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ORIGINAL ARTICLE

The Relationship Between Inflammatory Blood Cells and Executive Functions in Medication-Free Children with ADHD

İlaç Kullanmayan DEHB'li Çocuklarda İnflamatuar Kan Hücrelerinin Yürütücü İşlevler İle İlişkisi

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ABSTRACT

Background: The present study aimed to compare blood neutrophil, lymphocyte, platelet, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), erythrocyte and systemic inflammatory index levels in children with attention deficit hyperactivity disorder (ADHD) with typically developing (TD) healthy controls and to investigate the relationship between these levels and executive functions.
Materials and Methods: In this study, 79 ADHD children aged 8-14 years who did not use medication and 34 healthy controls were included. Participants' blood levels were based on routine complete blood count analysis. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) was used for clinical diagnosis in children, and the Stroop color test and serial digit learning test were applied to evaluate executive functions.
Results: No significant difference was found between the groups in neutrophil, lymphocyte, platelet, NLR, PLR, erythrocyte, and systemic inflammatory index levels. Compared to TDs, patients with ADHD were observed to perform significantly worse on executive function tests. Platelets, neutrophils, and lymphocytes were positively correlated with Stroop first section correction scores, platelets were positively correlated with Stroop second section time scores, lymphocytes were positively correlated with Stroop second section correction scores, NLR was negatively correlated with Stroop second section correction scores and platelets was positively correlated with Stroop third section time scores. Platelets and lymphocytes were positively correlated with Stroop section fourth time scores and NLR was positively correlated with Stroop section fourth error scores.
Conclusion: This study suggests that serum lymphocyte, neutrophil, NLR, and platelet levels may be associated with impaired executive tests in ADHD.

Keywords: Attention deficit hyperactivity disorder, child, executive function, systemic immune inflammation index

ÖZ

Arka plan: Bu çalışmanın amacı dikkat eksikliği ve hiperaktivite bozukluğu (DEHB) olan çocuklarda kan nötrofil, lenfosit, platelet, nötrofil-lenfosit oranı (NLR), platelet-lenfosit oranı (PLR), eritrosit ve sistemik inflamatuar index düzeylerini tipik olarak gelişen (TG) sağlıklı kontrollerle karşılaştırmak ve bu düzeylerin yürütücü işlevler ile ilişkilerini araştırmaktır.
Yöntemler: Bu çalışmaya 8-14 yaşları arasında ilaç kullanmayan 79 DEHB'li çocuk ve 34 TG sağlıklı kontrol dahil edilmiştir. Katılımcıların kan düzeyleri rutin tam kan sayımı analizine dayanmaktadır. Çocuklarda klinik tanı için Ruhsal Bozuklukların Tanısal ve Sayımsal El Kitabı, Beşinci Baskı (DSM-5) kullanılmış ve yürütücü işlevleri değerlendirmek için stroop renk testi ve sayı dizisi testi uygulanmıştır.
Bulgular: Nötrofil, lenfosit, platelet, NLR, PLR, eritrosit ve sistemik inflamatuar index düzeylerinde gruplar arasında anlamlı bir fark bulunmadı. Kontrol grubu ile karşılaştırıldığında, DEHB'li hastaların yürütücü işlev testlerinde anlamlı olarak daha kötü performans sergilediği gözlenmiştir. Platelet, nötrofil ve lenfositin stroop 1.bölüm düzeltme skorları ile pozitif, plateletin stroop 2.bölüm süre skorları ile pozitif, lenfositin stroop 2.bölüm düzeltme skorları ile pozitif korelasyon, NLR'nin ise stroop 2.bölüm düzeltme skorları ile negatif korelasyon, plateletin stroop 3.bölüm süre skorları ile pozitif korelasyon gösterdiği belirlenmiştir. Platelet ve lenfosit stroop 4.bölüm süre skorlarıyla pozitif, NLR stroop 4.bölüm hata skorlarıyla pozitif korelasyon göstermiştir.
Sonuç: Bu çalışma serum lenfosit, nötrofil, nötrofil-lenfosit oranı ve platelet düzeylerinin DEHB'deki bozulmuş yürütücü testlerle ilişkili olabileceğini göstermektedir.

