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ORIGINAL ARTICLE

Evaluation of the Mean Platelet Volume and Neutrophil/Lymphocyte Ratio, as Inflammatory Markers in Children with Autisim Spectrum Disorders

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Abstract

Introduction: Autism spectrum disorder (ASD) is a neurodevelopmental disorder that affects people's communication skills and world perception. Neuroinflammation and mitochondrial dysfunction have an extensive place in the etiology. Mean platelet volume (MPV) and neutrophil-lymphocyte ratio are used as inflammatory markers in many diseases. In this study, we aimed to compare platelet parameters and neutrophil-lymphocyte ratio (Neu/lymph) of children with ASD and healthy controls.

Methods: This is a single-center, retrospective, hospital-based, and case–control study. Patients diagnosed with ASD according to DSM5 criteria and healthy controls participated in the study. Hematocrit, platelet count, neutrophil count, MPV, and Neu/lymph data were statistically compared in both groups.

Results: A total of 53 patients (%38 male) with ASD and 53 healthy controls (20% male) were included in the study. The mean age of the ASD patients was 55.3±32.77 months and there was no statistical difference between the ASD group and healthy controls in terms of age and gender healthy controls had higher Neu/lymph ratio and MPV, but when the data were analyzed statistically no statistically significant parameter associated with autism was found.

Discussion and Conclusion: Platelet parameters and Neu/lymph ratio are not expected to alter in the ASD group.

Keywords: Attention deficit disorder; autism; mean platelet volume; neutrophil-lymphocyte ratio.

Autism spectrum disorder (ASD) is a neurodevelopmental disorder that affects people's communication skills and world perception[1]. Signs and symptoms include avoiding eye contact, not responding when called by name, pretending not to hear, no or little babbling, less variety of noises, not looking at the object or direction pointed, no or less mutual smile, inability to use or understand gestures, to be indifferent to imitating movements or facial expressions, lack of desire to be hugged, preferring to be alone rather than playing with others, avoiding interaction, not playing with toys as expected way (for example, just turning the wheels instead of driving the cars), repetitive play-

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ing styles, and overreaction to disrupted routines[2]. DMS5 diagnostic criteria are defined for the diagnosis[3]. One of 59 children in Türkiye is born with the risk of autism[4]. Genetic factors come to the fore in the etiology of autism. However, advanced maternal age, low birth weight, drug use during pregnancy, and past infections are risk factors for the development of ASD[5]. Apart from these factors, neuroinflammation and mitochondrial dysfunction have an extensive place in the etiology[6]. Neuroinflammation due to astrocyte microglial interaction has been demonstrated in animal models. Another meta-analysis showed that pro-inflammatory cytokines such as interleukin 1 and 6 were higher than healthy controls[7]. Platelets are the tiniest and most reactive component of blood[8]. Mean platelet volume (MPV) and neutrophil-lymphocyte ratio are used as inflammatory markers in many diseases[9]. In this study, we aimed to compare platelet parameters and neutrophil-lymphocyte ratio (Neu/lymph) of children with ASD and healthy controls.

Materials and Methods

This is a single-center, retrospective, hospital-based, and case–control study approved by the Ethics Committee of Kartal Dr. Lutfi Kirdar City Hospital with the number of 2022/514/223/7. The study was conducted in accordance with the principles of the Declaration of Helsinki.

We included all ASD-diagnosed patients according to DSM5 diagnostic criteria in pediatric neurology and pediatric psychiatry outpatient clinics between 2020 and 2022 who have available hemogram data which were obtained for their routine control. Furthermore, we built a control group among the healthy children who came to our hospital's pediatric outpatient clinics for routine health check-ups and whose hemogram data were available in the system, using randomized sampling method according to age groups and gender.

Hematocrit, platelet count, neutrophil count, MPV, and neutrophil-lymphocyte ratio (Neu/lymph) data were statistically compared in both groups.

Statistical Analysis

SPSS 21.0 (IBM) package program and Microsoft Excel 2010 programs were used to analyze the study results. In the creation of descriptive statistics, mean and standard deviation were used. The Chi-square test was used for categorical measurements. Numeric variables and histogram graph of the normal distribution that fits visually normality tests (Kolmogorov–Smirnov/Shapiro–Wilk) were tested using. The normal distribution is achieved in the comparison of independent variables when the independent samples t-test in cases where the normal distribution is not provided if you have two groups. Mann–Whitney U test was used. In the study, it was considered statistically significant that p value was <0.05.

Results

A total of 53 patients (%38 male) with ASD participated in our study. The mean age of the patients was 55.3±32.77 months. We included 53 healthy controls (20% male) in the control group. The mean age of the healthy controls was 61.3±31.2 months, and there was no statistical difference between the ASD group and healthy controls in terms of age and gender (Table 1). The diagnosis age of our patients with ASD ranges from 18 to 84 months, with an average of 29±32.77 months. There was a history of consanguinity in 30.1% of the patients. In 35.8% of the patients, there was pre-term birth history.

