INTERNATIONAL ANATOLIA ACADEMIC ONLINE JOURNAL
e-ISSN 2148-3159 HEALTH SCIENCES RESEARCH ARTICLE

KRONİK EFÜZYONLU KRONİK SÜPÜRATİF OTİTİS MEDİA HASTALARINDA TROMBOSİT-LENFOSİT ORANI (PLO) VE NÖTROFİL-LENFOSİT ORANI (NLO) KULLANILABİLİR Mİ?

Asst. Prof. MD Sevil ALKAN ÇEVİKER**, 0000-0003-1944-2477,**
Asst. Prof. MD Dursun Mehmet MEHEL, **0000-0002-5613-3393,**
Assoc. Prof**.** MD Doğukan ÖZDEMİR, **0000-0003-2008-163X,**
Assoc. Prof. MD Abdulkadir ÖZGÜR, **0000-0002-6155-5988,**
Prof MD Özgür GÜNAL, **0000-0002-7744-4123,**
Prof MD Süleyman Sırrı KILIÇ,**0000-0002-0238-8008.**

Geliş Tarihi/Received	Kabul Tarihi/Accepted	Yayın Tarihi/Published
14.02.2021	19.07.2021	30.08.2021

Correspondence: *Sevil ALKAN ÇEVİKER, Doktor Öğr. Üyesi, Çanakkale Onsekiz Mart Üniversitesi, Tıp Fakültesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji, sevil3910@gmail.com*

ÖZET

Giriş

Nötrofil Lenfosit Oranı (NLO) ve Trombosit Lenfosit Oranı (PLR) testleri, tüm hekimler tarafından hesaplanabilen ucuz testlerdir. Bu çalışmada, KSOM'nin akut alevlenmesinde NLO ve PLO'nın inflamatuar belirteç olarak kullanılıp kullanılamayacağını ve akut ataklarda erken tıbbi tedaviye karar vermedeki rolünü araştırmayı amaçladık.

Yöntem

Çalışmaya Ağustos 2015-Ağustos 2018 tarihleri arasında KSOM tanısı almış hastalar dahil edildi. Bu hastaların hemogram parametreleri hastane otomasyon sisteminden alınarak retrospektif olarak değerlendirildi. Her hasta için NLO ve PLO değerleri, nötrofili lenfosit ile, trombositi lenfosit sayılarıyla bölünerek hesaplandı. Demografik olarak yaş, cinsiyet, klinik tanı ve laboratuvar parametreleri değerlendirildi. Kontrol grubu, vaka grubundaki her hasta için kronik efüzyonlu KSOM tanısı olmayan bir hastadan oluştu

Bulgular

Yapılan analiz sonucunda; CRP, ESR, WBC, MPV, PLR, NLR değerleri trombosit sayısı dışında KSOM grubunda istatistiksel olarak anlamlı yüksek bulundu ($p < 0.05$), ancak ROC analizinde bu değerler anlamlı bulunmadı.

Tartışma
Literatürde KSOM hastalarında NLO ve PLO ile ilgili sınırlı sayıda çalışma vardır ve bu çalışmalarda bu testlerin henüz kullanılabileceğine dair yeterli kanıt yoktur. Standardizasyonu sağlamak ve bu NLO ve PLO oranlarının klinik önemini araştırmak için daha yüksek hasta sayılarına sahip randomize kontrollü çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Kronik Süpüratif Otitis Media, Nötrofil-Lenfosit Oranı, Trombosit-Lenfosit Oranı.

ARE PLATELET-LYMPHOCYTE AND NEUTROPHIL-LYMPHOCYTE RATIO VALID AS INFLAMMATORY MARKERS IN CHRONIC SUPPURATIVE OTITIS MEDIA WITH CHRONIC EFFUSION YET?

ABSTRACT

Introduction

Neutrophil to lymphocyte ratio (NLR) and Platelet-lymphocyte ratio (PLR) tests are inexpensive tests that can be calculated by all physicians. In this study, we aimed to investigate whether NLR and PLR could be used as inflammatory markers in acute exacerbation of CSOM and its role in deciding early medical treatment in acute attacks.

Method

In this study, patients diagnosed with CSOM between August 1, 2015 and August 1,2018 were included. Hemogram parameters of these patients were obtained from hospital system and evaluated retrospectively. The NLR and PLR values for each patient calculated as dividing neutrophil by lymphocyte, platelet by lymphocyte counts respectively. Demographically, age, gender, clinical diagnosis and laboratory parameters were evaluated. The control group consisted of one patient without a diagnosis of CSOM with chronic effusion for each patient in the case group.

