



Evaluation of Neutrophil-Lymphocyte Ratios, Mean Platelet Volumes, and Platelet-Lymphocyte Ratios in Pterygium

Onur Gokmen,¹ Azer Gokmen²

¹Department of Ophthalmology, Health Sciences University Van Training and Research Hospital, Van, Turkey

²Department of Internal Medicine, Health Sciences University Van Training and Research Hospital, Van, Turkey

Abstract

Objectives: To assess the neutrophil-to-lymphocyte ratio (NLR), mean platelet volumes (MPV), platelet-lymphocyte ratios (PLR) and other complete blood count parameters (CBC) as indicators of inflammation in patients with pterygium.

Methods: This study was carried out retrospectively in 111 consecutive pterygium patients and 106 control subjects. Laboratory and clinical parameters were obtained from the patient data management system. NLR and PLR were calculated by dividing neutrophil and platelet count by lymphocyte count.

Results: A significant difference was found in NLR and lymphocyte values between the pterygium and control groups ($p < 0.05$). However, there was no significant difference found in MPV, PLR and other parameters between groups ($p > 0.05$).

Conclusion: NLR may have an association with pterygium, which should be investigated at larger subgroups in further studies.

Keywords: Inflammation, mean platelet volume, neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, pterygium.

Introduction

Pterygium is a common fibrovascular disease of the bulbar conjunctiva that causes chronic irritation and astigmatism (1). The exact cause of pterygium is still unknown and ultra-violet radiation (UV) exposure is the only proven risk factor (2). Pterygium is not only a progressive fibrovascular mass triggered by chronic inflammation but also a neovascular formation (3).

Neutrophil-Lymphocyte Ratios (NLR) and Platelet-Lymphocyte Ratios (PLR) are inflammatory markers that can easily be acquired by a simple complete blood count (CBC) test. Research has shown an association of NLR with cardiovascular diseases, cancers, strokes, and their prognoses, which has a tendency to increase, and higher NLR ratios has shown as a poor prognostic factor in these chronic and

inflammatory conditions. As a result, they have become a topic for studies in many diseases (4–7). Additionally, it has been suggested that platelets play important roles in immune and/or inflammatory processes and mean platelet volume (MPV) is a potentially useful marker as an indicator reflecting platelet function and activity (8). MPV had also been shown to be an indicator of inflammation and a diagnostic factor for inflammatory diseases in studies (9–12). However, to our knowledge, there is no study that investigates the association between pterygium and NLR, MPV, and PLR even though it is a chronic inflammatory-triggered neovascular formation (3).

In this study, we aimed to analyze the diagnostic values of NLR, PLR, MPV, mean corpuscular volume (MCV), platelet distribution width (PDW), plateletcrit (PCT) and hematocrit (HCT) of pterygium patients to establish if these values can be an indicating marker.

Address for correspondence: Onur Gökmen, MD. Sağlık Bilimleri Üniversitesi Van Eğitim ve Araştırma Hastanesi, Oftalmoloji Bölümü, Van, Turkey

Phone: +90 507 467 07 67 **E-mail:** onurgokmen@gmail.com

Submitted Date: June 22, 2019 **Accepted Date:** September 15, 2019 **Available Online Date:** December 25, 2019

©Copyright 2019 by Beyoglu Eye Training and Research Hospital - Available online at www.beyoglu-eye.com

OPEN ACCESS This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.



Methods

Data Collection

This retrospective study included blood sample test results of male and female patients diagnosed with pterygium and control subjects at the Health Sciences University Van Education and Training Hospital between 2014 and 2018. Pre-operative CBC results of patients scheduled for pterygium surgery and similar results for control subjects were retrospectively scanned from the patient data management system. This study was approved by the local ethics committee. This research adhered to the tenets of the Declaration of Helsinki.

Measurement Methods

Pterygium patients and healthy control subjects were separated into two groups, and the groups were compared with each other. Blood samples were taken from the antecubital vein at 8 a.m. after an overnight fast. Lymphocyte counts (LY), neutrophil counts (NEU), platelet counts (PLT), PDW, PCT, HCT, and MPV values were taken from the CBCs of subjects and NLR and PLR ratios were calculated over these values. CBCs measurement instrument was an automated blood cell counter (Sysmex XN-1000, Sysmex Corporation, Kobe, Japan).

