Research article

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The neutrophil-lymphocyte ratio in children with atopic dermatitis: a case-control study

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Abstract

Background. Neutrophil-lymphocyte ratio(NLR) is a novel marker for the evaluation of inflammation and has not been evaluated previously in patients with AD.

Objective. To investigate the relationship between NLR and the clinical findings of AD.

Methods. Sixty-six children with AD were included in the study. The control group was included 66 children who have no allergic and chronic diseases.The immunoglobulin(Ig)E levels and complete blood count were measured. Skin prick tests were performed using the same antigens for all patients.

Results. NLR was not significant between the patient and control groups (p>0.05).The patients with AD were divided into 3 groups according to their SCORAD score as mild, moderate and severe AD.No statistically significant difference was present between groups in terms of demographic and clinical characteristics,eosinohil-lymphocyte ratio,eosinophil-neutrophil ratio,the percentage of eosinophil, IgE,the sensitivity of skin tests(p>0.05). However,NLR and sensitivity to house dust mite were significantly different among groups(respectively,p=0.037,p:0.043).SCORAD scores were weak positively correlated with NLR levels,eosinophil-lymphocyte ratio and the sensitivity of house dust mite (respectively,r:0.329;p:0.007,r:0.264;p:00035,r:0.325;p:0.008).

Conclusion. We didn't found significant difference in term of mean NLR betweeen patients with AD and control group. NLR was found significantly higher in severe AD patients than mild AD patients.The house dust mite sensitivity, eosinohil-lymphocyte ratio and NLR were correlated with AD severity. ***Clin Ter 2017; 168(4):e262-265. doi: 10.7417/CT.2017.2017***

Key words: *Atopic dermatitis, neutrophil-lymphocyte ratio, child, severity*

Introduction

Atopic dermatitis (AD) is an inflammatory disease of the skin. Pruritus, scratching, and chronic, relapsing, or both eczematous lesions are major hallmarks of the disease. 10-20% of children and 1-3% of adults are affected. The exact cause of AD is not well understood. Like other allergic diseases, atopic dermatits is caused by the influence of genetic and environmental factors. Many cells and cytokines are involved in the pathogenesis (1, 2). In patient with AD has been shown to be a correlation between severity of AD and various substances such as serum thymus and activation-regulated chemokine and serum interleukin 17, 23 and 10 (3, 4). However, these substances can not be routinely examined. Neutrophil-lymphocyte ratio (NLR) is a novel marker for the evaluation of inflammation. NLR is readily available, cost effective and could be calculated easily. NLR has been associated with some conditions such as chronic inflammation in cardiovascular diseases, hypertension, diabetes mellitus, malignancies, Familial Mediterranean Fever, and hepatic cirrhosis, and it has been suggested that NLR has a prognostic importance (5-9). Atopic dermatitis is also an inflammatory disease of the skin. There are two different inflammation types in pathogenesis. The acute phase is characterized by TH2 inflammation. In the chronic phase is involved both Th1 and Th2-type inflammation (1). Patients with AD have been shown to have a neutrophilic inflammation with eosinophilic inflammation (10-12). In a recent study, they found that the atopic dermatitis gene set score correlated with systemic and local measures of allergic inflammation including serum IgE, blood eosinophil count, and tissue eosinophils. Similarly, potent neutrophil chemoattractant gene sets have been found a positive correlation with neutrophils count in the blood (10). These studies indicate that neutrophilia is a sign in atopic dermatitis. In the study of Hon et al. (12) determined that the relationship between the severity of AD and neutrophil count, but counts of lymphocytes are inversely correlated with disease severity. In another study, Yoshida et al. (13) was found that neutrophil count in patient with AD were not statistically different in comparision of control. Although neutrophilia is not showed to inflammation alone, NLR is a parameter that is indicating the inflammation. Despite in the study of Hon et al. (12) the eosinohil/lymphocyte ratio was asssessed in patient with AD, NLR has not been evaluated previously in patients with AD. In this study, we aimed to investigate neutrophil-lymphocyte in patients with AD and the relationship between NLR and the clinical findings of AD.