The relationship between the age and laboratory data of the children included in the study and autism is given in Table 2. When the results were examined, it was observed

Table 1. Data on gender and age distribution according to autism status

Features	Autism Status		
	Yes (n)/SD	No (n)/SD	p
Male	38	20	0.304
Female	15	33	0.339
Age (month)	55.3±32.77	61.3±31.2	
Total	53	53	

Chi-square test.

Table 2. Distribution of laboratory data according to autism status

Features	Autism status		
	Yes (Mean±SD)	No (Mean±SD)	p
Wbc/uL	9243±2728	9126±2648	0.823
Hgb g/dL	12.5±1.1	12.4±1	0.691
Hct %	37.9±3.4	38.3±2.8	0.519
Neu mm^3	3988±2242	4180±2058	0.648
Lenf mm^3	4120±1346	3933±1527	0.381*
Neu/lenf	1.12±0.9	1.42 ±1.8	0.286
Plt /uL	328622±78077	361943±86930	0.077*
Mpv μm^3	9.65±1.24	9.46±0.99	0.399*

Independent samples test * Mann–Whitney U test; Wbc: White blood cell count; Hgb: Hemoglobin; Hct: Hematocrit; Neu: Neutrophil count; Lenf: Lymphocyte count; Plt: Platelet count. Mpv: Mean platelet volume.

that the mean age, Hct mean, neutrophil mean, neu/lymph mean, and platelet mean were higher in healthy children than patient with autism, but when the data were analyzed statistically, no parameter was found to be significantly associated with autism.

Discussion

Platelets, as granule-secreting cells, have been revealed to be a useful cellular model for studying neuropathologic diseases. Dense granules of platelets contain neurotransmitters such as serotonin and gamma-aminobutyric acid[10]. Platelets and neurons have same features about granule activation and secretion. Platelet integrin receptor αIIbβ3 is responsible for serotonin transport. In addition, platelets do not synthesize serotonin but take it from the circulation through the SLC6A4 pathway. In other words, the excess serotonin is stored in the dense granules of the platelets. The serotonin blood level is one of the biomarkers of ASD[11]. Platelets have been studied in many neuropsychiatric diseases because they are easily accessible cells obtained from the blood and have similarities with neurons. However, the number of studies on the MPV and autism is as few as the fingers of one hand in the literature.

Apart from the relationship between platelets and serotonin, MPV and NRL ratios also provide information about the inflammatory status and prognosis prediction in coronary artery disease[12]. Furthermore, they can be used as inflammatory markers in neoplasms and rheumatological syndromes such as ankylosing spondylitis and systemic lupus erythematosus[13]. While genetic and environmental factors play a role in the etiology of ASD, inflammation seems to be one of the factors affecting these factors[14,15]. It is reported that peripheral cytokine networks regulate the hemostasis of the central nervous system. Gruol et al.[16] suggested that although IL6 levels support neuronal development during astrogliosis, high IL6 levels are associated with ASD. Chronic elevation of TNF-α has harmful effects on memory and is associated with ASD. In addition, Laing et al.[17,18] reported that chemokines – a cytokine subgroup – (CCL2/MCP-1, CCL3/MIP-1α, CCL4/MIP-1β, CCL5/RANTES, and CCL11/Eotaxin) have a role in physiologic and pathologic interactions between astrocyte, microglia, and neuronal cells. Therefore, peripheral inflammatory markers have significant effects on the central nervous system.

MPV and NRL ratios can determine the prognosis of inflammatory events and following up diseases. Korniluk et al.[13] suggested in their 2019 study that MPV can be used as a parameter to predict cardiovascularly and stroke risk, and MPV cutoff values are helpful parameters in predicting the risk of thrombolytic events.

Avcil et al.[19] investigated the effects of MPV neutrophile/lymphocyte ratios in attention deficit hyperactivity (ADHD) disorder and found that the MPV and NRL ratios were higher in ADHD patients than in the control group. Likewise, Önder et al.[20] found the MPV and NRL ratios higher in ADHD patients compared to the control group. Güneş et al.[21] found higher MPV and NRL ratios in patients with generalized tonic-clonic seizures compared to the control group.

However, no significant difference was found in MPV and NRL rates in ASD patients compared to the control group in our study. To the best of our knowledge, the number of literature describing how MPV and NRL parameters are affected in ASD patients is very few. Garipardic et al.[22] reported no significant correlation between the patient group and MPV in their prospective and case–control study, including 36 ADHD and 18 ASD patients, concordant with our results. Çoban et al.[23] showed that platelet functions were affected more in ASD patients than in healthy controls.

As a result, there was no significant difference between MPV and NRL parameters in ASD patients compared to healthy controls. Unlike the ADHD group patients, the lack of significant difference in MPV and NRL rates in the ASD group with the control group may indicate that inflammation is more prominent in the etiopathogenesis of ADHD. Furthermore, since MPV findings are not expected to alter in the ASD group, the MPV cutoff value changes detected in ASD patients may indicate that these patients need follow-up for cardiovascular risk.