Anahtar kelimeler: Çocuk, dikkat eksikliği hiperaktivite bozukluğu, sistemik immün inflamasyon indeksi, yürütücü işlev

Introduction

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by persistent symptoms of inattention, hyperactivity, and impulsivity (1). One widely accepted theory of ADHD symptomatology states that children and adolescents with this disorder show immature executive function development (2). In cognitive functioning, ADHD is most consistently associated with deficits in executive functions such as sustained attention, working memory, timing, psychomotor speed, and reaction time variability (3). Increased serum inflammatory markers have been reported to be associated with impaired executive function tests (4). In addition, in recent years, there has been increasing interest in investigating the role of systemic inflammation and immune dysregulation in the pathogenesis of ADHD (5). Genetic studies have also shown links between ADHD and polymorphisms

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in genes associated with inflammatory pathways (6). Studies to date have shown that inflammatory cytokine levels in patients with ADHD are higher than in healthy individuals (7). Increased levels of cytokines in the central nervous system (CNS) can lead to neuroinflammation and consequent impairment of neuronal plasticity or alterations in synaptic processes (8). Increased risk of ADHD has been reported in children of mothers with inflammatory and immune system diseases (9). Changes in inflammatory cytokines have been shown to cause neurotransmission changes in dopaminergic pathways in the brain similar to those seen in ADHD (10). It has also been reported that there are inconsistent findings in studies on inflammatory changes in ADHD (11).

Ongoing inflammatory processes in the body can be recognized by complete blood count (CBC) tests, which are frequently used in clinical practice. CBC includes levels of erythrocytes, white blood cells (WBCs), neutrophils, lymphocytes, and platelets (12).

The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) reflect the balance between adaptive immune responses and can be used to assess their use in routine clinical practice in chronic low-grade inflammation (13, 14). In recent years, NLR and PLR have been reported to be elevated in patients with depressive, bipolar, or non-affective psychosis (15). A recent meta-analysis showed that ADHD patients had higher NLR and PLR values compared to controls, and no significant difference was observed in inflammatory markers in studies including analyses according to ADHD subtypes. (16). However, higher WBC, neutrophil and NLR levels have been reported in women with ADHD compared to men with ADHD (17).

Changes in platelet function can affect common pathways with neurons by triggering inflammatory processes (18). PLR is a widely used marker that is thought to be associated with malignancies and infections (19).

A new index defined as the systemic immune inflammation index (SII) has been developed concerning inflammation variability. This index (Platelet × Neutrophil/Lymphocyte) is based on platelet, neutrophil, and lymphocyte counts (20). High SII appears to be associated with subclinical low-grade inflammation (21).

This study aimed to investigate whether neutrophil, erythrocyte, NLR, PLR, lymphocyte, platelet, and SII levels, which are an easy option for use in clinical practice in children with ADHD who have not received drug treatment, are different from typically developing (TD) healthy children and whether this is associated with inflammatory response and ADHD. In addition, the relationship between these parameters and executive functions in ADHD will be evaluated.

Materials and Methods

In the Child and Adolescent Psychiatry Outpatient Clinic of the Faculty of Medicine at Selcuk University, patients diagnosed with eating disorders, visual and hearing loss, chronic blood disease, organic brain damage, chronic physical illness, obesity, overweight, active infection, specific learning disability, genetic disorders, intellectual disability, substance abuse, schizophrenia, major depressive disorder (MDD), autism spectrum disorder (ASD) and language disorders and patients who had previously used any psychiatric medication were excluded from the study. Children with ADHD were included in the study considering the above-mentioned conditions. The selection process of participants with ADHD is shown in Figure 1.