Results

As a result of the analysis it was found that; CRP, ESR, WBC, MPV, PLR, NLR values were statistically significantly higher in the CSOM except platelet count ($p < 0.05$), but in ROC analysis these values were not found to be significant.

Discussion

There are a limited number of studies in the literature on NLR and PLR for CSOM patients, and there is not enough evidence in these studies that these tests can be used yet. Randomized controlled studies with higher patient numbers are needed to ensure standardization and to investigate the clinical significance of these NLR and PLR ratios.

Key words: Chronic Suppurative Otitis Media, Neutrophil-Lymphocyte Ratio, Platelet-Lymphocyte Ratio.

INTRODUCTION

Chronic Suppurative Otitis media (CSOM) is a chronic infection and chronic inflammation of the of the middle ear (the mucosa covering the inner surface of the tympanic cavity), mastoid air cells and Eustachian tube. The basis of the clinical presentation is otorrhea, perforated tympanic membrane and conductive hearing loss. It usually develops following recurrent acute otitis attacks and/or chronic otitis media with effusion, but tubal dysfunction, allergies, nasopharyngeal and paranasal infections also facilitate the development of the disease. Despite the studies, the mechanisms of CSOM formation are still not clearly explained. In addition, a treatment strategy such as when to give medical treatment and when to perform surgery has not been established yet. In general, the presence of otorrhea for more than three months is considered as a sign of chronicity. The goals of treatment are to eradicate the infection, prevent complications, repair the eardrum, and restore hearing. Medical treatment is done to control infection and prevent discharge. Repair of the eardrum and restoration of hearing are mostly provided by surgical treatment. If the disease is not recognized in the early period or if appropriate treatment is not performed, serious complications may develop. Improperly treated CSOM may cause life-threatening complications (meningitis, intracranial abscess, etc.) (1-3).

The number of white blood cells (WBC) studied in the whole blood count (CBC) test, which is an easy and inexpensive test, neutrophil, lymphocyte, platelet count (PLT) and mean platelet volume (MPV) values and whose rates are used as inflammatory markers. Neutrophil lymphocyte ratio (NLR) and platelet lymphocytes ratio (PLR) are some of the most important of these markers and in the current literature, there are several studies on whether it has predictive value of NLR and PLR for many diseases such as inflammatory diseases, malignancies, hypertension (HT), such as diabetes mellitus (DM) (4).

The aim of this study was to investigate the relationship between NLR and PLR in CSOM patients with chronic effusion and its role in predicting early medical treatment in acute attacks.

METHODS

In this study, patients diagnosed with CSOM in our outpatient clinics of our hospital, between August 1, 2015 and August 1,2018 were included. The results of hemogram parameters were obtained from the automation system records of our hospital. Demographically, age, gender, clinical diagnosis (according to ICD code) and laboratory parameters were evaluated. The control group consisted of one patient without a diagnosis of chronic suppurative otitis media with chronic effusion for each patient in the case group.

C-reactive protein (CRP), Erythrocyte sedimentation rate (ESR) values and mean platelet volume (MPV) values in the hemogram parametres which are known as the inflammation parameters were examined. In addition hemogram parameters of these patients were evaluated retrospectively for calculations. To obtain NLR values, the neutrophil count was divided by the lymphocyte count. Platelet count was divided by lymphocyte count to obtain PLR values. All data were recorded for statistical analysis.

The laboratory parameters of the patients were studied in the biochemistry laboratory of our hospital.

Statistical analysis: SPSS 21.0 (SPSS, Chicago, IL, *USA*) program was used for statistical evaluation of the data. The data of patient and control groups were analyzed using the Kolmogorov-Smirnov test and Shapiro-Wilk tests. Descriptive statistics were presented as mean ± standard deviation, categorical variables as number of cases and%. The values of the normal and non-normal control and patient groups were shown as mean ± SD and the difference between the groups was evaluated by Independent Student-t test and Mann-Whitney U test, respectively. The correlation coefficients and statistical significance were calculated by ear Spearman correlation test since the variables did not fit the normal distribution. Pearson correlation test and Spearman correlation test were used to analyze the correlation of platelet lymphocyte ratio. $p<0.05$ was considered statistically significant.

