

# Could neutrophil-to-lymphocyte ratio be an important parameter in children and adolescents with obsessive compulsive disorder?

*Çocuk ve ergen obsesif kompulsif bozukluk tanılı hastalarda nötrofil lenfosit oranı önemli bir parametre olabilir mi?*

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## SUMMARY

**Objective:** The number of studies that suggest the possible role of immune abnormalities in the pathogenesis of obsessive-compulsive disorder(OCD) are increasing. Our aim here is to determine the relationship between neutrophil lymphocyte ratio(NLR) and children and adolescents with OCD.NLR and platelet lymphocyte ratio(PLR) are new, inexpensive, easily reproducible indicators used for the determination of low grade inflammation. **Method:** In this study, retrospective records of 32 children and adolescents with OCD were screened, and the NLR, PLR,monocyte lymphocyte ratio (MLR) data obtained from the pre-treatment complete blood count were compared with the same data of the healthy control group with similar characteristics. **Results:** The NLR was found lower in children and adolescents with OCD compared to the control group; yet PLR and MLR were not significantly different. **Discussion:** Inflammation might play a role in the etiopathogenesis of OCD. The NLR may be potential inflammation markers for OCD in children.

**Key Words:** Obsessive-Compulsive Disorder, Child psychiatry, Inflammation, Neutrophil to lymphocyte ratio

## ÖZET

**Amaç:** Obsesif kompulsif bozukluğun(OKB) patogeneğinde immün anormalliklerin olası rolünü öne süren çalışmaların sayısı gün geçtikçe artmaktadır. Buradaki amacımız çocuk ve ergenlerde nötrofil lenfosit oranı (NLO) ile OKB arasındaki ilişkiyi belirlemektir. NLO ve trombosit lenfosit oranı (TLO) düşük dereceli inflamasyonun belirlenmesinde kullanılan yeni, ucuz, kolay tekrarlanabilir göstergelerdir. **Yöntem:** Bu çalışmada OKB tanılı 32 çocuk ve ergenin retrospektif kayıtları tarandı ve tedavi öncesi tam kan sayımından elde edilen NLO, PLO, MLO verileri; benzer özellikli sağlıklı kontrol grubunun aynı verileriyle karşılaştırıldı. **Bulgular:** NLO; OKB tanısı olan çocuk ve ergenlerde kontrol grubuna göre düşük bulundu; Ancak TLO ve MLO anlamlı olarak farklı değildi. **Sonuç:** Enflamasyon OKB'nin etiopatogeneğinde rol oynayabilir. NLO, çocuklarda OKB için potansiyel inflamasyon belirtici olabilir.

**Anahtar Sözcükler:** Obsesif-Kompulsif Bozukluk, Çocuk psikiyatri, İnflamasyon, Nötrofil Lenfosit oranı

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## INTRODUCTION

Obsessive-compulsive disorder (OCD) is characterized by obsessions defined as repetitive thoughts, impulses, or fantasies, which are involuntary, inconvenient and unsettling; and compulsions defined by repetitive behaviors or mental actions, in which a person can not prevent himself as a reaction to obsession. There are studies showing that the lifetime prevalence of obsessive-compulsive disorder in adolescents is between 2% and 3%(1). Although the etiological processes of the pathophysiology of obsessive-compulsive disorder are not fully understood; neuroanatomic, neurochemical, genetic, environmental-personal, cognitive, behavioral and psychosocial factors have been suggested. The number of evidence for the role of inflammation in the etiology of early-onset obsessive-compulsive disorder has increased in recent years (2). There is evidence that inflammatory processes may play a direct role in the pathophysiology of some OCD subtypes, such as pediatric autoimmune neuropsychiatric diseases associated with streptococcal infection (PANDAS). In a study of miRNA, which was thought to be effective in the regulation of cytokines, chemokines and transcription factors involved in the inflammatory etiology of OCD, miRNA levels were significantly higher among OCD group compared to the control group(3). There are also studies showing that free radical, oxidant and antioxidant defense system disorders have pathogenic effects on neural tissues in humans and therefore may play a role in the development of obsessive compulsive disorder(4). Neutrophils are the first defensive cells of the natural immune system and contribute to phagocytosis and apoptosis by promoting inflammatory mediators. Lymphocytes represent the regulatory and protective part of acquired immunity. Neutrophil to lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) are inexpensive and reproducible tests that can be easily calculated from hemogram analysis, which can be determined under simple laboratory conditions. The NLR has been proposed as a new marker of chronic low-grade inflammation and as a predictor of clinical course in neuroimmune disorders(5). Leukocytes were studied for NLR and PLR, inflammatory diseases, malignancies, hypertension (HT), diabetes mellitus (DM) and some psychiatric disorders(6). There is a grow-

