to ischemic stroke ($p = 0.005$) (Table 2).

Discussion

Stroke is a heterogeneous disease, of which ischemic stroke is the most common subgroup. Brain tissue damage develops due to perfusion disorder resulting from thromboembolism or atheroembolism. As a result of this damage, many cytokines and neurotransmitters are released from the infected tissue, and the hypothalamic-pituitary axis and sympathetic nervous system are activated. Cortisone and noradrenaline released from these systems cause cells to migrate from lymphoid organs to peripheral blood. As a result of changes in the number of immune cells in the peripheral blood, leukocytosis, neutrophilia and lymphopenia occur, which changes the NLR. The stroke induced immunodepression (SIRS) definition is used for the immune change that develops as a result of stroke (16). Many studies have

observed similar mechanisms in subarachnoid and intraparenchymal hemorrhages (17,18). In our study, in line with the findings in the literature, while leukocytosis, neutrophilia and lymphopenia were detected in the stroke group compared to the non-stroke group, a statistically significant increase in the NLR was also found ($p < 0.001$).

An increased NLR has been indicated as a poor prognostic factor in many diseases in which inflammation is observed in the pathogenesis, such as stroke (10-13). In this study, the NLR was higher in the stroke group compared to the non-stroke group, in accordance with the literature. However, it is known that the NLR value, which indicates inflammation, increases in the presence of infection (18-19). Stroke-associated pneumonia (SAP) is more common in stroke patients due to infection, especially impaired swallowing reflex and accompanying immunodepression (21,22). Not evaluating the presence of infection in our study was considered the most important limitation of the study.

The NLR value was found to be higher in the hemorrhagic stroke group than in the ischemic stroke group ($p = 0.001$). This finding is consistent with the literature and has been associated with higher sympathetic discharge and metabolic stress in the hemorrhagic stroke group compared to the ischemic stroke group (23,24). Due to metabolic stress and sympathetic discharge, more neutrophils and leukocytes migrate from lymphoid tissues to peripheral blood. This condition explains the higher NLR value in the hemorrhagic stroke group.

Since the mortality rates of patients with hemorrhagic stroke are higher and the severity of hemorrhagic stroke is relatively higher, the frequency of admission to the emergency department for this group is higher than for the ischemic group and is an expected condition (26). In our study, in accordance with the literature, the frequency of admission to the emergency department and hospitalization in the hemorrhagic stroke group was found to be higher than in the ischemic stroke group ($p = 0.005$).

High levels of hemoglobin, hematocrit and red blood cells (RBC) are considered to be associated with ischemic stroke. This is probably associated with the increase in viscosity (27). In our study, it was found statistically significant that hemoglobin, hematocrit and RBC values were lower in the stroke group compared to the non-stroke group ($p < 0.001$). In the literature, this situation was found to be associated with a long hospitalization (28); however, it was not associated with mortality and stroke severity. In our study, hemoglobin and

hematocrit levels were found to be higher in the hemorrhagic stroke group than in the ischemic stroke group. There is not enough data in the literature to explain this situation clearly, although there are findings indicating that it mostly develops secondary to hypertension, which is found in the etiology of intracerebral hemorrhage (29).

In our study, the platelet count was found to be lower in the group with stroke compared to the group without stroke, and this was considered statistically significant ($p < 0.001$). There is limited information on this subject in the literature. The low platelet count is explained by platelet aggregation due to endothelium damage and a decrease due to consumption (30), but more data are needed on this topic.

A hemogram examination using peripheral blood can be easily repeated when necessary and for monitoring purposes. However, the clinical significance of NLR values, when the procedure is repeated and evaluated in follow-up, is predicted to be affected by many parameters. In our study, blood samples were taken within the first 24 hours and evaluated. In studies conducted in the literature, blood was taken within 6-24 hours and the samples obtained were then evaluated (10-15,17,18,26). In the results of these studies, patients with high NLR rates in the data obtained from blood taken in the first 24 hours were associated with high mortality rates or poor clinical outcomes (10-13,15,17,18,26). There is not enough evidence to explain the relationship between the NLR values evaluated after the first 24 hours and the patient's clinical situation, and the available evidence is thought to contain bias in many aspects (10,17,18,26,31).

Conclusion

There is no biomarker for clinical outcome and mortality estimation that has entered routine clinical use in the follow-up of stroke patients. Although the NLR can potentially be affected by many parameters, it is thought that due to its noninvasive and inexpensive nature, the NLR can be used in the prediction of mortality and clinical outcomes when blood samples from stroke patients taken in the first 24 hours are studied.

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