Ethical approval: The study was approved by the local ethics committee of Samsun Education and Research Hospital, Health Sciences University, at date of 26 March 2019 with number 2019/7.

RESULTS

The demographic and biochemical data of the 108 patients are summarized in Table 1. A total of 108 cases; 53 (50%) patients with CSOM with chronic effusion, 53 (50%) control group were included in the study. There was 27 females (50.9%) and 26 males (49.1%) in the CSOM group; control group consisted of 27 women (50.9%) and 26 men (49.1%). The median age was 42.54±15.87 years in case group and 39.24±17.10 in control group. The mean age of the patients and controls were 42.54 ± 15.87 and 39.24 ± 17.10, respectively, but there was no significant difference in term of age between two groups ($p> 0.05$). Additionally, there was no significant difference between the groups in terms of gender numbers ($p> 0.05$). As a result of the analysis it was found that; CRP, ESR, WBC, MPV, Platelets / Lymphocyte Ratio, Neutrophil /

Lymphocyte Ratio values were statistically significantly higher in the chronic otitis media group except platelet count ($p<0.05$) (Table 1).

Table 1. Demographic and biochemical data (mean ± standard deviation).

	Chronic supurative otitis media with chronic effusion group	**Control group**	**p value**
Age (years) (mean ± SD)	42.54±15.87	39.24±17.10	.218*
Gender **-woman** **-male**	W/M 27 (50.9%) 26 (49.1%)	W/M 27 (50.9%) 26(49.1%)	1.000***
CRP (mg / L) (mean ± SD)	69.37±36.46	22.0±15.15	.000*
ESR (mm/h) (mean ± SD)	59.88±24.50	37.18±20.20	.000*
WBC (mean ± SD)	14528.30±4732.10	6878.86±1743.70	.000*
MPV (mean ± SD)	9.92±2.02	8.08±1.53	.000*
Platelets (mean ± SD)	214924.52±79793.92	222726.41±70679.70	.323*
Platelets / Lymphocyte (PLR)	118.18±15.25	93.46±14.18	.000**
Neutrophil /	3.18±0.94	2.08±0.50	.000*

lymphocyte (NLR)			

• * Mann-Whitney U test, ** Independent - Sample T test, *** Chi-square tests were used.

While there was a weak relationship between the 3 values and the neutrophil / lymphocyte ratio, there was no significant relationship between the p values. The relation of Neutrophil / Lymphocyte ratio with the others in the chronic otitis media group, respectively, is not significant. There was a positive correlation between NLR and WBC value, and a negative correlation between sedimentation and PLR. However, no statistically significant relationship was found according to p values (p> 0.05) (Table 2).

Table 2. Correlation table of blood parameters in the patient group.

	Neutrophil / Lymphocyte (NLR)	
	r	***p**
Platelet (x10^3 µL)	.166	.233
CRP (mg/L)	.006	.964
MPV (fl)	-.026	.852
Sedimentation	-.084	.552
WBC	.221	.112
Platelet / Lymphocyte ratio	-.112	.423

** Spearman correlation test, CRP: C-reactive protein, MPV: mean platelet volume, WBC: white blood cell.

There was a negative correlation between PLR and PLT and NLR. However, no significant correlation was found in p values (p> 0.05) (Table 3).

