Evaluation of Neutrophil / Lymphocyte Ratio and Platelet / Lymphocyte Ratio in Pseudoexfoliation Syndrome

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ABSTRACT

Purpose: To evaluate the Neutrophil to Lymphocyte ratio (NLR) and Platelet to Lymphocyte ratio (PLR) in patients with pseudoexfoliation syndrome (PES).

Material and Methods: Fifty-five patients with PES and 33 patients with no problems other than cataract and refractive error were included in the study.

Results: The mean NLR was found 2.59±1.48 in patients with PES and 1.75±0.6 in the control group. The difference was statistically significant (p=0.002). The mean PLR was 119,95±65,93 in patients with PES and 114,84±39,88 in the control group. The difference between the two groups was not statistically significant (p=0,29).

Conclusion: Inflammation has an important role in the formation of PES. Therefore, NLO can be used as a new inflammatory biomarker which is simple and easily accessible in the diagnosis and follow-up of PES.

Key Words: Pseudoexfoliation Syndrome, Biomarker, Neutrophil, Lymphocyte, Platelet.

INTRODUCTION

Pseudoexfoliation syndrome (PES) is a systemic disease characterized by excessive production of grayish-white abnormal fibrillary extracellular substances and accumulation in anterior segment elements such as iris, lens, cornea, ciliary body, trabecular network and lens zonules and extra-ocular organs such as skin, aorta, lung, kidneys, connective tissue and peripheral vessels.[1-3] It increases by advancing age. It affects more than 30% of individuals aged >60 years.[4] Most common ocular findings include open-angle glaucoma secondary to pseudoexfoliation, cataract, difficulty in pupil dilatation, zonule problems and lens luxation.[1,5]

Although pathogenesis has not been fully elucidated in PES which was first described by Lindber in 1917[1,6,7] it is thought than genetic factors as well as aging process, inflammation, oxidative stress, ultraviolet irradiation and autoimmune disease play role in the development of PES.[8-10] As inflammation is involved in the etiology, inflammatory biomarkers have become important in the PES.

Both increased neutrophil level and lymphopenia are biomarkers of acute inflammation. In recent years, neutrophil: lymphocyte ration (NLR) and platelet: lymphocyte ratio (PLR) has been introduced as a finding of subclinical systemic inflammation as similar to C-reactive protein.[11,12] The NLR and PLR have become an established predictor in the prognosis and progression of many cancers and cardiovascular disorders.[13,14] However, there is limited number of studies investigation effects of these biomarkers in the progression and prognosis of cases with PES.

In our study, we aimed to demonstrate relationship between PES and NLR and PLR which are accepted as inflammatory biomarkers in recent studies.

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MATERIAL AND METHOD

This retrospective study was conducted at Ophthalmology Department of Van Yuzuncu Yil University, Medicine School. Data were collected by screening records of the patient who presented to ophthalmology outpatient clinic between January, 2016 and December, 2018. The study was approved by Ethics Committee of Van Yuzuncu Yil University, Medicine School. The study was conducted in accordance to Helsinki Declaration. All participants gave written informed consent before study.

The subjects were assigned into 2 groups: Group 1, 55 patients diagnosed as PES in routine ophthalmological examination; and group, 33 patients with no ocular disorder other than cataract and refractive error.

The PES diagnosis was made by oof grayish-white exfoliation material in anterior capsule and/or pupillary border in one or both eyes after pupil dilatation by 1% tropicamide eye drop in slit-lamb examination.

The patients with acute or chronic infectious disease, those with autoimmune disorder, cardiac disease, cerebrovascular disease, hematological disorder or malignancy, those undergoing radiotherapy or chemotherapy, those on systemic steroids, those with inflammatory eye disorder such as uveitis, scleritis or keratitis, those with diabetes mellitus and patients with intraocular pressure>21 mmHg were excluded.