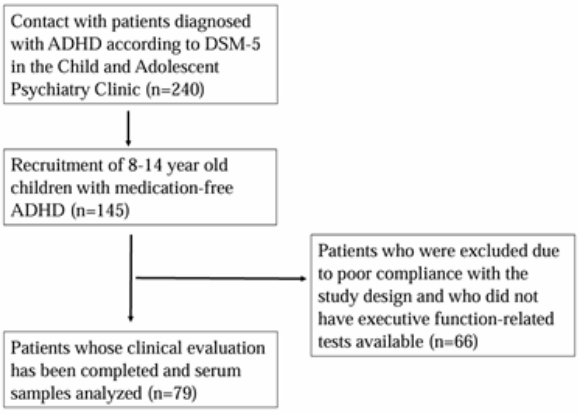

Figure 1. Flowchart of the patients' inclusion. ADHD: attention deficit hyperactivity disorder, n: number.

The TD control group consisted of healthy children who came to our clinic for consultation and were randomly selected under the exclusion criteria. Seventy-nine children were included in the ADHD group and 34 children were included in the TDs.

After the examination, sociodemographic data forms were completed by the clinician for both groups. Written informed consent was obtained from the parents of the children in both groups. The ages of the children ranged between 8 and 14 years. Children in both groups were similar in terms of age, height, weight, and body mass index (BMI).

The study was conducted under the Declaration of Helsinki and approved by the ethics committee of the Selçuk University Faculty of Medicine (Date: July 30, 2024, number: 2024/14).

Clinical assessment

The children in both groups were evaluated by a certificated interview using the Schedule for Affective Disorders and Schizophrenia for School-Age Children, Present and Lifetime Version (KSADS-PL) and diagnosed based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), criteria (22, 23). The validity and reliability of the K-SADS-PL for Turks were confirmed by Ünal et al. (24).

Stroop Test and Serial Digit Learning Test (SDLT) were administered to the participants by the clinician (25). Validity and reliability studies of the Stroop Test for the Turkish population were performed by Karakaş et al (26).

The SDLT was first proposed by Zangwill (1943) as a method for assessing short-term memory deficits (27). Studies on the standardization of the SDLT to Turkish culture were carried out by Karakaş et al (26). In the evaluation, the number of attempts by which the mastery learning was achieved and the total score were considered (28).

Blood Samples

Blood samples were taken from all children in both groups between 09.00 and 10.00 hours after 9 hours of fasting. All blood analyses were performed in the Biochemistry Laboratory of Selcuk University Medical Faculty Hospital using an automatic hematological analyzer (BC 6200). SII, NLR, and PLR values were obtained from CBC results based on quantitative analysis of blood cells.

Statistical analysis

The Statistical Package for Social Sciences, software version 24.0 (SPSS Inc., Chicago, IL) was used for the statistical analysis. Clinical, demographic, and blood variables were compared between the groups according to their distributions, as determined using the Student t-test or Mann-Whitney U test. The chi-square test was used for categorical data, and skewness and kurtosis values between −2 and +2 were used to determine a normal distribution (George, 2011). A p-value <0.05 was accepted as significant at the 95% CI. Effect sizes (ESs) were estimated using Cohen's d (parametric-nonparametric comparisons) and Cramér's V (categorical variables; Ess: ≥0.8, large; 0.5–0.7, intermediate; 0.2–0.4, small; and <0.2, no effect) (29). The Pearson and Spearman tests were used to determine any correlations between the blood parameters and executive function tests.

Results

A total of 113 children (34 in the TDs and 79 in the ADHD group) were included in the study. There was no statistically significant difference between ADHD and TD control groups in terms of weight, height, age, and BMI, but a significant difference was observed in terms of sex.

Regarding executive functions, Stroop's third, fourth, and fifth section times were significantly longer in the ADHD group than in the TDs. Stroop third, fourth, and fifth segment corrections were significantly higher in the ADHD group than in the TDs. Serial Digit Learning Test scores were significantly lower in the ADHD group compared to TDs.

