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RESEARCH

PROGNOSTIC RELATIONSHIP BETWEEN COMPLETE BLOOD COUNT PARAMETERS AND TRANSIENT ISCHEMIC ATTACK, ISCHEMIC STROKE AND HEMORRHAGIC STROKE

ABSTRACT

Introduction: In this study, it was aimed to be investigated the relationship between complete blood count parameters such as leukocyte, neutrophil, lymphocyte, monocyte, platelet counts, red blood cell distribution width, platelet distribution width, and mean platelet volume values and transient ischemic attack, ischemic stroke and hemorrhagic stroke.

Materials and Method: A total of 215 patients including 171 with ischemic stroke, 24 with hemorrhagic stroke (non-traumatic subarachnoid hemorrhage and intraparenchymal hemorrhage) and 20 with transient ischemic attack, along with 60 healthy volunteers were enrolled in the study. Leukocyte, neutrophil, lymphocyte, monocyte, and platelet counts, and red blood cell distribution width, platelet distribution width, and mean platelet volume values of the transient ischemic attack, ischemic stroke and hemorrhagic stroke patients were compared with the control group, and between the groups themselves.

Results: The mean age of patients was 67.5 (min 22-max 96), while 138 (64.2%) patients were over the age of 65. Men constituted 53% of all patients. Mean platelet volume levels of the ischemic stroke group were significantly higher than the control group (median values of 9.7 and 9.4) (p=0.003). The number of neutrophils in the transient ischemic attack group was significantly higher than the ischemic stroke group (p=0.011) and the hemorrhagic stroke group (p=0.014). Leukocyte levels were significantly higher in the transient ischemic attack group than the control group (p=0.037).

Conclusion: Mean platelet volume may be an important indicator of prognosis in ischemic stroke, whereas leukocyte and neutrophil counts may be important prognostic indicators of transient ischemic attack. There were no significant differences in the complete blood count parameters that we studied for the hemorrhagic stroke group.

Key Words: Stroke, Ischemic Attack, Transient; Blood Cell Count; Prognosis.

ARAŞTIRMA

GEÇİCİ İSKEMİK ATAK, İSKEMİK İNME VE HEMOROJİK İNME İLE TAM KAN SAYIMI PARAMETRELERİ ARASINDAKİ PROGNOSTİK İLİŞKİ

ÖZ

Giriş: Bu araştırmada lökosit sayısı, nötrofil sayısı, lenfosit sayısı, monosit sayısı, platelet sayısı, eritrosit dağılım genişliği, trombosit dağılım genişliği ve ortalama trombosit hacmi değerleri gibi tam kan sayımı parametreleriyle geçici iskemik atak, iskemik inme ve hemorojik inme arasındaki ilişkinin incelenmesi amaçlanmıştır.

Gereç ve Yöntem: Yüz yetmiş biri iskemik inme, 24'ü hemorajik inme (travmatik olmayan subaraknoid kanama ve intraparankimal kanama), ve 20'si geçici iskemik atak olmak üzere toplam 215 hasta ile 60 sağlıklı gönüllü çalışmaya dahil edildi. Acil servise başvuru anında alınan tam kan sayımındaki lökosit sayısı, nötrofil sayısı, lenfosit sayısı, monosit sayısı, platelet sayısı, eritrosit dağılım genişliği, trombosit dağılım genişliği ve ortalama trombosit hacmi değerleri kontrol grubu ile geçici iskemik atak, iskemik stroke ve hemorojik strok arasında ve grupların kendi aralarında karşılaştırıldı.

Bulgular: Hastaların yaş ortalaması 67.5 (min 22- max 96) iken 138 (%64.2) hasta 65 yaşın üstünde idi. Erkekler tüm hastaların % 53'ünü oluşturmaktaydı. Kontrol grubuyla iskemik inme hastaları arasında ortalama trombosit hacmi düzeyleri iskemik inme grubunda anlamlı ölçüde yüksekti (ortanca değerleri 9.7 ve 9.4) (p=0.003), geçici iskemik atak grubu, iskemik inme grubuna göre (p=0.011) ve hemorajik inme grubuna göre (p=0.014) daha fazla nötrofil sayısına sahipti. Lökosit düzeyleri geçici iskemik atak grubunda Kontrol grubuna göre istatistiksel olarak anlamlı ölçüde daha yüksekti (p=0.037).