Venous blood samples were drawn from patient and control groups. The samples were studied in K2-EDTA tubes (Ethylene Diamine Tetra Acetic Acid) by Nihon Kohden Celltac G MEK-9100 automated analyzer using commercial kits (Hemolynac -310 and 510 Lysing reactive)

Statistical analysis:

Statistical analyses were performed using SPSS version 23.0. Descriptive statistics were used for age, gender, and mean NLR and PLR values. Normal distribution was assessed by Kolmogorov-Smirnov test. To compare groups regarding age, neutrophil, lymphocyte, platelet, NLR and PLR, Student's t test was used for data with normal distribution whereas Mann Whitney U test for those with skewed distribution. Chi-square test was used to compare groups regarding gender. ROC analysis was performed for NLR and PLR values.

FINDINGS

The study included 55 patients with pseudoexfoliation in one or both eyes (group 1) and 33 age- and sex-matched healthy individuals as controls (group 2). In group 1, there was bilateral pseudoexfoliation material in 36 whereas unilateral pseudoexfoliation material in 19 of 55 patients.

Mean NLR was calculated as 2.59±148 in group 1 and 1.75±0.6 in group 2, indicating significant difference (=0.002) (Figure 1a). Mean PLR was calculated as 119.95±65.93 in group 1 and 114.84±39.88 in group 2, indicating no significant difference (p=0.29) (Figure 1b). No significant difference was detected in NLR and PLR between patients with bilateral or unilateral pseudoexfoliation material. ROC analysis was performed for NLR and PLR values.

The area under curve (AUC) was found as 0.68±0.6 for NLR (p=0.04). The cut-off value was calculated as 1.86. The sensitivity and specificity were 0.62 and 0.38, respectively (Figure 2). The ROC analysis did not revealed a significant outcome for PLR. No significant difference was detected between groups regarding age and gender. Table 1 summarizes clinical characteristics and laboratory results in the patient and control groups.
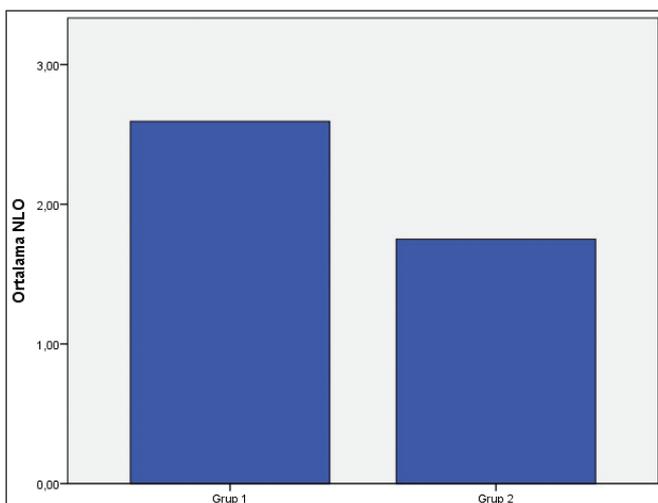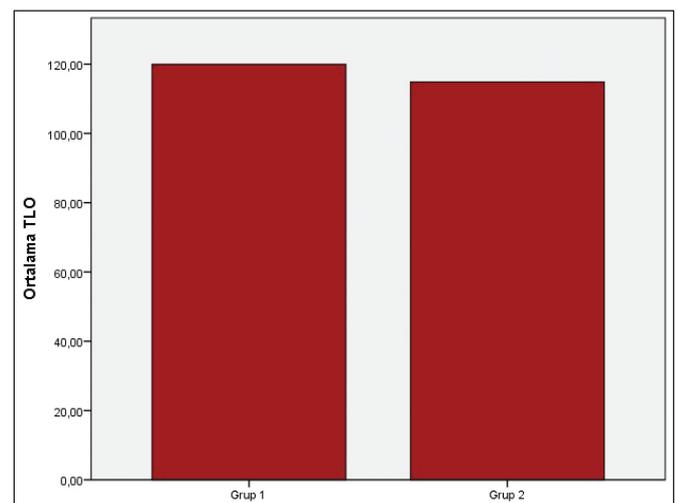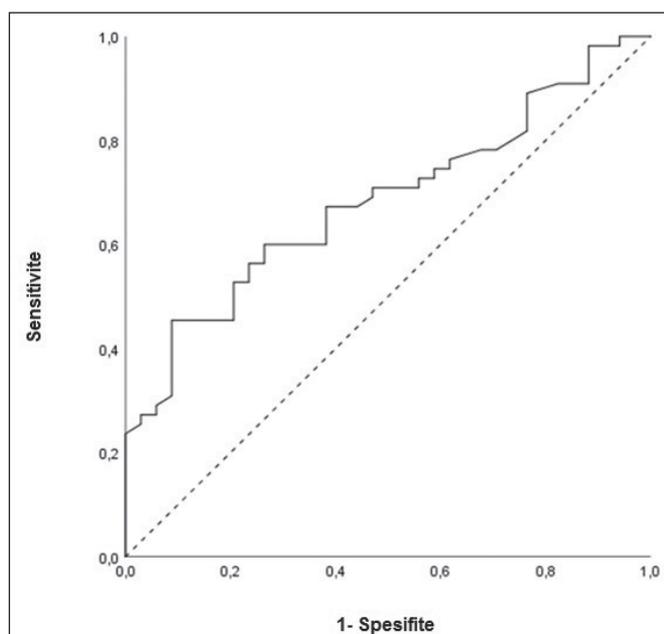