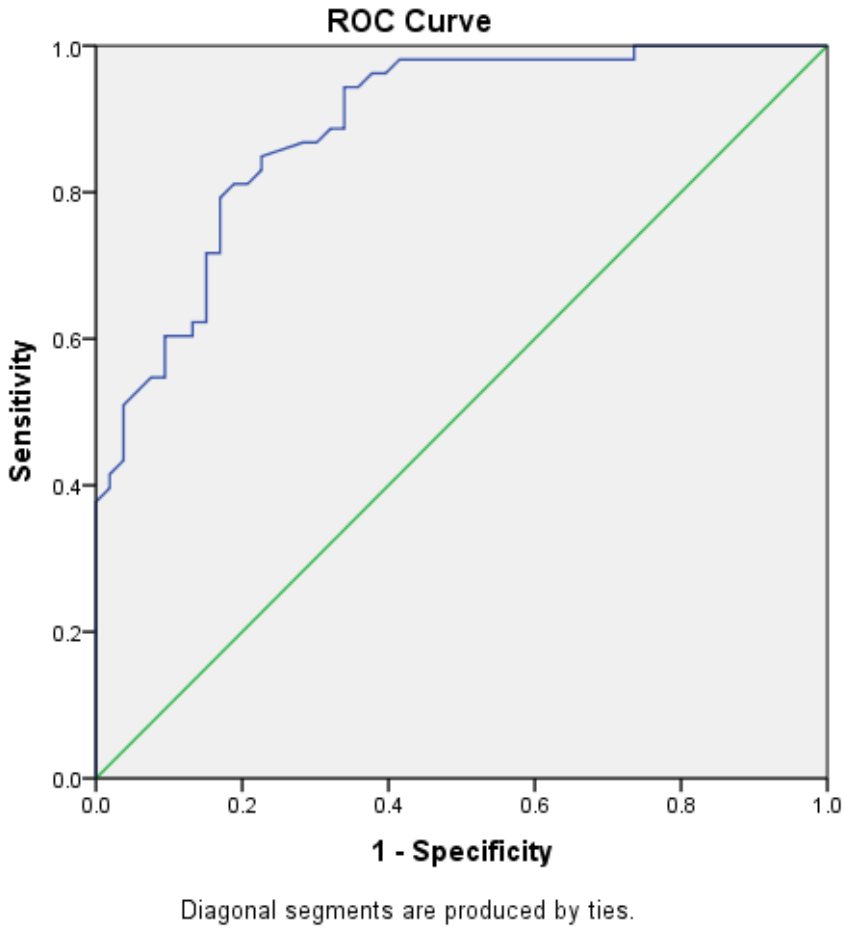
Table 3. Correlation table of PLR and PLT and NLR in the patient group.

	Platelet / Lymphocyte ratio (**PLR)**	
	r	**p**
CRP (mg/L)	.229	.100*
MPV (fl)	.154	.270*
Platelet (x10^3 µL)	-.193	.167**
Sedimentation	.209	.133*
WBC	.206	.139*
Neutrophil / Lymphocyte (NLR)	-.112	.423**

* Pearson Correlation Test, ** Spearman Correlation Test, $p<0.05$ is considered significant.

The diagnostic decision-making properties of serum PLR and NLR values in chronic otitis media were examined by "Receiver Operating Characteristics" (ROC) curve analysis. In the presence of significant breakpoints, sensitivity, specificity, positive and negative predictive values of these limits were calculated. In the evaluation of the area under the curve, it was interpreted that the diagnostic value of the test was statistically significant in cases with $p <0.05$. (Figure 1,2,3). Confidence intervals were found between 0.82 and 0.94 for PLR and 0.83 to 0.95 for NLR. As a result of the analysis, no superiority to each other was determined as the area they covered.

Figure 1. ROC analysis of Platelet / Lymphocyte Ratio between two groups.



Area Under the Curve

Test Result Variable(s): PLT_LEN Ratio

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.889	.031	.000	.829	.949

Figure 2. ROC analysis of Neutrophil / Lymphocytebetween two groups.

Area Under the Curve

Test Result Variable(s): NLO

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.892	.031	.000	.831	.953

The test result variable(s): NLR has at least one tie between the positive actual state group and the negative actual state group.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

