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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

HETEROZİGOT BETA TALASEMİLİ HASTALARDA TAM KAN SAYIMININ ROLÜ

THE ROLE OF COMPLETE BLOOD COUNT IN PATIENTS WITH HETEROZYGOUS BETA THALASSEMIA

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ÖZET

AMAÇ: Çalışmanın amacı heterozigot beta talasemili (HBT) olgularla sağlıklı çocuklardaki Tam Kan Sayımı parametrelerini değerlendirerek Ortalama Trombosit Hacmi (MPV), Trombosit Lenfosit oranı (PLR) ve Nötrofil Lenfosit oranını karşılaştırmaktır.

GEREÇ VE YÖNTEM: Temmuz 2016 ve Eylül 2019 tarihleri arasında HBT tanısı konulan çocuk hematoloji onkoloji polikliniğine başvuran 60 hasta ile benzer yaş ve cinsiyette 60 sağlıklı kontrol olgusu retrospektif olarak incelendi. Bir yaşın üzerindeki çocuklar arasında hemoglobin A2 düzeyi% 3.5'in üzerinde olanlar çalışmaya alındı.

BULGULAR: Toplam 120 olgu çalışmaya dahil edildi. HBT grubunda 60 olgu (32 erkek ve 28 kadın) ve kontrol grubunda da 60 (36 erkek ve 24 kadın) olgu bulunmaktaydı. İki grup arasında yaş ve cinsiyet açısından anlamlı fark yoktu (p = 0,29 ve p = 0,27). Trombosit sayısı, MPV, lenfosit ve ferritin HBT grubunda anlamlı olarak daha yüksekken, hemoglobin HBT grubunda kontrol grubuna göre anlamlı olarak daha düşüktü.

SONUÇ: Sağlıklı HBT'li hastalarda MPV ve trombosit sayısındaki artış hiperkoagulabiliteye neden olabilir ve erişkin olgularda tromboza yatkınlıkta diğer risk faktörleriyle birlikte rol oynayabilir. HBT olgularda tromboembolik olayların insidansı konusunda çok az çalışma vardır, erişkin HBT olgularını özellikle tromboembolik olaylar açısından izlemek ve daha fazla olgu ile çalışma yapmak gerekmektedir.

ANAHTAR KELİMELER: Heterozigot Beta Talasemi, Ortalama Trombosit Hacmi, Tam Kan Sayımı, Trombosit

ABSTRACT

OBJECTIVE: The goal of this study was to compare the Mean Platelet Volume (MPV), Platelet Lymphocyte ratio, and Neutrophil Lymphocyte ratio by evaluating the parameters of Complete Blood Count in healthy children and patients with heterozygous Beta-thalassemia (HBT).

MATERIAL AND METHODS: Between July 2016 and September 2019, 60 patients admitted to the pediatric hematology-oncology outpatient clinic diagnosed with HBT and 60 healthy control subjects of similar age and sex were analyzed retrospectively. Children over one year old, whose hemoglobin A2 levels were above 3.5% were included in the study population.

RESULTS: A total of 120 subjects were enrolled in this study. The HBT group included 60 subjects (32 males and 28 females) and the control group included 60 (36 males and 24 females). There were no significant differences between the two groups in terms of age and gender (p=0.29 and p=0.27). Platelet count, MPV, lymphocyte, and ferritin were significantly higher in the HBT group, whereas hemoglobin was significantly lower in the HBT group as compared with the control group.

CONCLUSIONS: Increased MPV and platelets in healthy HBT patients may cause hypercoagulability and may play a role with other risk factors in the predisposition of thrombosis in adult cases. There are very few studies on the incidence of thromboembolic events in cases with HBT. It is necessary to monitor adult HBT cases especially in terms of thromboembolic events, and to study with more cases.