No significant difference was found between the two groups in terms of neutrophil, erythrocyte, lymphocyte, NLR, PLR, SII, and platelet levels (z = −0,644; p =0,519, z = 0,136; p = 0,892, t = 0,705; p = 0,482, t = 1,201; p= 0,232, z = −0,745; p= 0,456, z = −0,472; p =0,637, t =-0,080; and p= 0,936, respectively).

Height, sex, weight, age, BMI, blood variables, and executive function-related test data of the two groups are shown in Table 1.

Platelets, neutrophils, and lymphocytes were positively correlated with Stroop 1 correction scores (p= 0,048; r= 0,223, p= 0,047; r= 0,224, p= 0,011; r= 0,286, respectively), platelets were positively correlated with Stroop 2 times scores, lymphocytes were positively correlated with Stroop 2 correction scores, NLR was negatively correlated with Stroop 2 correction scores (p= 0,037; r= 0,235, p= 0,007; r= 0,299, p= 0,015; r= -0,273, respectively) and platelets were positively correlated with Stroop 3 times scores (p=0,017; r= 0,267) (Table 2).

Platelet and lymphocyte correlated positively with Stroop section 4 time scores and NLR correlated positively with Stroop section 4 error scores (p= 0,002; r= 0,344, p= 0,016; r= 0,271, p= 0,014; r= 0,277, respectively) (Table 3).

Discussion

To the best of our knowledge, this is the first study to examine the relationship between neutrophil, erythrocyte, lymphocyte, NLR, PLR, SII, platelet levels,

Table 1. Data regarding the comparison of serum neutrophil, lymphocyte, NLR, PLR, erythrocyte, platelet, and SII levels and demographic and clinical variables of the two groups.

	ADHD (79)	TD (34)	p	$t/x^2/z$	d
Age (years)	10.43±2.57	10.74±2.24	0.550	-0.600	0.012
Sex	Erkek (47) Kız (32)	Erkek (13) Kız (21)	0.038	4.313	0.195[a]
Height	142.97 ±13.32	139.20 ±13.19	0.169	1.383	0.028
Weight[b]	38.98 ±11.44	37.58 ±15.44	0.758	-0.308	0.010
BMI	18.72±3.19	18.72 ±4.04	1.000	0.000	0.000
S1T[b]	13.95 ±5.47	10.98±2.59	0.251	-1.148	0.069
S1E	-	-	-	-	-
S1C[b]	0.13±0.46	0.06±0.23	0.598	-0.527	0.018
S2T[b]	14.78±6.25	12.59±3.42	0.537	-0.617	0.043
S2E[b]	0.03 ±0.17	-	-	-	-
S2C[b]	0.32 ±0.69	0.09 ±0.28	0.311	-1.012	0.043
S3T	19.81±5.40	17.59±4.71	0.041	2.072	0.043
S3E[b]	0.11±0.42	0.09 ±0.28	0.655	-0.447	0.005
S3C	1.20±1.31	0.38±0.65	0.001	3.454	0.079
S4T	30.16±10.95	21.28±5.11	<0.001	4.512	0.103
S4E[b]	0.30±1.07	0.15±0.35	0.711	-0.371	0.018
S4C	2.30±1.95	0.68±0.72	<0.001	4.716	0.110
S5T	44.12±18.24	29.37±8.12	<0.001	4.517	0.104
S5E[b]	1.37±2.83	0.59±0.65	0.848	-0.191	0.037
S5C[b]	3.75±2.71	1.26±0.89	0.036	-2.095	0.123
SDLT[b]	4.95±6.44	19.85±4.99	<0.001	-7.578	0.258
Neutrophil[b]	3.95±1.46	3.40±0.96	0.519	-0.644	0.044
Lymphocyte	2.88±0.77	2.77±0.66	0.482	0.705	0.014
NLR	1.43±0.61	1.29±0.50	0.232	1.201	0.025
PLR[b]	115.47±31.91	121.48±37.94	0.456	-0.745	0.017
Erythrocyte[b]	4.89±0.35	4.88±0.32	0.892	0.136	0.002
Platelet	318.84±71.14	319.97±64.31	0.936	-0.080	0.001
SII[b]	459,96±221,29	422,01±217,57	0,637	-0,472	0.172