ing interest in the analysis of different neurobiological markers in psychiatric disorders. A recent meta-analysis in the field of adult psychiatry supports the hypothesis that NLR and PLR may be useful to detect inflammatory activation in mood disorders(7). NLR is inexpensive, easy to apply and it is a data which is calculated with the data obtained from routine hemogram test. In this study was hypothesised that NLR was significantly different in children and adolescents with OCD compared to healthy controls; and therefore NLR values of the patient and control groups were examined. As far as we know, NLR in childhood OCD has not been previously evaluated; so this is the first study evaluating whether there is a relationship between OCD and NLR.

## METHOD

The study was conducted by screening the files of patients who were admitted to Manisa Celal Bayar University Medical Faculty Hospital Children and Adolescent Psychiatry outpatient clinic between September 2015 and September 2018. By excluding patients with non-OCD psychiatric disorders and any health problems and those with leukocyte counts higher than 10,000 and less than 4000, a total of 35 patients aged 9-18 years (mean: 14,08) were included in the study. We excluded leukocyte counts higher than 10,000 and less than 4000, because we want to avoid affected NLR with leukocytosis or leukopenia. A total of 32 healthy children aged 11-17 (mean: 14.4), who applied to the health control committee of the same hospital for various reasons and reported as completely healthy were included in the study. Age, sociodemographic data, previous drug use, coexistent physical or mental illness, or family history of psychiatric disease were evaluated. Leukocyte, platelet, lymphocyte, monocyte, neutrophil data of healthy controls and routine pre-treatment group were reviewed. NLR was determined by comparing the absolute neutrophil and absolute lymphocyte counts; while monocyte-lymphocyte ratio(MLR) was obtained by comparing the ratio of absolute monocytes and absolute lymphocytes.

SPSS for Windows version 15.0 (2006; SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Frequency analysis and cross tables were established for descriptive data and variables. Mean and standard deviations were measured for numerical variables. Chi-square test was used to compare the independent variables. Kolmogorov-Smirnov test was used to test the normality of intergroup data; whereas Student's t-test was used to compare the normal variables. Man-Whitney U test was used for numerical variables which did not show normal distribution. A value of  $P < 0.05$  was considered statistically significant.

## RESULTS

The study included 35 OCD patients with a mean age of  $14,08 \pm 2,53$  (9-18), and a control group of 32 healthy individuals with a mean age of  $14,40 \pm 1,82$  (11-17). There was no significant difference between two groups in terms of age and gender ( $p = 0.558$ ;  $p = 0.994$ ). (Table 1). Firstly, Kolmogorov-Smirnov test was used in order to check whether the distribution of data was normal. Distribution was normal. Platelet, neutrophil and lymphocyte counts of the two groups were not significantly different ( $p > 0.05$ ). Significant difference was present only for the number of monocytes ( $p = 0.016$ ) (Table 2). When analyzed with the data obtained from the pre-treatment routine blood samples, a significant decrease in NLR was observed in OCD patients compared to the control group. The mean value of NLR was  $1.38 \pm 0.49$  and  $1.80 \pm 0.71$  in OCD patients and healthy control group, respectively. This difference was significant. ( $t = -2.831$ ;  $p = 0.006$ ). The value of PLR was low in OCD

patients compared to the control group; but it was not significant. The mean values of MLR were similar in both groups and there was no significant difference ( $P > 0.05$ ) (Table 3).

## DISCUSSION

In order to understanding the inflammatory etiology of OCD, we aimed to evaluate the use of NLR as a simple and inexpensive biomarker in OCD. We evaluated NLR, MLR and PLR, which are considered as new clinical markers of inflammation in various medical conditions including neuropsychiatric disorders. NLR was significantly lower in OCD patients compared to healthy control group. Due to the fact that neutrophils are leukocytes that play a major role in acute inflammation and that lymphocytes are the main contributors to chronic inflammation, the lowness of this ratio suggests that chronic inflammatory process may have a role in the etiology of obsessive-compulsive disorder. In a study conducted by Rao et al. in 2015, some plasma cytokine levels (IL-2, IL-4 and TNF-alpha) were significantly higher in patients with comorbid OCD without comorbidities compared to healthy controls(9). These cytokines are known to stimulate proliferation of lymphocytes. Increased lymphocyte ratio may decrease NLR, which supports our results. Colak et. al. found significantly higher TNF-alpha levels in pediatric OCD patients compared to healthy controls(8). The fact that Th1 lymphocyte-mediated TNF-alpha was detected at high levels suggests that activation of T lymphocytes may result in a significant reduction in NLR. In contrast to these findings, there are also studies showing a significant decrease in TNF-alpha ( $p$