Figure 1a. *Mean NLR in the patient and control group.*

Figure 1b. *Mean PLR in the patient and control group.*

Figure 2: *ROC analysis of NLR.*

DISCUSSION

In this study, we demonstrated that there is a relationship between NLR and patients with PES but no relationship between PLR and same study population.

It has been thought that many factors such as inflammation, ischemia and hypoxia are involved in the pathogenesis of PES. However, its etiopathogenesis hasn't been fully elucidated.

As inflammation has come to forefront, many studies investigating inflammatory biomarkers in patients with PES have been conducted in recent years. In a study, Garweg et al.[15] studied 40 inflammatory cytokines in aqueous humor of the patients with PES and control group and showed that the cytokines were markedly higher in PES patients with lens subluxation when compared to remaining groups.

Again, Sarenac Vulovic et al.[16] evaluated nitric oxide (NO) and tumor necrosis factor-alpha (TNF-α) levels in the serum and aqueous humor of PES patients, PES patients with glaucoma (PESG) and patients without PES. Authors found that NO and TNF-α levels in the aqueous humor were significantly higher in PSG group than remaining groups the aqueous humor but there was no marked difference in serum levels among groups. In another study, it was shown that there is a correlation between serum and aqueous humor YKL-40 levels in patients with PES.[17] In a study by Cumurcu et al.[18] it was emphasized that elevated serum alpha-1 antitrypsin levels could be used as a marker in patients with PES.

There are many studies indicating that blood cell ratios such as NLR and PLR can be used biomarker to define risk factors in some ocular disorders such as diabetic retinopathy and AMD, coronary heart disease and malignancies as well as in the follow-up as similar to our study.[19-24]

There is limited number of studies investigated NLR and PLR as biomarker in PES. As similar to our study, Kurtul et al.[2] found that NLR was markedly higher in patients with PES and PESG when compared to control group. Ozgonul et al.[25] compared NLR and PLR values among PES, PESG and control groups. Authors found that there was significant difference in NLR values between PES, PESG and control while only significant difference in PLR value was detected between PSEG and controls. Mirza et al.[5] assessed monocyte: HDL ratio (MDR) and lymphocyte: monocyte ratio LMR and showed that MDR was significantly higher while LMR was significantly lower in PES and PESG groups when compared to control.

Elevated neutrophil count or lymphopenia alone is one of the significant findings of inflammation. In our study, it was found that neutrophil count was significantly higher while lymphocyte count was significantly lower in PES group when compared to controls.

There are some limitations in our study. Firstly, we did not assess patients with PES glaucoma as a third group. Secondly, we did not measure and compare other pro-inflammatory cytokines with NLR and PLR. Finally, number of controls differed from patient group.

In conclusion, it is well-known that inflammation plays an important role in PES development. Thus, in PES, NLR can be used as a novel, simple and readily available biomarker in the diagnosis and follow-up.

There is a need for further studies evaluating serum NLR levels in cases of glaucoma or lens subluxation caused by pseudoexfoliation in PES.

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