Patient Selection

Inclusion criteria were having a pterygium and providing a blood sample within three days before pterygium surgery, being over 18 and having no other ocular or systemic disease or infectious disease for the pterygium group. The control group included complete blood count (CBC) samples of blood provided by subjects who came to Van Education and Training Hospital polyclinics for reasons other than ophthalmological.

Patients having an ophthalmologic disease other than pterygium, and having any ocular surgery history for the pterygium group were excluded from this study. Exclusion criteria for both groups were having any other known systemic diseases, such as diabetes or hypertension, having any hematinic deficiency, cardiovascular disease, and cancer, being pregnant, having a history of steroid or oral contraceptive use, being a smoker, and showing any infectious disease symptoms when the blood was drawn.

Statistical Analyses

Statistical analysis was performed using SPSS V.20.0. For each variable, normality was checked using the Kolmogorov Smirnov test. T-tests and Kruskal-Wallis tests were used to evaluate the statistical differences between the pterygium and control groups of neutrophil, lymphocyte and platelet

counts, MCV, PDW, PCT, HCT, MPV values and neutrophil/lymphocyte and platelet/lymphocyte ratios. Values of $p < 0.05$ were considered statistically significant. Descriptive statistics were presented as frequency, percent, mean, SD, and range (minimum–maximum).

Results

In total, 987 patients operated on for diagnoses of pterygium between 2014 and 2018 were scanned retrospectively, and 876 patients were eliminated due to the absence of blood samples taken within three days before surgery or having one of the conditions mentioned in the exclusion criteria. This study included 111 eyes of 111 pterygium patients and 106 eyes of 106 control subjects. In the pterygium group, 52 (46.8%) patients were male and 59 (53.2%) female, while in the control group 50 (47.2%) male and 56 (52.8%) female subjects were included. The mean age of the pterygium group was 42.6 ± 13.8 (range 18-82), while in the control group, it was 41.2 ± 13.1 (range 19-76), and there was no statistically significant difference between the age and sex distribution of the groups (all $p > 0.05$).

HCT, MCV, PLT, MPV, NEU, PDW, PCT, and PLR differences were not statistically significant between the pterygium and control groups. However, the LY count was significantly lower in the pterygium group ($p = 0.03$), and the NLR value was significantly higher in the pterygium group ($p = 0.04$). Descriptive statistics of the CBC parameters of the pterygium and control groups are shown respectively in Table 1 and Table 2, while comparisons of the groups are given in Table 3 and Table 4.

Discussion

Pterygium is a common fibrovascular proliferation of the ocular surface that arises from chronic inflammation (13). Pterygium's inflammatory process is triggered by UV exposure and concludes with activated local cascades of cytokines, such as IL-1, IL-6, IL-8 and TNF- α and production of growth factors, such as VEGF, PDGF, b-FGF, and TGF- β in epithelial and endothelial cells, fibroblasts, and leukocytes (14, 15).

Anguria et al. (16) also showed chronic inflammatory cell activation and presentation in pterygium pathology specimens. In addition, the cell counts were related to the severity of the inflammation and UV exposure was suspected as being responsible for the induced inflammatory cells in pterygium tissues.

NLR is a marker for chronic systemic inflammation and NLR has shown an increase in many systemic diseases such as diabetes, systemic hypertension, cardiovascular diseases and strokes. Its prognostic value has also been proven in many cancers (5, 17, 18).