Sonuç: Ortalama trombosit hacmi iskemik inmeden sonra prognozun önemli belirleyicisi olabilirken lökosit sayısı ve nötrofil sayısıda geçici iskemik atak grubunun prognozunda önemli belirleyici olabilir. Hemorojik inmede çalıştığımız tam kan sayımı parametreleri açısından anlamlı bir fark yoktur.

Anahtar Sözcükler: İnme; Geçici İskemik Atak; Tam Kan Sayımı Parametreleri; Prognoz.

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Introduction

Stroke is the third most common cause of death worldwide and is a major cause of serious morbidity and mortality. (1) In the U.S., approximately 795,000 persons experience a new or recurrent strokes yearly. Approximately 610,000 of these are first attacks, and 185,000 are recurrent attacks (2). Ischemic strokes constitute 87% and hemorrhagic strokes constitute 13% of all strokes (3).

Platelets play an important role in the pathogenesis of atherosclerotic complications by contributing to thrombus formation (4), Furthermore, platelet hypofunction may cause intracranial hemorrhage (5). MPV is an indicator of platelet function; larger platelets are more reactive, more easily produce prothrombotic factor and are more adherent.

The inflammatory response plays an important role in secondary injury following ischemia and stroke. Leukocytes, including neutrophils and macrophages, are believed to contribute to inflammatory tissue injury in acute stroke. Many reports have demonstrated leukocyte accumulation, initiation of thrombosis and exacerbation of ischemic brain injury after stroke.

The white blood cell (WBC) count has been established as a marker of inflammation, and although the WBC count and its subtypes have not been targeted for specific therapies, it does correlate with outcome in both elevation myocardial infarction and non-ST elevation myocardial infarction (6,7). The association between neutrophilia and impaired microvascular perfusion may be a manifestation of neutrophil-mediated microvascular plugging (8). In our study, we aimed to investigate the relationship between complete blood count parameters such as leukocyte, neutrophil, lymphocyte, monocyte, and platelet counts, RDW, PDW, and MPV values and TIA, ischemic stroke and hemorrhagic stroke.

Materials and Method

A total of 215 patients who were diagnosed with stroke and TIA, according to brain tomography and physical examination findings and the World Health Organization criteria (sudden onset of neurological deficit persisting for 24 hours in case of a stroke or less than 24 hours in case of a TIA), in the Ankara Atatürk Training and Research Hospital Emergency Department between 1 January 2011 and 1 January 2012 participated in the study. The patients who appropriate to the criteria defined by The American Heart Association in 2009 was admitted as TIA (9). The patient group included 171 ischemic stroke patients, 24 hemorrhagic stroke patients (nontraumatic subarachnoid hemorrhage and intraparenchymal hemorrhage) and 20 TIA patients. The files of these patients were reviewed retrospectively after approval of the hospital ethics committee. Sixty healthy volunteers who were not suspected to have stroke or TIA and who were free of exclusion criteria variables were included in the study as a control group.

The files included demographic data (age, gender); complaint; the type of admission; additional diseases; physical examination findings; Glasgow Coma Score; duration of hospitalization; leukocyte, neutrophil, lymphocyte, monocyte, and platelet counts; and RDW, PDW, and MPV values at the time of admission to the emergency department.

Blood samples of both the patient group and the control group were taken in ethylene diamine tetra acetic acid blood (EDTA) tubes and analyzed in the first hour in a Roche Sysmex X-2100 analyzer device.

Exclusion Criteria

- Patients who were admitted 24 hours after the onset of symptoms of stroke
- Patients with stroke due to trauma, tumor, infection, infarction or bleeding
- Patients presenting with lacunar infarct
- Patients presenting with epidural hematoma, or traumatic subarachnoid hemorrhage
- Patients with symptoms of acute coronary syndrome, pulmonary embolism, acute renal failure, and chronic renal failure besides stroke
- Patients with known thyroid disease
- Patients with known hematological disorders
- Patients brought to the emergency room because of cardiopulmonary arrest

Statistical Analysis

Statistical analysis was performed with the SPSS 15.0 software package. Compliance with normal distribution was evaluated with the Shapiro-Wilk test. The Kruskal-Wallis test was used to compare three groups for continuous variables which do not comply with the normal distribution; the data were expressed in median values and 25-75% quarterly values. A Mann-Whitney U test was used to compare two groups for continuous variables which do not comply with the normal distribution. Pearson's chi-square test was used for categorical data analysis; the data were expressed as numbers and percentages. A p value of <0.05 was considered statistically significant.