KEYWORDS: Heterozygous Beta-thalassemia, Mean Platelet Volume, Complete Blood Count, Platelet

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INTRODUCTION

Beta thalassemia is an inherited congenital hemoglobin synthesis disorder characterized by defective beta chains of hemoglobin that reduces the production of hemoglobin (1). It is the most common preventable hereditary blood disease worldwide. There are three types of beta thalassemia according to the clinical symptoms (2); thalassemia major, thalassemia intermedia, and thalassemia minor (heterozygous Beta-thalassemia). Thalassemia major causes life-threatening anemia; recurrent blood transfusions and iron chelation treatment are needed. Mild to moderate anemia can be seen in patients with thalassemia intermedia, the need for transfusion is less than in thalassemia major. Mild anemia is usually seen in patients with heterozygous Beta-thalassemia (HBT). Although hemoglobin levels vary between 9-11 g/dl, normal hemoglobin levels may be detected in some patients. If the HbA2 level is more than 3.5%, the patient is diagnosed with HBT. The incidence of arterial and venous thromboembolism increases in thalassemia patients compared to the healthy population (3). The increased risk of thrombosis occurs especially in patients with Beta-thalassemia intermedia and/or thalassemia major with splenectomy.

Hypercoagulability is known to occur in patients with thalassemia, which explains the increase in the prevalence of thromboembolic events (4).

The presence of a high incidence of thromboembolic events has led to the identification of a hypercoagulable state in these patients. There are many factors in the pathophysiology of these thrombotic events. Platelet activation is one of the reasons for hypercoagulability (5).

Mean platelet volume (MPV) is a highly sensitive marker for platelet activation. MPV in healthy humans varies between 7.2-11.7 fl. It is a significant marker to show platelet turnover. Larger platelets are younger and more reactive than normal platelets. Increased MPV indicates platelet production and in vivo platelet activation. The relationship between increased MPV and venous thromboembolism (VTE) has been shown in previous studies. And also some studies suggest that MPV can be a predictive marker for detecting VTE (6). Hemogram is an easily accessible, simple, and inexpensive test that provides information about the quantitative and qualitative properties of many blood cells such as platelets, neutrophils, and lymphocytes. High platelet-lymphocyte ratio (PLR) and neutrophil-lymphocyte ratio (NLR) are effective in thromboembolic events and inflammation.

Recent reports show that PLR and NLR can be used as markers to predict susceptibility to thrombosis (7, 8). The purpose of our study was to establish the susceptibility to thrombotic events by comparing MPV, PLR, and NLR in HBT and the healthy population.

MATERIAL AND METHOD

Between July 2016 and September 2019, 60 patients admitted to the pediatric hematology-oncology outpatient clinic diagnosed with HBT and 60 healthy children of similar age and gender were studied retrospectively. Age, gender, body weight, drug use, hemogram, ferritin, hemoglobin electrophoresis results were recorded from patients' files. The study population consisted of children over one year of age whose hemoglobin A2 level was above 3.5%. Patients with acute and chronic infections, antiaggregant and anticoagulant drugs, solid tumors, hematologic malignancies, and iron deficiency anemia were excluded from the study.

Healthy children over one year of age with normal hemoglobin values were included in the control group. All results were analyzed using SPSS 18 (SPSS, Chicago, IL, USA). Subjects were split into two groups as HBT and control. Categorical variables are described as percentages and numbers while numerical variables are expressed as a minimum, maximum, and mean ± SD. The categorical independent variables were compared between groups using the χ 2 test. The one-sample Kolmogorov- Smirnov test was used to determine if the numerical independent variables were normally distributed.

The chi-squared and Mann–Whitney U tests were used for non-normally distributed variables. The students-test was used to compare normally distributed parametric data. In every instance, a p-value< 0.05 was considered statistically significant.

Ethical Committee

The study was approved by the Ethics Committee of Afyonkarahisar Health Science University (2019/376). All subjects gave written informed consent for the study.

RESULTS

A total of 120 subjects were enrolled in this study. The HBT group consisted of 60 subjects (32 males, 28 females) and the control group consisted of 60 subjects (36 males, 24 females). There were no significant differences between the two groups in terms of age and gender (p=0.29 and p=0.27). Baseline characteristics and laboratory parameters of the study groups were given in **(Table 1)**.