Few studies are investigating the relationship between

Table 1. CBC parameters of pterygium group

	Number	Range	Minimum	Maximum	Mean	SD
HCT %	111	25.40	28.60	54.00	43.28	4.71
MCV fL	111	38.90	55.20	94.10	83.28	6.36
PLT 10 ³ /uL	111	372.00	119.00	491.00	267.98	66.27
MPV %	111	5.10	7.90	13.00	10.31	1.15
NEU 10 ⁹ /L	111	12.92	1.54	14.46	4.78	2.22
LY 10 ⁹ /L	111	3.3	0.75	4.05	2.20	0.67
PDW fL	111	9.90	8.70	18.60	13.40	2.47
PCT %	111	3.84	0.10	3.94	0.62	0.89
NLR	111	18.14	0.74	18.88	2.53	2.27
PLR	111	349.95	46.30	396.25	134.65	59.71
Total	111					

CBC: Complete Blood Count; NLR: Neutrophil–Lymphocyte Ratios; PLR: Platelet-Lymphocyte Ratios; MPV; Mean Platelet Volume; MCV: Mean Corpuscular Volume; PDW: Platelet Distribution Width; PCT: Plateletcrit; HCT: Hematocrit; LY: Lymphocyte Counts; NEU: Neutrophil Counts; PLT: Platelet Counts; SD: Standard Deviation.

Table 2. CBC parameters of the control group

	Number	Range	Minimum	Maximum	Mean	SD
HCT %	106	25.50	32.10	57.60	42.43	3.97
MCV fL	106	43.60	63.40	107.00	84.35	6.40
PLT 10 ³ /uL	106	323.00	156.00	479.00	276.03	65.40
MPV %	106	5.26	7.94	13.20	10.42	0.95
NEU 10 ⁹ /L	106	11.40	1.98	13.38	4.54	1.68
LY 10 ⁹ /L	106	3.27	0.84	4.11	2.40	0.65
PDW fL	106	11.70	8.50	20.20	13.14	2.19
PCT %	106	2.66	0.14	2.80	0.44	0.55
NLR	106	6.73	0.83	7.56	2.04	1.03
PLR	106	240.86	62.30	303.16	122.90	44.36
Total	106					

CBC: Complete Blood Count; NLR: Neutrophil–Lymphocyte Ratios; PLR: Platelet-Lymphocyte Ratios; MPV; Mean Platelet Volume; MCV: Mean Corpuscular Volume; PDW: Platelet Distribution Width; PCT: Plateletcrit; HCT: Hematocrit; LY: Lymphocyte Counts; NEU: Neutrophil Counts; PLT: Platelet Counts; SD: Standard Deviation.

NLR and ocular diseases. Ilhan et al. found higher NLR in age-related macular degeneration (19). Ozturk et al. found increased NLR values in Behcet disease (BD), which is a systemic inflammatory vasculitis, also affecting the eyes by causing panuveitis, although NLR is also associated with BD activity. (20) Celik and Sekeryapan et al. found higher NLR values in dry eyes (21, 22). Dursun et al. (23) found higher NLR values in retinal vein occlusion. In our study, we found higher NLR values in pterygium patients ($p < 0.05$). Chronic inflammatory and neovascular activity in pterygium may be the cause of increased NLR levels in the current study.

MPV is a laboratory marker that shows the activity of platelets, and its increase has been seen generally in vascular diseases, such as strokes, peripheral artery diseases, cerebrovascular diseases, and inflammatory diseases (24). In our study, we found no significant difference between groups in MPV, PCT and PDW values ($p > 0.05$). PCT is a parameter derived from the platelet count and MPV; PDW is a parameter that measures platelet size distribution and activity (25). Platelet activity and MPV values generally increase in vascular diseases. However, pterygium has a more dominant fibrous component and greater fibroblast activity than vascu-

Table 3. Comparison of NEU, LY, PLT, NLR, PLR, MPV and HCT values between groups

	t-test		
	p	Mean Difference	Std. Error Difference
NEU	0.386	0.23	0.27
LY	0.034	-0.19	0.09
PLT	0.369	-8.05	8.94
NLR	0.040	0.50	0.24
PLR	0.102	11.76	7.17
MPV	0.481	-0.10	0.14
HCT	0.152	0.85	0.59

NLR: Neutrophil-Lymphocyte Ratios; PLR: Platelet-Lymphocyte Ratios; MPV: Mean Platelet Volume; HCT: Hematocrit; LY: Lymphocyte Counts; NEU: Neutrophil Counts; PLT: Platelet Counts.