Table 1— Basic Demographic Characteristics of the Patients, Comorbidities and Drugs Used.

	Ischemic Stroke n (%) median	Hemorrhagic Stroke n (%) median	TIA n (%) median
Age	72 (60-80)	57 (43.25-75.00)	67 (59-80)
Male sex	87 (50.9%)	16 (66.7%)	11 (55.0%)
Diabetes Mellitus	59 (34.5%)	5 (20.8%)	11 (55.0%)
Hypertension	108 (63.2%)	13 (54.2%)	16 (80.0%)
Previous Ischemic Stroke	22 (12.9%)	2 (8.3%)	1 (5.0%)
Previous Hemorrhagic Stroke	1 (0.6%)	-(-)	-(-)
Coronary Artery Disease	40 (23.4%)	7 (29.2%)	4 (20.0%)
Atrial fibrillation	19 (11.1%)	1 (4.2%)	0 (0.0%)
The use of aspirin	64 (37.4%)	8 (33.3%)	8 (40.0%)
The use of warfarin	10 (5.8%)	1 (4.2%)	3 (15.0%)
The use of oral antidiabetic	53 (31.0%)	3 (12.5%)	8 (40.0%)
The use of antihypertensive	108 (63.2%)	12 (50.0%)	15 (75.0%)
Cigarettes	22 (12.9%)	3 (12.5%)	1 (5.0%)
Alcohol	3 (1.8%)	-(-)	-(-)

Results

A total of 215 patients and 60 healthy volunteers were enrolled in the study. The patient group included 171 (79.5%) with ischemic stroke, 24 (11.2%) with hemorrhagic stroke, and 20 (9.3%) with TIA. The demographic characteristics of the patients are presented in Table 1. There was no statistically significant difference among the three groups in terms of gender (p=0.343). There were no significant differences between the groups in terms of the numbers of patients with a prior diagnosis of diabetes mellitus and hypertension (p=0.059 and 0.196). However, there was a significant difference between the groups in terms of ages of the patients (p=0.003). That is, the median age of the ischemic stroke group was significantly higher than that of the TIA group (p=0.001). In addition, average age of the patients was 67.5 (min 22-max 96), while 138 (64.2%) patients were over the age of 65. The number of patients over 65 was significantly greater than the number of patients under the age of 65. Men accounted for 53% of all patients. There were no significant differences between patients above and below age 65 in terms of prior diagnosis of diabetes mellitus (p=0.878), hypertension (p=0.056), ischemic stroke (p=0.207), history of atrial fibrillation (p=0.137) and mortality (p=0.325). Coronary artery disease was more common among patients who were over age 65 (p=0.043). The demographic data and laboratory test results of patients under and above 65 years of age are given in Table 2.

Regarding admissions to the emergency department, 137 of the patients with ischemic stroke (80.1%), 9 of the patients with hemorrhagic stroke (37.5%), and 19 of the patients with TIA (95.0%) were admitted to the emergency department by ambulance.

Some of the complete blood count values of the ischemic stroke, hemorrhagic stroke and TIA groups are presented in Table 3. The number of neutrophils was significantly higher in the TIA group than in either the ischemic stroke group (p=0.011) or the hemorrhagic stroke group (p=0.014). No statistically significant difference was observed between the number of neutrophils in the ischemic stroke and hemorrhagic stroke groups. There were no significant differences between the groups in terms of the other parameters.

The median age of the control group of 60 healthy volunteers who were included in the study was 66.50 (59.25-72.25). No significant age difference was observed between the patient group and the control group (p = 0.072). In the control group, the median value of MPV was 9.4 (8.8-9.9), leukocyte count was 8,200 (6,600 to 10,175), and platelet count was 223,000 (201500-273250). In terms of leukocyte and platelet counts, no significant differences were observed between the control group and ischemic stroke group (p=0.853 and p=0.248, respectively), but the MPV levels of the ischemic stroke group were significantly higher (median values of 9.7 and 9.4; p=0.003, respectively). On the other hand, the median age of the control group was significantly higher than that of ischemic stroke group (p=0.010). No sig-

Table 2— Demographic Data of Patients Under and Above 65 Years of Age, and Laboratory Results.