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Methods

Sixty-six children who were followed-up with the diagnosis of with AD in Pediatric Allergy and Immunology Clinic of University of Health Sciences, Zeynep Kamil Health Training and Research Center were included in the study. Patients were evaluated retrospectively between January 2014 and December 2014. The control group was included 66 children who have no allergic diseases. Patients who have had an acute/chronic infection, obesity and patients with any other systemic disease such as hepatic, renal, cardiovascular diseases, diabetes mellitus, cancer and systemic inflammatory disorders were excluded. In addition, patients with anemia / polycythemia, leukopenia / leukocytosis, thrombocytopenia / thrombocytosis in complete blood count analysis were excluded from the study. A detailed allergic history, including the age and a familial atopy history were recorded. Familial atopy was accepted as positive when having an allergic disease in first-degree relatives (parents and siblings). The diagnosis of AD was evaluated according to Hanifin & Rajka criteria (14). AD severity was graded by the Severity Scoring of Atopic Dermatitis (SCORAD) index. An objective SCORAD score of <15 was classified as mild, 15-40 as moderate, and >40 as severe (15). The immunoglobulin (Ig) E levels and complete blood count were measured. The study was approved by the local ethics committee of the same institue and adhered to the principles of Helsinki Decleration. An oral consent was obtained from all subjects and / or their parents.

Skin Prick Tests

Skin prick tests were performed using the same antigens for all patients. Patients were considered eligible for the skin test if they have not received antihistamines for at least one week. Skin prick tests were applied on the anterior forearm. Histamine (10 mg/ml) and physiological saline were used as positive and negative references, respectively. Skin reactions were evaluated at the 15th minute of the application, and indurations ≥3mm were considered as a positive reaction. Skin prick tests for common aeroallergens (*Dermatophagoides pteronyssinus, Dermatophagoides farinea*, grasses mix, cereals mix, trees mix, weed-mix, *Alternaria alternaria*, cockroaches, cat dander, dog dander and foods (milk, egg yolk, egg white, potato, wheat flour) (Stallergenes SA, 92160 Antony, France) were performed by using stallerpoint (Stallergenes SA, 92160 Antony, France) (16).

Laboratory analysis

Hemoglobin, platelet, leukocyte, neutrophil, and lymphocyte count measurements were performed within approximately 60 minutes after blood sampling with Coulter Hmx Hematology Analyzer (Beckman Coulter, Inc. CA, USA) with original method and reagents. The ratios of blood cells were calculated by dividing the percentage of cells in complete blood count analysis.

Statistical Analyses

Statistical Package for Social Sciences (SPSS for Windows 15.0 Chicago, USA) program was used to analyse the data. Results were given as either mean ± standard deviation (SD) or as median and interquartile range (IQR) according to the distribution. Student-t test and ANOVA were used for the comparison of normally distributed variables. Chi-square, Mann-Whitney U tests and Kruskal-Wallis test were used for non-normally distributed variables. Pearson's and Spearman's correlation test were used for the correlation analyses of variables. $p < 0.05$ was considered as significant.

Results

This study consisted of 40 (60.6%) male and 26 (39.4%) female patients with a mean age of 5.6±2.8 years (1-13 years) as the patient group, and 34 (51.5%) male and 32 (48.5%) female patients with a mean age of 5.6±2.5 years (1-13 years) as the control group. There was no difference between patient and control group regarding age and gender ($p>0.05$). The median (interquartile range) of NLR was 1.11 (0.54-1.38) in the study group and 1.0 (0.47-1.57) in the control group. NLR was not significant between the patient and control groups ($p>0.05$). But, the Eosinohil/Lymphocyte ratio (ELR) and Eosinophils/Neutrophils ratio (ENR) of patient group were higher than control groups (Table 1).