Table 4. Comparison of MCV, PCT AND PDW values between groups

	MCV	PDW	PCT
Mann-Whitney U	5456.50	5575.00	5326.50
Wilcoxon W	11672.50	11246.00	11542.50
Z	-0.923	-0.666	-1.205
p	0.356	0.505	0.228

MCV: Mean Corpuscular Volume; PDW: Platelet Distribution Width; PCT: Plateletcrit.

lar components and activities and these findings may explain the non-significant MPV, PLT, PCT, PDW, and PLR values in pterygium (25, 26).

Other CBC parameters that we investigated in the groups but found insignificant were HCT and MCV ($p > 0.05$). HCT and MCV are markers related to red blood cells showing red blood cell ratio to total blood volume and erythrocyte volume, respectively, and they are used clinically to assess anemias and reduced oxygen-carrying capacity (27). Pterygium occurs on a chronic inflammatory surface that is more related to white blood cells, and insignificant HCT and MCV levels in the current study may show that pterygium has no relationship with red blood cells.

A bias of our study may be taking the blood samples of preoperative patients, taking non-recurrent cases and cases of pterygium showing no inflammation symptoms. In addition, acute inflamed pterygiums, recurrent pterygiums, and small pterygiums without surgery indications may influence the results and can be investigated in future studies.

There are a few limitations to our study. Firstly, this study had a cross-sectional design, but pterygium may be affected

by environmental and genetic factors that may alter the findings. Secondly, the number of subjects is limited with a retrospective design and thirdly, NLR, NEU, LY, MPV and PLR are not specific markers for pterygium and may be affected by many inflammatory conditions.

Despite the limitations and bias, to our knowledge, our study is the first in the literature that investigates the NLR and PLR in pterygium. In conclusion, NLR, MPV, and PLR are cost-effective tests that can be measured with a simple CBC and can be calculated easily. As a result, NLR may have an association with pterygium, which should be investigated at larger subgroups in further studies.

Disclosures

Ethics Committee Approval: The Ethics Committee of Van Training and Research Hospital provided the ethics committee approval for this study (2017/17).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Involved in design and conduct of the study (OG); preparation and review of the study (OG, AG); data collection (OG); and statistical analysis (OG).

References

- Han SB, Jeon HS, Kim M, Lee SJ, Yang HK, Hwang JM, et al. Risk Factors for Recurrence After Pterygium Surgery: An Image Analysis Study. *Cornea* 2016;35:1097-103.
- Liu L, Wu J, Geng J, Yuan Z, Huang D. Geographical prevalence and risk factors for pterygium: a systematic review and meta-analysis. *BMJ Open* 2013;3:e003787.
- Chen J, Maqsood S, Kaye S, Tey A, Ahmad S. Pterygium: are we any closer to the cause? *Br J Ophthalmol* 2014;98:423-4.
- Namikawa T, Munekage E, Munekage M, Shiga M, Maeda H, Kitagawa H, et al. [The Clinical Role of the Neutrophil/Lymphocyte Ratio in Patients with Advanced Gastric Cancer Treated with Protein-Bound Polysaccharide K and Chemotherapy]. [Article in Japanese]. *Gan To Kagaku Ryoho* 2015;42:2081-3.
- Imtiaz F, Shafique K, Mirza SS, Ayoob Z, Vart P, Rao S. Neutrophil lymphocyte ratio as a measure of systemic inflammation in prevalent chronic diseases in Asian population. *Int Arch Med* 2012;5:2.
- Na N, Yao J, Cheng C, Huang Z, Hong L, Li H, et al. Meta-analysis of the efficacy of the pretreatment neutrophil-to-lymphocyte ratio as a predictor of prognosis in renal carcinoma patients receiving tyrosine kinase inhibitors. *Oncotarget* 2016;7:44039-46.
- Brooks SD, Spears C, Cummings C, VanGilder RL, Stinehart KR, Gutmann L, et al. Admission neutrophil-lymphocyte ratio predicts 90 day outcome after endovascular stroke therapy. *J Neurointerv Surg* 2014;6:578-83.
- Murat SN, Duran M, Kalay N, Gunebakmaz O, Akpek M, Doger C, et al. Relation between mean platelet volume and severity of atherosclerosis in patients with acute coronary syndromes.