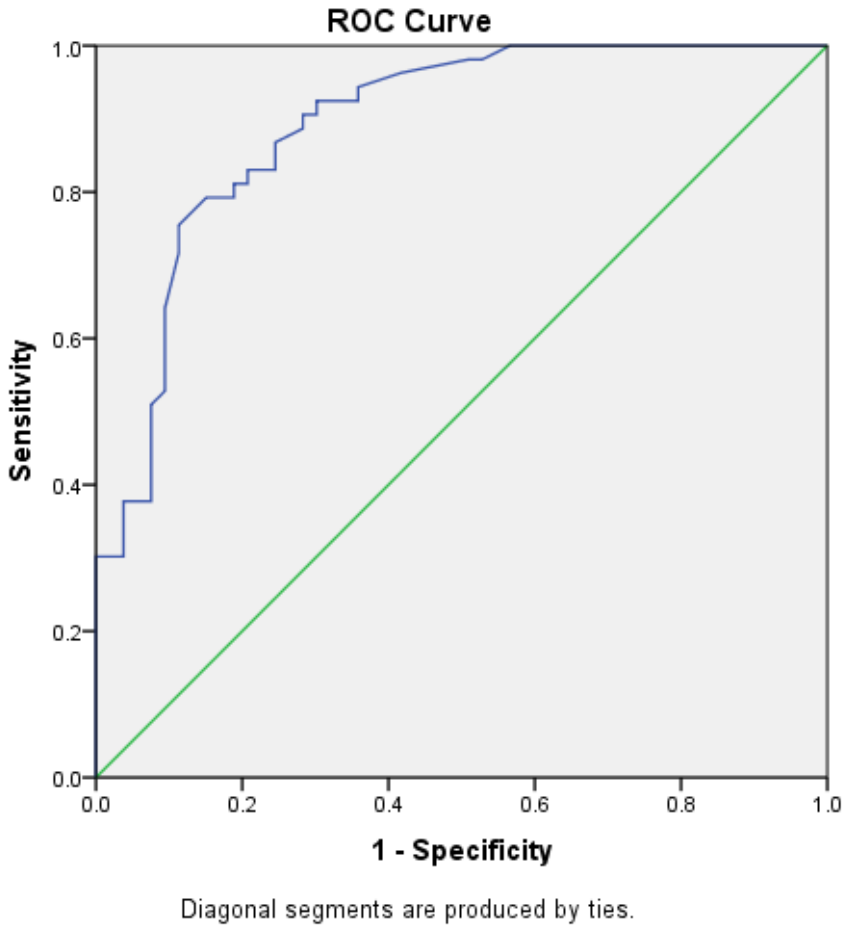
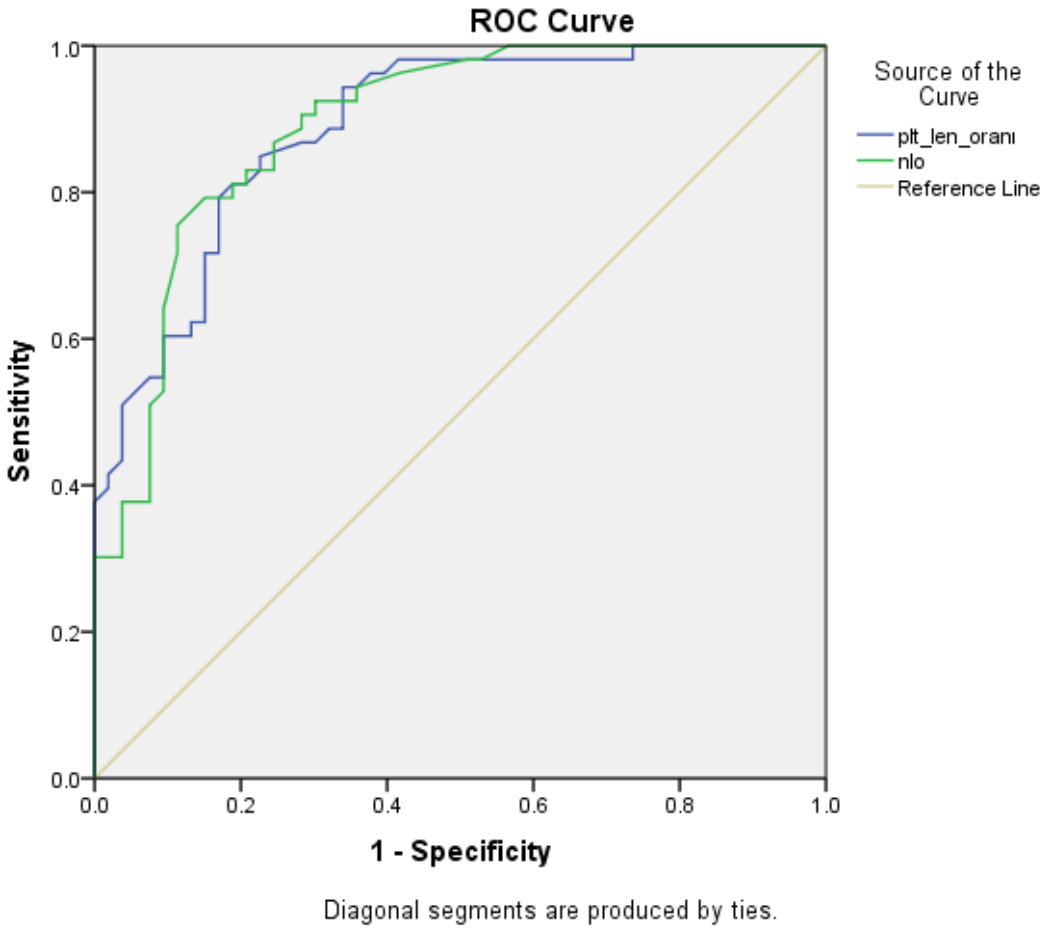


Figure 3. ROC analysis of Neutrophil / Lymphocyte and Platelet / Lymphocyte Ratio due to reference line.