Table 1: Characteristics and laboratory parameters of the study groups

	HBT	Control	p
Age	6,42-4,17(1,00-15,00)	7,23-4,43(1,00-16,00)	0,292
Hemoglobin	10,21-0,70(8,20-11,90)	13,38-1,01(12,00-16,40)	<0,001
Mean Platelet Volume	10,02-1,06(8,00-13,20)	8,67-0,76(7,00-9,80)	<0,001
Leukocyte	8,51-2,13(4,39-13,04)	7,83-1,66(4,43-12,05)	0,052
Neutrophil	4,62-1,53(1,86-7,60)	4,30-1,14(2,10-7,30)	0,368
Lymphocyte	3,28-0,91(1,50-5,40)	2,83-0,92(1,00-5,40)	0,008
Platelet	393,00-144,77(195,00-817,00)	303,63-85,15(177,00-556,00)	<0,001
Ferritin	39,51-19,56(14,40-92,00)	32,25-16,25(12,93-79,20)	0,014
Neutrophil/lymphocyte	1,48-0,54(0,44-3,43)	1,66-0,65(0,59-4,09)	0,264
Platelet/lymphocyte	131,47-73,41(48,75-508,00)	125,90-81,73(41,16-545,00)	0,358

Platelet count, MPV, lymphocyte, and ferritin were significantly higher in the HBT group whereas hemoglobin was significantly lower in the HBT group as compared with the control group.

DISCUSSION

The incidence of thromboembolic events in thalassemia patients increases compared to the healthy population. The risk is higher, especially in patients with Beta-thalassemia intermedia and splenectomy. The reason for the increase in the prevalence of thromboembolic events is thought to be associated with hypercoagulability (9). The causes of hypercoagulability are, as follows; increased platelet aggregation, and expression of activation markers, impairment of platelet morphology, increased platelet count, and activation in patients with splenectomy (10). High platelet count seems to be a predictor of increased thromboembolic event risk in patients with thalassemia intermedia and thalassemia who underwent splenectomy (4). Although platelets are thought to be playing a central role in arterial thrombosis, it is also thought to be effective in the pathogenesis of venous thrombosis. Recent studies have shown that it is effective in deep vein thrombosis (11).

In our study, platelet levels were higher in patients with HBT than in the control group. Platelet size reflects platelet activation. Large platelets are more metabolic and enzymatically active than small ones (12). The MPV is an important platelet volume indicator and is a simple and reliable parameter showing platelet activation and function (13). The relationship between increased MPV and VTE has been demonstrated and it was thought that MPV can be a valuable marker for VTE (12).

In a study performed by Braekkan et al. it was shown that high MPV levels were identified as a marker for VTE and the importance of platelet activity in the pathogenesis of VTE (14). In a study on platelet indices in 2013 patients with acute deep vein thrombosis; Cay et al. found that MPV values were higher than the control group and they stated that the presence of DVT may be closely related to increased platelet activation (15). In another study, including 147 patients, examining the relationship between acute DVT and MPV in hospitalized patients, MPV values were found high in these patients and it was recommended that this was an independent predictor (16). In our study, MPV values were significantly higher in the HBT group than in the control group. Numerous studies have been conducted to research the increased incidence of thromboembolic events in thalassemia patients with splenectomy and thalassemia intermedia (17). However, there is limited data on thrombosis status in HBT. In the meta-analysis of arterial thromboembolic events in thalassemia carriers, it was concluded that Beta-thalassemia carriage may play a role as a protective factor against arterial cardiovascular and cerebrovascular disease in male patients (18). In the study of 2356 HBT and 9424 control cases performed in Taiwan between 2001 and 2010, the incidence of arterial thromboembolic events and myocardial ischemia is significantly higher in HBT cases (19). In a study performed in adult patients with 48 HBT and 51 control

subjects, MPV was found to be significantly higher than the control group (13). Similarly, in our study, MPV was found to be higher in patients with HBT than in the control group. Increased PLR values show inflammatory status and platelet activation (20). Previous studies have shown that high NLR and PLR may be associated with thrombosis and are valuable as an independent marker for the development of central venous sinus thrombosis, pulmonary emboli, and acute DVT (11, 21). Unlike in our study, NLR and PLR levels in HBT and control groups were not statistically significant. We acknowledge that the limits of our study are mainly represented by the retrospective setting and the small cohort.

In our study, we found increased MPV and platelet levels in healthy HBT patients. This may cause hypercoagulability and play a role with other risk factors in the predisposition of thrombosis in adult cases. There are very few studies on the incidence of thromboembolic events in cases with HBT, it is necessary to monitör adult HBT cases especially in terms of thromboembolic events, and to study with more cases.

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