The patients with AD were divided into 3 groups according to their SCORAD score as mild AD (Group I-SCORAD<15), moderate AD (Group II-SCORAD: 15-40) and severe AD (Group III-SCORAD>40). No statistically significant difference was present between groups in terms of gender, age, familial atopy, duration of disease, the presence of asthma, the presence of allergic rhinitis, eosinohil-lymphocyte ratio, eosinophil-neutrophil ratio, the percentage of eosinophil, serum IgE, the sensitivity of skin tests (pollens, dander, *A.alternata*, cockroaches and food) (p>0,05). Ho-

Table 1. Comparison of socio-demographic features and neutrophil-lymphocyte ratio between patients and control groups.

	Study Group (n=66)	**Control Group (n=66)**	***P***
Gender (n) Male/Female	40/26	34/32	0.381*
Age (years) Mean±standart deviation	5.6±2.8	5.6±2.5	0.932**
Neutrophil-lymphocyte ratio Median (interquartile range)	1.11 (0.54-1.38)	1.0 (0.47-1.57)	0.935***
Eosinohil-lymphocyte ratio Median (interquartile range)	0.10 (0.04-0.19)	0.03 (0.01-0.06)	0.000***
Eosinophil-neutrophil ratio Median (interquartile range)	0.10 (0.04-0.16)	0.03 (0.02-0.07)	0.000***

*Chi-squared ** Student T test ***Mann Whitney U test

Table 2. Comparison of socio-demographic features, clinical and laboratory findings of the patient with mild atopic dermatitis (Group-I), moderate atopic dermatitis (Group-II), and severe atopic dermatitis (Group III).

	Group I n:13	Group II n:32	Group III n:21	P
Gender, Male/Female	8/5	20/12	12/9	0.924*
Age, month[a]	45.5 (25,5-80,5)	68 (46-92)	78 (52-102)	0.483**
Familial atopy, n (%)	4 (30.8)	13 (40.6)	12 (57.1)	0.280*
The presence of asthma, n (%)	4 (30.8)	8 (25)	9 (42.9)	0.392*
The presence of allergic rhinitis, n (%)	5 (38.5)	13 (40.6)	12 (57.1)	0.424*
The duration of disease, month[a]	24 (8.2-27)	24 (24-36)	48 (24-60)	0.112**
Neutrophil-lymphocyte ratio[b]	0.84±0.57	1.14±0.56	1.37±0.56	0.037***
Eosinophil-lymphocyte ratio[b]	0.11±0.13	0.12±0.86	0.18±0.12	0.137***
Eosinophil-neutrophil ratio[b]	0.12±0.10	0.12±0.89	0.13±0.90	0.878***
The percentage of eosinophil [a]	3.6 (1.9-5.6)	4.2 (2.3-6.5)	6.2 (3.1-8.7)	0.260**
Serum immunoglobuline E, (IU/ml)[a]	139 (31-216)	151 (28-342)	496 (111-1200)	0.074**
Sensitivity to house dust mite, n (%)	2 (15.4)	11 (34.4)	12 (57.1)	0.043*
Sensitivity to pollens, n (%)	2 (15.4)	3 (9.4)	1 (4.8)	0.576*
Sensitivity to dander, n (%)	1 (7.7)	1 (3.1)	1 (4.8)	0.799*
Sensitivity to *A. alternata,* n (%)	1 (7.7)	2 (6.2)	2 (9.5)	0.907*
Sensitivity to cochrach, n (%)	1 (7.7)	2 (6.2)	0	0.470*
Sensitivity to foods, n (%)	1 (7.7)	4 (12.5)	4 (19)	0.623*

[a]Median (interquartile range) [b]Mean±Standart deviation *Chi-square test **Kruskal Wallis test ***ANOVA

wever, mean NLR and sensitivity to house dust mite (HDM) were significantly different among groups (respectively, p=0.037, p:0.043) (Table 2).

In terms of NLR and sensitivity to HDM in the pairwise comparison of the groups, while there was statistically significant differences between Group I and Group III (respectively, p=0.027, p:0.034), there were no significant difference between Group I-Group II and Group II-Group III (p>0.05). Objective SCORAD score were weak positively correlated with NLR levels, eosinophil-lymphocyte ratio and the sensitivity of house dust mite (respectively, r:0.329; p:0.007, r:0.264; p:00035, r:0.325; p:0.008).