[a]Cramer's V effect size, [b]Mann-Whitney U. ADHD: Attention deficit hyperactivity disorder, TD: Typically developing healthy controls, BMI: Body mass index, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, S1T: Stroop 1. Part-Time, S1E: Stroop 1. Part Error, S1C: Stroop 1. Part Correction, S2T: Stroop 2. Part-Time, S2E: Stroop 2. Part Error, S2C: Stroop 2. Part Correction, S3T: Stroop 3. Part-Time, S3E: Stroop 3. Part Error, S3C: Stroop 3. Part Correction, S4T: Stroop 4. Part-Time, S4E: Stroop 4. Part Error, S4C: Stroop 4. Part Correction, S5T: Stroop 5. Part-Time, S5C: Stroop 5. Part Correction, S5E: Stroop 5. Part Error, SDLT: Serial Digit Learning Test, SII: Systemic inflammatory index, d: Cohen's d effect size,

and executive functions in children with ADHD who are not taking medication. In our study, no significant difference was found between the two groups in terms of neutrophil, erythrocyte, lymphocyte, NLR, PLR, SII, and platelet levels.

Platelets, neutrophils, and lymphocytes were positively correlated with Stroop first section correction scores, platelets were positively correlated with Stroop first section time scores, lymphocytes were positively correlated with Stroop second section correction scores, NLR was negatively correlated with Stroop second section correction scores. Also, platelets were positively correlated with Stroop's third section time scores. Platelets and lymphocytes were positively correlated with Stroop section four-time scores and NLR was positively correlated with Stroop section fourth error scores.

Previous studies between children with ADHD and controls revealed that NLR and PLR values in the ADHD group were significantly higher than in controls (30, 31). Although a recent meta-analysis reported that ADHD patients had higher NLR and PLR values compared to controls, another recent review reported inconsistent results regarding adolescents with ADHD (16, 32).

Tablo 2. Correlation coefficients between blood variables and Stroop test subscores.

		S1T	S1C	S2T	S2C	S3T	S3E
SII	p	0.110	0.285	0.395	0.130	0.747	0.826
	r	0.181	0.122	0.097	-0.172	0.037	0.025
Ntrphl	p	0.131	**0.047**	0,454	0,576	0,860	0,962
	r	0.171	**0,224**	0,085	-0,064	-0,020	0,006
Lymp	p	0,481	**0,011**	0,261	**0,007**	0,113	0,875
	r	0,080	**0,286**	0,128	**0,299**	0,180	0,018
NLR	p	0,380	0,996	0,949	0,015	0.506	0.956
	r	0,100	-0,001	0,007	-0.273	-0.076	0.006
PLR	p	0.292	0.262	0.453	0.126	0.327	0.650
	r	0.120	-0.128	0.086	-0.174	0.112	0.052
Erythc	p	0.904	0.422	0.774	0.427	0.510	0.744
	r	-0.014	0.092	0.033	0.091	0.075	0.037
Platelet	p	0.058	**0.048**	**0.037**	0.116	**0.017**	0.413
	r	0.214	**0.223**	**0.235**	0.178	**0.267**	0,093

NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, S1T: Stroop 1. Part-Time, S1C: Stroop 1. Part Correction, S2T: Stroop 2. Part-Time, S2C: Stroop 2. Part Correction, S3T: Stroop 3. Part-Time, S3E: Stroop 3. Part Error, SII: Systemic inflammatory index, Ntrphl: Neutrophil, Lymp: Lymphocyte, Erythc: Erythrocyte

Tablo 3. Correlation coefficients between blood variables and Stroop and serial digit learning test subscores.