	Patients Under the Age of 65	Patients Over the Age of 65	p
Age	52 (47-59)	76 (72-81)	**<0.001**
Male sex	45 (59.2%)	69 (49.6%)	0.179
Duration of hospitalization (days)	5.5 (2-10)	6 (4-10)	**0.016**
GCS	15 (14-15)	15 (14-15)	0.433
Leukocyte counts	8750 (7100-10425)	7780 (6325-10275)	0.087
Platelet counts	232500 (193000-273000)	216500 (180500-256750)	**0.021**
Monocyte counts	600 (500-900)	600 (500-900)	0.354
Lymphocyte counts	2280 (1500-2900)	1505 (1000-2000)	**<0.001**
Neutrophil counts	5200 (4367-6825)	5400 (4100-7800)	0.689
MPV	9.6 (9.2-10.1)	9.8 (9.0-10.4)	0.239
RDW	44.5 (41.5-46.5)	46.5 (44.1-49.7)	**<0.001**
PDW	12.1 (11.1-13.1)	12.5 (11.2-14.1)	0.099

GCS: Glasgow Coma Score, MPV: Mean Platelet Volume, RDW: Red Blood Cell Distribution Width, PDW: Platelet Distribution Width.

Table 3— Distribution of Laboratory Values Across Patient Groups.

	Ischemic Stroke Median (25-75%)	Hemorrhagic Stroke Median (25-75%)	TIA Median (25-75%)	p
Platelet counts	222000 (182000-264000)	221000 (194500-252000)	232000 (187000-299000)	0.745
Monocyte counts	600 (500-880)	600 (550-900)	700 (600-1000)	0.270
Lymphocyte counts	1690 (1100-2400)	1600 (1335-2650)	1600 (1200-2200)	0.617
Leukocyte counts	8000 (6500-10500)	8500 (7000-9500)	9000 (8000-11900)	0.089
Neutrophil counts	5240 (4100-7300)	4900 (3650-7600)	6200 (5700-10200)	0.025
MPV	9.7 (9.1-10.4)	9.90 (9.20-10.15)	9.5 (8.7-10.0)	0.397
RDW	46.1 (43.5-48.7)	44.50 (40.35-46.45)	48.1 (44.7-51.6)	0.123
PDW	12.3 (11.2-14.0)	12.60 (11.45-14.75)	11.9 (10.4-13.7)	0.490

MPV: Mean Platelet Volume, RDW: Red Blood Cell Distribution Width, PDW: Platelet Distribution Width.

nificant differences were observed between the hemorrhagic stroke group and control group in terms of leukocyte platelet count and MPV values (p=0.855, p=0.386, p=0.056 respectively), although the median age of the control group was significantly higher than that of hemorrhagic stroke group (p=0.014).

No significant differences were found between the control group and the TIA group in terms of age, MPV values and platelet counts (p=0.423, p=0.714, p=0.973 respectively), but leukocyte levels were significantly higher in the TIA group (p=0.037). In the follow up, 172 patients were hospitalized in the clinic (80.0%) and 24 patients were hospitalized in the intensive care service (11.2%), while 19 patients (8.8%) were discharged after follow-up in the emergency department. There was no significant correlation between MPV levels of these patients and hospitalization (p = 0.948). Twenty-three patients (10.7%) died in the hospital.

Discussion

The prevalence of stroke between the ages of 45 and 64 is 2.9% person; it rises to 6.3% person for people aged 65-74 and then rises to 10.6% person for those above the age of 75 (10). It is 2-3 times more common among men between the ages of 55 and 64, whereas this difference decreases after the age of 85. Due to this prevalence, new and different treatment methods have been introduced, especially in the treatment of ischemic stroke, and rapid diagnosis of the patients has become even more important. In order to detect the existence of ischemic brain injury, many biochemical markers, as

well as complete blood count parameters, have been investigated. In our study, we investigated whether leukocyte, neutrophil, lymphocyte, monocyte, and platelet counts, and RDW, PDW, and MPV values have any diagnostic value in TIA, hemorrhagic stroke, and ischemic stroke. In our patient group, 64.2% were over the age of 65, the average age was 67.5 years, and the majority of the patients were men (53%). These data, consistent with the literature, reveal that the majority of stroke patients are over age 65.