Ethics Committee Approval: This is a single-center, retrospective, hospital-based, and case–control study approved by the Ethics Committee of Kartal Dr. Lutfi Kirdar City Hospital with the number of 2022/514/223/7. The study was conducted in accordance with the principles of the Declaration of Helsinki.

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References

1. Lord C, Elsabbagh M, Baird G, Veenstra-Vanderweele J. Autism spectrum disorder. Lancet 2018;392:508–20.
2. Greenspan SI, Brazelton TB, Cordero J, Solomon R, Bauman ML, Robinson R, et al. Guidelines for early identification, screening, and clinical management of children with autism spectrum disorders. Pediatrics 2008;121:828–30.
3. Banaschewski T, Döpfner M. Attention-deficit/hyperactivity disorder. Z Kinder Jugendpsychiatr Psychother [Article in German] 2014;42:271–7.
4. Susuz Ç, Güçiz DB. Autism spectrum disorder with public health perspective. Halk Sağlığı Derg [Article in Turkish] 2020;5:297–310.
5. Bölte S, Girdler S, Marschik PB. The contribution of environmental exposure to the etiology of autism spectrum disorder. Cell Mol Life Sci 2019;76:1275–97.
6. Sharma SR, Gonda X, Tarazi FI. Autism spectrum disorder: Classification, diagnosis and therapy. Pharmacol Ther 2018;190:91–104.
7. Masi A, Quintana DS, Glozier N, Lloyd AR, Hickie IB, Guastella AJ. Cytokine aberrations in autism spectrum disorder: A systematic review and meta-analysis. Mol Psychiatry 2015;20:440–6.
8. Williams O, Sergent SR. Histology, platelets. Available at: https://www.ncbi.nlm.nih.gov/books/NBK557800/. Accessed Sep 21, 2023.
9. Leader A, Pereg D, Lishner M. Are platelet volume indices of clinical use? A multidisciplinary review. Ann Med 2012;44:805–16.
10. Anderson GM, Hertzig ME, McBride PA. Brief report: Platelet-poor plasma serotonin in autism. J Autism Dev Disord 2012;42:1510–4.
11. Padmakumar M, Van Raes E, Van Geet C, Freson K. Blood platelet research in autism spectrum disorders: In search of biomarkers. Res Pract Thromb Haemost 2019;3:566–77.
12. Pafili K, Penlioglou T, Mikhailidis DP, Papanas N. Mean platelet volume and coronary artery disease. Curr Opin Cardiol 2019;34:390–8.
13. Korniluk A, Koper-Lenkiewicz OM, Kamińska J, Kemona H, Dymicka-Piekarska V. Mean Platelet Volume (MPV): New perspectives for an old marker in the course and prognosis of inflammatory conditions. Mediators Inflamm 2019;2019:9213074.
14. Bhandari R, Paliwal JK, Kuhad A. Neuropsychopathology of autism spectrum disorder: Complex interplay of genetic, epigenetic, and environmental factors. Adv Neurobiol 2020;24:97–141.
15. Gevezova M, Sarafian V, Anderson G, Maes M. Inflammation and mitochondrial dysfunction in autism spectrum disorder. CNS Neurol Disord Drug Targets 2020;19:320–33.
16. Gruol DL. IL-6 regulation of synaptic function in the CNS. Neuropharmacology 2015;96:42–54.
17. Matta SM, Hill-Yardin EL, Crack PJ. The influence of neuroinflammation in autism spectrum disorder. Brain Behav Immun 2019;79:75–90.
18. Laing KJ, Secombes CJ. Chemokines. Dev Comp Immunol 2004;28:443–60.
19. Avcil S. Evaluation of the neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, and mean platelet volume as inflammatory markers in children with attention-deficit hyperactivity disorder. Psychiatry Clin Neurosci 2018;72:522–30.
20. Önder A, Gizli Çoban Ö, Sürer Adanır A. Elevated neutrophil-to-lymphocyte ratio in children and adolescents with attention-deficit/hyperactivity disorder. Int J Psychiatry Clin Pract 2021;25:43–8.
21. Güneş M, Büyükgöl H. Relationship between generalized epileptic seizure and neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, and neutrophil mediated inflammation. Int J Neurosci 2020;130:1095–100.
22. Garipardic M, Doğan M, Bala KA, Mutluer T, Kaba S, Aslan O, et al. Association of attention deficit hyperactivity disorder and autism spectrum disorders with mean platelet volume and vitamin D. Med Sci Monit 2017;23:1378–84.
23. Coban N, Gokcen C, Akbayram S, Calisgan B. Evaluation of platelet parameters in children with autism spectrum disorder: Elongated collagen-adenosine diphosphate and collagen-epinephrine closure times. Autism Res 2019;12:1069–76.