Area Under the Curve

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
PLR	.889	.031	.000	.829	.949
NLR	.892	.031	.000	.831	.953

The test resultvariable(s): PLT LEN Ratio, NLR has at least one tie between the positive actual state group and the negative actual state group.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

DISCUSSION

Platelet-Lymphocyte Ratio (PLR) and Neutrophil-Lymphocyte Ratio (NLR) are inflammatory parameters, since they are values that do not require extra costs and can be easily calculated from peripheral blood analysis, and have inspired many studies in various fields of medicine from cancer to infection, rheumatic diseases, etc. in recent years in order to investigate many inflammatory processes (4-8). Although rare, there are studies investigating the effectiveness of these values in CSOM in adults (9). It has been determined that many studies have been conducted investigating the correlations between the inflammatory markers in otitis media in the literature. However, the results of the study did not generally lead to a clear conclusion (4-9). In this study, we aimed to investigate whether NLR and PLR could be used as inflammatory markers in acute exacerbation of CSOM and its role in deciding early medical treatment in acute attacks.

Elbistanli et al. (10) investigated, the mean NLR and PLR rates in 126 pediatric patients diagnosed with CSOM with chronic effusion and inserted a ventilation tube. In this study, NLR and PLR values were found to be significantly higher in the case group than in the control group. Also, in this study, NLR and PLR values have been reported to be a laboratory indicator that supports typing the viscosity of the fluid accumulated in the middle ear, in addition to having a predictive value for otitis media with effusion. Boztepe et al.(11) reported that, in their retrospective study including 81 COM patients, NLR increased significantly in middle ear effusions, and an NLR value lower than 1.38 and a PLR value lower than 97.96 could indicate mucoid effusion. Atan et al. (12) found that NLR and PLR were higher in otitis media with effusion in a study they conducted with 77 patients.

Eryilmaz et al. (13) reported that the presence of other inflammatory diseases such as chronic rhinosinusitis and allergic rhinitis can change the NLR and the PLR in children who need a ventilation tube for otitis media. Tansuker et al. (14) compared 2 groups (active COM and inactive COM) with and without mastoidectomy in their study. They suggested that, there

was not significantly difference of NLR between the groups. Eğilmez et al. (9) were investigated the real potential role of neutrophil, platelet, Eosinophil / Lymphocyte Ratio (ELR) and mean platelet value (MPV) in the diagnosis of otitis media with effusion in their study. There was no statistically significant difference between the two groups in terms of NLR, PLR, ELR and MPV values in this study, too. Similarly, Bakshi (15) investigated that the change in neutrophil-lymphocyte and thrombocyte-lymphocyte ratios in otitis media with effusion can be used to predict the viscosity of the secretions, but it is difficult to determine the importance of standardization because the NLR may differ from person to person due to age and body mass index. In our study, it was found that; CRP, ESR, WBC, MPV, Platelets / Lymphocyte Ratio, Neutrophil / lymphocyte Ratio values were statistically significantly higher in the chronic otitis media group except platelet count ($p < 0.05$), but in ROC analysis these values were not found to be significant either.

CONCLUSION

There are a limited number of studies in the literature on NLR and PLR rates for CSOM patients, and there is not enough evidence in these studies that these tests can be used yet. Randomized controlled studies with higher patient numbers are needed to ensure standardization and to investigate the clinical significance of these NLR and PLR ratios.

Conflict of Interest: We declare that there is no conflict of interest.

Limitations of our study: The limitation of our study is that it has a single center, a limited number of patients and a retrospective study.

Peer-review: Externally peer-reviewed.

Financial support: None.

Author Contributions: Concept – S.A.Ç, D.M.M., D.Ö.; Design - S.A.Ç, D.M.M.; Supervision - A.Ö,Ö.G; Resource - S.A.Ç, D.M.M.; Materials - D.M.M..; Data Collection and/or Processing – D.M.M..; Analysis and/or Interpretation - D.M.M., D.Ö.;.; Literature Search –S.A.Ç, D.M.M.,.; Writing - S.A.Ç, D.M.M.,; Critical Reviews - S.S.K, Ö.G., A.Ö, ÖG, SSK.