Discussion

In our study, the mean NLR in children with AD was not statistically significant compared to control group. NLR was not evaluated in patients with previously. Although AD is an inflammatory skin disease and NLR is a marker of inflammation, the reason of the nonsignificant NLR values between groups may be due to small number of patients and having mostly mild to moderate AD. Another important result in our study, we determined that ELR and ENR of patient were higher than control group. The number of eosinophils in atopic dermatitis may be more than normally (1). For this reason, we think that we found a significant difference between the groups in terms of ELR and ENR.

When we evaluated according to the severity of atopic dermatitis in children with AD; NLR and HDM sensitivity were significantly higher in patients with severe AD. NLR was used as an indicator in so many inflammatory diseases as mentioned above (5-9). Neutrophilic inflammation is also shown with eosinophilic inflammation in patients with AD (10-12). Choy et al. (10) demonstrated that a positive correlation between potent neutrophil chemoattractant gene set scores and neutrophils in the blood of patients with AD. While neutrophilic inflammation was detected only in lesional areas, it was not demonstrated in perilesional areas. Furthermore, it has been found a correlation between the number of neutrophils and crust presence. Besides the extent of lesions in AD, SCORAD scale is also used in assessing the severity of the lesions. The crust is also one parameter indicating the presence of density. In another study, Hon et al. (12) was demonstrated that the relationship between the severity of AD and neutrophil count. These results show that neutrophilia is more common in severe AD. In contrast to these studies, the study of Yoshida et al. (13) was found that did not different in terms of the counts of neutrophils in the blood between atopic eczema of patients and controls. In the result of high neutrophil counts, NLR becomes higher. We found that NLR higher in severe AD patients. In addition, we determined a weak positive correlation between the severity of AD and NLR. Despite NLR has not been evaluated previously in patients with AD, Hon et al. (12) were determined that AD severity was positively correlated with the counts of neutrophils, and negatively correlated with the counts of lymphocytes. Indirectly, there is a positive relationship between NLR and AD severity. There is a need for a comprehensive study to be able to say more clearly the relationship between NLR and the severity of AD. Eosinohil/lymphocyte ratio ratio didn't differ among the different groups in terms of AD severity, But eosinohil/lymphocyte ratio was positively correlated with total SCORAD level. This result is consistent with studies of Hon et al. (12)

We found that sensitivity to HDM in patients with severe AD patients higher than in patients with mild AD. HDM sensitivity is a common aeroallergen sensitivity in AD patients. Although there is no proven benefit of reducing and avoidance from house mite dusts, HDM is correlated with

the severity of AD (17-19). In the study of Kutlu et al. (18) they found a correlation between HDM sensitivity and AD severity in a 45 patients with AD. Likewise, patients with strong SPT positivity to HDM had a higher total SCORAD score and subjective symptoms score (p<0.05) (18). Similarly, Adham et al. (19) have been shown to be a correlation between AD severity and HDM sensitivity is also shown. Consistent with these results, we determined HDM sensitivity significantly higher in children with severe AD.

The limitation of our study is small participant number. The less number of cases was due to be held in a single center and crossectional. However, we believe that our study is important because it is the first study evaluating the NLR in patients with AD. The other limiting factor our study is that there is no threshold value for NLR such as CRP. However, as mentioned above, we think that NLR would be useful while evaluating the severity of disease in patients with AD as in so many other inflammatory diseases.

As a result, we did not a significant difference in term of mean NLR between patients with AD and control group. However, NLR was found significantly higher in severe AD patients than mild AD patients. The house dust mite sensitivity, eosinohil/lymphocyte ratio and NLR are correlated with AD severity. NLR can be used to assess the severity in patients with atopic dermatitis. However, a larger series of studies is needed to examine the relationship between NLR and severity of AD.

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