		S3C	S4T	S4E	S4C	S5T	S5E	S5C	SDLT
SII	p	0.463	0.739	0.055	0.957	0.864	0.694	0.366	0.843
	r	-0.084	0.038	0.217	-0.006	0.020	0.045	0.103	-0.023
Ntrphl	p	0.378	0.882	0.078	0.973	0.752	0.487	0.899	0.881
	r	-0.101	0.017	0.199	-0.004	-0.036	-0.079	0.015	0.017
Lymp	p	0.338	**0.016**	0.421	0.423	0.501	0.176	0.861	0.729
	r	0.109	**0.271**	-0.092	0.091	0.077	-0.154	0.020	-0.040
NLR	p	0.177	0.291	0.014	0.461	0.703	0.807	0.904	0.496
	r	-0.153	-0.120	0.277	-0.084	-0.044	0.028	-0.014	0.078
PLR	p	0.951	0.721	0.243	0.834	0.398	0.125	0.326	0.582
	r	-0.007	0.041	0.133	-0.024	0.096	0.174	0.112	-0.063
Erythc	p	0.171	0.992	0.520	0.552	0.379	0.785	0.913	0.492
	r	0.156	-0.001	-0.073	0.068	-0.100	-0.031	0.013	0.078
Platelet	p	0.293	**0.002**	0.958	0.256	0.193	0.829	0.071	0.145
	r	0.120	**0.344**	-0.006	0.129	0.148	0.025	0.204	-0.166

NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, S3C: Stroop 3. Part Correction, S4T: Stroop 4. Part-Time, S4E: Stroop 4. Part Error, S4C: Stroop 4. Part Correction, S5T: Stroop 5. Part-Time, S5C: Stroop 5. Part Correction, S5E: Stroop 5. Part Error, SDLT: Serial Digit Learning Test, SII: Systemic inflammatory index, Ntrphl: Neutrophil, Lymp: Lymphocyte, Erythc: Erythrocyte

Neutrophil, platelet, and SII levels have been reported to be higher in children with ADHD compared to controls in various studies (33, 34). However, similar to the results of our study, it was reported that there was no significant difference in platelet, WBC, NLR, PLR, and SII levels in adults and children with ADHD when compared with healthy controls (35-37).

It is known that increased inflammation may be associated with the development of psychopathology or resistance to treatment (9). Regarding other inflammatory markers, recent meta-analyses have shown that peripherally measured IL-6 levels are significantly higher and tumor necrosis factor-alpha (TNF-a) levels are lower in individuals with ADHD compared to healthy controls (11, 38). Contradictory results have been reported in studies on c-reactive protein (CRP) in children with ADHD (39, 40). Other studies showed that there was no significant difference

in IL-1 and TNF- a levels between participants with ADHD and controls (41, 42).

NLR, PLR, and platelet levels can be easily calculated from CBC analysis (43). NLR, platelets, and PLR are observed to be associated with inflammatory pathways and have been used as a diagnostic biomarker model in various psychiatric disorders (44, 45). However, increased SII levels may contribute to increased neuronal apoptosis in ADHD brains by causing the release of reactive oxygen species in neutrophils (46). There is a reciprocal relationship between platelets and inflammation. Numerous inflammatory cytokines released during inflammation, such as IL-1, may contribute to platelet activation (47).

Systemic inflammation has been suggested to play an important role in psychiatric disorders such as ASD and ADHD; however, the relationships between these neurodevelopmental disorders and systemic inflammation are still poorly understood (48). In contrast to ASD, less evidence has been presented to date for targeting inflammation in ADHD (49). The fact that the blood parameters examined in our study did not differ from the controls may be due to methodological differences such as sample characteristics, measurement methods, and study design. Conflicting results in the literature may also contribute to this situation. In addition, the fact that children with ADHD did not use medication in our study may affect blood parameters. Due to the retrospective design of other studies, active or chronic infections and autoimmunity-related conditions that may affect inflammatory markers may not be assessed. Further studies including repeated measurements with a larger study group are needed to demonstrate this situation.