**Table-1 DEMOGRAPHIC CHARACTERISTICS OF THE SUBJECTS**

	OCD Patients n=35	Control Group n=32	P value
<b>Gender: male / female (n)</b>	12 / 23	11 / 21	0,994*
<b>Age(years): mean / <math>\pm</math> SD</b>	14,08 / 2,53	14,40 / 1,82	0,558**
<b>Age Range min / max</b>	9 / 18	11 / 17	

OCD: Obsessif-Compulsif Disorder SD: Standart Deviation \* Chi-Square Tests, \*\* Student T Tests

**Table-2** COMPARISON OF BLOOD COUNT PARAMETERS

	Control Group	OCD Patients	t value <sup>(b)</sup>	p value <sup>(a)</sup>
	Mean	Mean		
Leukocyte 10 <sup>9</sup> /µL	7337,19	7313,43	-,0608	0,9517
Lymphocyte 10 <sup>9</sup> /µL	2465,94	2787,14	1,9429	0,0564
Neutrophil 10 <sup>9</sup> /µL	4176,88	3646,86	-1,8411	0,0702
Monocyte 10 <sup>9</sup> /µL	444,38	537,43	2,4709	0,0161
Platelet 10 <sup>9</sup> /µL	280593,75	287800,00	0,3918	0,6965

OCD: Obsessif-Compulsive Disorder

a Student T tests p<0,05 was considered statistically significant.

b Student T tests p<0,05 was considered statistically significant.

<0.0001) in OCD patients compared to healthy controls(10). Although a 2018 meta-analysis in which 6 cytokines (TNF-α, IL-1β, IL-6, IL-4, IL-10 and IFN-1) were evaluated among patients with OCD found that the results of the studies were contradictory and that there was no consistent evidence for the involvement of immune mediators in the pathophysiology of OCD; this suggests the lability of cytokines(11). It has also been suggested that neutrophil and lymphocyte levels, which are more stable in chronic inflammation than blood cytokine levels, NLR may be a reliable proinflammatory marker. It has been found that proinflammatory susceptibility may be present in early-onset OCD patients due to the excessive reactivity of monocytes which are natural immune response cells (12). In our study, monocyte counts were significantly higher in OCD group compared to healthy controls. (p=0.016)

One research including the comparison of OCD group and healthy controls revealed higher numbers of neutrophil-lymphocyte ratio and platelet-lymphocyte ratio values in the study group, was published on February 2019 (13). These findings different from ours. In a study neutrophil count was found to be reduced in adult pure OCD patients (14). These data support our findings.

To our knowledge, our study is one of the few study among to compare the NLR, PLR and MLR levels as a predictive marker between children diagnosed with OCD and a healthy control group. Our findings should be evaluated according to the limitations of this study. Data can be enriched with structured interviews. Our study may not be generalized due to these limitations: NLR symptom correlation was not examined, the lymphocyte subtype was not evaluated, no correlation with the markers of

**Table-3** COMPARISON OF BLOOD COUNT PARAMETERS

	Control Group n=32	OCD Patients n=35	t value	p value*
PLR(mean) <sup>(a)</sup>	120,6029	107,3501	-1,6913	0,0956
MLR(mean) <sup>(b)</sup>	0,1920	0,2029	0,5748	0,5674
NLR(mean) <sup>(c)</sup>	1,8006	1,3811	-2,8315	0,0062

OCD: Obsessif Compulsive Disorder

\*Student T tests. p<0,05 was considered statistically significant.

a PLR: Platelet-Lenfosit Ratio

b MLR: Monosit-Lenfosit Ratio

c NLR: Nötrofil-Lenfosit Ratio

inflammation (such as crp and sediment) and limited time interval. Additional research is warranted. On the other hand, the significant result in the NLR, which is easily reproducible from the complete blood count parameters and accepted as new clinical markers of systemic inflammation, has increased our motivation for future studies. Our findings showed that NLR levels were lower in children with isolated OCD compared to healthy control group. This finding suggests that low NLR

levels may play a role in the chronic inflammatory pathophysiology of childhood OCD and may be a predictable test.

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