REFERENCES

1. Paksoy M, Aydın S, Hardal Ü, Çelebi Ö, Eken M. KronikOtitisMediadaKemik Zincir, Kulak Zarı Perforasyonları ve işitme Kayıpları ile ilişkisi, Otoscope. 2005; 2: 51 - 57.
2. Incesulu A. Chronic suppurative otitis media. Turkiye Klinikleri J Surg Med Sci 2005;1:66-70.
3. Verhoeff M, van der Veen EL, Rovers MM, Sanders EA, Schilder AG. Chronic suppurative otitis media: a review. Int J Pediatr Otorhinolaryngol. 2006 Jan;70(1):1-12.
4. Balta S, Demirkol S, Unlu M, Arslan Z, Celik T. Neutrophil to lymphocyte ratio may be predict of mortality in all conditions. Br J Cancer 2013;109(12):3125-26.
5. Djordjevic D, Rondovic G, Surbatovic M, Stanojevic I, Udovicic I, Andjelic T, et al. Neutrophil-to-Lymphocyte Ratio, Monocyte-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio, and Mean Platelet Volume-to-Platelet Count Ratio as Biomarkers in Critically Ill and Injured Patients: Which Ratio to Choose to Predict Outcome and Nature of Bacteremia? Mediators Inflamm. 2018;2018:3758068. doi: 10.1155/2018/3758068.
6. Buettner S, Spolverato G, Kimbrough CW, Alexandrescu S, Marques HP, Lamelas J, et al. The impact of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio among patients with intrahepatic cholangiocarcinoma. Surgery. 2018;164(3):411-418. doi: 10.1016/j.surg.2018.05.002.
7. Zhang JY, Ge P, Zhang PY, Zhao M, Ren L. Role of Neutrophil to Lymphocyte Ratio or Platelet to Lymphocyte Ratio in Prediction of Bone Metastasis of Prostate Cancer. Clin Lab. 2019;65(5). doi: 10.7754/Clin.Lab.2018.181040.
8. Hammad M, Shehata OZ, Abdel-Latif SM, El-Din AMM. Neutrophil/lymphocyte ratio and platelet/lymphocyte ratio in Behçet's disease: which and when to use? Clin Rheumatol. 2018;37(10):2811-2817. doi: 10.1007/s10067-018-4194-z.
9. Eğilmez OK, Güven M, Yılmaz MS, Demir D, Çelik B. NRL, PLR, ELR, MPV veEfüzyonlu Otitis Media. SakaryaTıpDergisi 2019;9(2):297-301.
10. Elbistanli MS, Koçak HE, Acipayam H, Yiğider AP, Keskin M, Kayhan FT. The Predictive Value of Neutrophil-Lymphocyte and Platelet-Lymphocyte Ratio for the Effusion Viscosity in Otitis Media With Chronic Effusion. J Craniofac Surg. 2017;28(3):e244-e247. doi: 10.1097/SCS.0000000000003452.
11. Boztepe OF, Demir M, Gün T, Bilal N, Ensari NA, Doğru H. A novel predictive marker for the viscosity of otitis media with effusion. Int J PediatrOtorhinolaryngol. 2015;79(12):2355-8. doi: 10.1016/j.ijporl.2015.10.043.

12. Atan D, Apaydin E, Ozcan KM, Dere H. New diagnostic indicators in chronic otitis media with eff usion: neutrophil to lymphocyte ratio and thrombocyte lymphocyte ratio. ENT Updates.2016;6:12–15
13. EryilmazA, Basal Y. Neutrophil to lymphocyte ratio for evaluating the viscosity of otitis media with effusion: Which method has more benefit on clinic? International Journal of Pediatric Otorhinolaryngology. 2016: 83,218. doi:10.1016/j.ijporl.2016.01.015
14. Tansuker HD, Eroğlu S, Yenigün A, Taşkin Ü, Oktay MF. Can Serum Neutrophil-to-Lymphocyte Ratio Be a Predictive Biomarker to Help Differentiate Active Chronic Otitis Media From Inactive Chronic Otitis Media? J Craniofac Surg. 2017;28(3):e260-e263. doi: 10.1097/SCS.0000000000003484.
15. Bakshi SS. Neutrophil-to-Lymphocyte ratio in patients with cirrhosis Clin Gastroenterol Hepatol. 2019: 17(4);799