In our study, platelets, neutrophils, and lymphocytes were positively correlated with Stroop first section correction scores, platelets were positively correlated with Stroop second section duration scores, lymphocytes were positively correlated with Stroop second section correction scores, NLR was negatively correlated with Stroop second section correction scores, and platelets were positively correlated with Stroop third section duration scores. Platelets and lymphocytes were positively correlated with Stroop section fourth duration scores and NLR was positively correlated with Stroop section fourth error scores. A negative correlation between NLR and Montreal Cognitive Assessment has been reported in patients with Parkinson's disease (50). It was reported that NLR and PLR were inversely significantly correlated with the working memory test (Direct Digit Span) but not with the Stroop test in women (51). High NLR is associated with visuospatial impairments and executive function deficits (52, 53). An association between high levels of NLR and cognitive impairment in Alzheimer's disease has been reported (54, 55). It has been reported that higher neutrophil counts are associated with an increased risk of dementia and higher lymphocyte counts are associated with a lower risk of dementia (56). While a significant negative correlation was observed between NLR and Stroop interference score in bipolar patients, no statistically significant difference was found between patients and controls in terms of NLR and PLR (57).

Elevated inflammatory cytokines are associated with worse cognitive function in patients with bipolar disorder (58). Increased neutrophil and NLR values and decreased lymphocyte levels were significantly associated with worsening Stroop interference in women with schizophrenia (59). Concerning this condition, studies provide preliminary evidence that elevated inflammatory status negatively affects frontotemporal cognitive abilities such as memory, attention, and executive functions (60). The correlation of platelet, lymphocyte, neutrophil, and NLR levels with the scores in the Stroop color test in our study may refer to previous studies. To clearly show the relationship between inflammatory response and executive tests, further studies are needed to understand this situation with repeated blood measurements throughout the day and related advanced executive function tests. The strengths of this study include the fact that the patients did not receive any medical treatment and the blood parameter measurements were performed within a certain period. To the best of our knowledge, this is the first study to examine the relationship between neutrophil, erythrocyte, lymphocyte, NLR, PLR, SII, platelet levels, and executive functions in children with ADHD who are not taking medication.

However, this study also has limitations. Considering neuroinflammation in our study, further repeated measurements of tests related to executive functions in patients with ADHD were not performed and comorbid psychiatric disorders that may occur with prospective follow-up could not be examined and other inflammatory cytokines were not investigated. Anxiety disorders and other depressive disorders comorbid with ADHD that may affect blood values were not excluded, and the severity of these symptoms was not assessed in participants with ADHD. Furthermore, daily

variations in blood levels have not been analyzed or correlated with executive function-related tests through repeated measurements. To understand the inflammatory variability in the participants, we measured only complete blood counts and did not measure other body fluids such as saliva cerebrospinal fluid, or neuronal tissue.

Conclusion

This study suggests that lymphocyte, neutrophil, neutrophil-to-lymphocyte ratio, and platelet levels in the blood may be related to impaired executive tests in ADHD. Neutrophil, erythrocyte, lymphocyte, NLR, PLR, SII, and platelet levels in ADHD patients aged 8-14 years who did not use medication did not differ significantly compared to the TD control group.

However, further studies are needed to examine the roles of inflammatory cytokines and blood cells in ADHD etiopathogenesis and their ability to identify executive dysfunctions in ADHD.

Authors' Contribution Statement

MET: Conceptualization, data curation, formal analysis, investigation, methodology, supervision, validation, visualization, writing – original draft, writing – review and editing.

EKB: Conceptualization, formal analysis, methodology, supervision, writing – original draft, writing – review and editing.

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Declaration of Competing Interest

The authors have no conflict of interest to declare.

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