- Angiology 2013;64:131–6.
9. Fan Z, Zhang Y, Pan J, Wang S. Acute Appendicitis and Mean Platelet Volume: A Systemic Review and Meta-analysis. *Ann Clin Lab Sci* 2017;47:768–72.
 10. Peng YF, Huang YX, Wei YS. Altered mean platelet volume in patients with polymyositis and its association with disease severity. *Braz J Med Biol Res* 2016;49:e5168.
 11. Zheng X, Hao R, Wang Y. [Analysis the relationship of mean platelet volume and nasal obstructive disease]. [Article in Chinese]. *Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi* 2014;28:1662–4.
 12. Shi X, Li WC, Mo LJ, Li XH, Luo YZ, Qin LQ, et al. Altered mean platelet volume in children with Henoch-Schonlein purpura and its association with disease activity. *Ann Clin Biochem* 2018;55:368–72.
 13. Di Girolamo N, Wakefield D, Coroneo MT. UVB-mediated induction of cytokines and growth factors in pterygium epithelial cells involves cell surface receptors and intracellular signaling. *Invest Ophthalmol Vis Sci* 2006;47:2430–7.
 14. Kurt A, Kılıç R, Tad M, Polat OA. YKL-40 expression in pterygium: a potential role in the pathogenesis. *International ophthalmology. Int Ophthalmol* 2019;39:1445–50.
 15. Bradley JC, Yang W, Bradley RH, Reid TW, Schwab IR. The science of pterygia. *Br J Ophthalmol* 2010;94:815–20.
 16. Anguria P, Carmichael T, Ntuli S, Kitinya J. Chronic inflammatory cells and damaged limbal cells in pterygium. *Afr Health Sci* 2013;13:725–30.
 17. Deng M, Ma X, Liang X, Zhu C, Wang M. Are pretreatment neutrophil-lymphocyte ratio and platelet-lymphocyte ratio useful in predicting the outcomes of patients with small-cell lung cancer? *Oncotarget* 2017;8:37200–7.
 18. Min K, Kwon S, Cho SY, Choi WJ, Park SU, Jung WS, et al. Atrial Fibrillation is Strongly Associated With the Neutrophil to Lymphocyte Ratio in Acute Ischemic Stroke Patients: A Retrospective Study. *J Clin Lab Anal* 2017;31.
 19. Ilhan N, Daglioglu MC, Ilhan O, Coskun M, Tuzcu EA, Kahraman H, et al. Assessment of Neutrophil/Lymphocyte Ratio in Patients with Age-related Macular Degeneration. *Ocul Immunol Inflamm* 2015;23:287–90.
 20. Ozturk C, Balta S, Balta I, Demirkol S, Celik T, Turker T, et al. Neutrophil-lymphocyte ratio and carotid-intima media thickness in patients with Behcet disease without cardiovascular involvement. *Angiology* 2015;66:291–6.
 21. Celik T. Assessment of Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio in Patients with Dry Eye Disease. *Ocul Immunol Inflamm* 2018;26:1219–22.
 22. Sekeryapan B, Uzun F, Buyuktarakci S, Bulut A, Oner V. Neutrophil-to-Lymphocyte Ratio Increases in Patients With Dry Eye. *Cornea* 2016;35:983–6.
 23. Dursun A, Ozturk S, Yucel H, Ozec AV, Dursun FG, Toker MI, et al. Association of neutrophil/lymphocyte ratio and retinal vein occlusion. *Eur J Ophthalmol* 2015;25:343–6.
 24. Balta S. Mean Platelet Volume, Neutrophil-Lymphocyte Ratio, and Long-Term Major Cardiovascular Events. *Angiology* 2019;70:289–90.
 25. Wiwanitkit V. Plateletcrit, mean platelet volume, platelet distribution width: its expected values and correlation with parallel red blood cell parameters. *Clin Appl Thromb Hemost* 2004;10:175–8.
 26. Kim KW, Park SH, Kim JC. Fibroblast biology in pterygia. *Exp Eye Res* 2016;142:32–9.
 27. Strauchen JA, Alston W, Anderson J, Gustafson Z, Fajardo LF. Inaccuracy in automated measurement of hematocrit and corpuscular indices in the presence of severe hyperglycemia. *Blood* 1981;57:1065–7.