Although the effects of dysfunction or number of platelets in the pathophysiology of hemorrhagic stroke are not fully understood, platelets do play an important role in the pathophysiology of stroke. The relationship between MPV and severity and prognosis of stroke is still controversial (11,12). There are several studies indicating the prognostic impact of MPV, while other studies report no relationship between MPV and the prognosis of stroke (13,14). Bath et al. in their study reported that MPV is primarily associated with ischemic stroke, but there is no association between MPV and hemorrhagic stroke and strokes with unknown cause (11,15,16). However, in another study that investigated only the relationship between MPV and hemorrhagic stroke, MPV was reported to have prognostic impact (11,12). In our study, MPV was significantly higher in ischemic stroke, compared to hemorrhagic stroke and TIA. Given our results, we suggest that MPV may have a prognostic impact on ischemic stroke, but does not have any prognostic impact on hemorrhagic stroke and TIA.

Circulating platelets show a broad spectrum of values, and an inverse relationship between platelet count and mean platelet volume is known to exist (11,13). An increase in mean platelet volume has been reported in acute myocardial infarction (17). Toghi et al., in their study with lacunar stroke patients, reported a decrease in the platelet PDW in the acute and sub-acute phases (18). The significance of hematologic and biochemical parameters associated with spontaneous intracerebral hemorrhage has not been studied extensively (19). Impaired platelet function has been associated with an increased risk for intracerebral hemorrhage, and platelet count on the first day was found to be a good predictor of mortality, but the role of platelet count and dysfunction in the pathogenesis of hemorrhagic stroke is still poorly understood (19,20,21). In our study we did not observe any prognostic relationship between the number of platelets and PDW and ischemic stroke, hemorrhagic stroke, and TIA.

Inflammatory processes pose a risk for ischemic stroke, and also play an important role in the pathophysiology of cerebral ischemia. Brain ischemia and following reperfusion causes an inflammatory response in microcirculation, which is responsible for cell destruction (22). On the other hand, it is reported that systemic inflammation plays an important role in the development of atherosclerosis, and is associated with a high risk for coronary heart disease and stroke (22,23). However, the role of the inflammatory response is not clear in hemorrhagic stroke.

In one study, monocyte counts were higher in patients with both TIA and ischemic stroke, and leukocyte counts were significantly higher in TIA patients, whereas there was no significant difference between the groups in terms of monocyte and neutrophil counts (24). In another retrospective study with 1041 patients with ischemic stroke and TIA, the number of neutrophils and leukocytes were significantly higher in both groups (25). In our study, leukocyte and the neutrophil counts were significantly higher in the TIA group than the control group, whereas there were no significant differences between ischemic stroke and hemorrhagic stroke in terms of RDW, WBC, neutrophil and lymphocyte counts.

VCAM-1 is one of the many endothelium-derived adhesion molecules and binds monocytes and T cells. These cells connect to the endothelium, pass through subendothelial area and accumulate there. This accumulation causes lipid accumulation and results in atherosclerosis. In a study conducted with TIA and ischemic stroke patients, the number of monocytes were significantly high in both groups (25). We did not observe any significant change in terms of the number of monocytes in any of the three groups.

RDW is an important parameter used in the differential diagnosis of the underlying cause of anemia. Apart from this, in recent years it has been suggested that RDW may have a role in the pathogenesis of inflammation. The relationship between RDW and the prognosis of myocardial infarction, heart failure, and stroke has been investigated and an association between RDW and poor prognosis has been suggested (26). Ani et al. showed that the mean RDW was significantly higher among persons with a stroke compared to individuals without a stroke, but these associations are still controversial (26). In our study, we did not find a significant difference in terms of RDW among any of the three groups.

In conclusion, MPV may be an important indicator of prognosis in ischemic stroke, whereas leukocyte and neutrophil counts may be important indicators of prognosis in TIA. There is no significant difference in terms of complete blood count parameters in hemorrhagic stroke. But more evidence is needed to determine whether this results in a clinically important effect. Assuming that the peripheral inflammatory response is a result of brain tissue damage may be a premature conjecture.

Study Limitations: The lack of distinction between the anterior and posterior circulation and the infarct volume which have prognostic value in ischemic stroke.

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