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Original Article

The Role of Systemic Inflammation in Acquired Nasolacrimal Duct Obstruction

Yasar Dag,[1] Yakup Acet[2]

[1]Department of Ophthalmology, Başakşehir Çam and Sakura City Hospital, İstanbul, Türkiye
[2]Department of Ophthalmology, Mardin Training and Research Hospital, Mardin, Türkiye

Abstract

Objectives: This study aims to investigate the influence of systemic inflammation on adult patients with acquired nasolacrimal duct obstruction (ANLDO).

Methods: Peripheral venous blood analysis was performed on adult patients who underwent dacryocystorhinostomy for ANLDO between June 2020 and December 2022, during their remission period just before the surgery. Platelet, Neutrophil, Lymphocyte, Monocyte, White Blood Cell (WBC) count, Platelet/Lymphocyte ratio (PLR), Neutrophil/Lymphocyte ratio (NLR), Monocyte/Lymphocyte ratio (MLR), and systemic inflammatory index (SII) (calculated as platelet × (neutrophil/lymphocyte)) were compared with a volunteer control group.

Results: The study included 54 adult patients with ANLDO and 54 individuals in the control group. The mean age was 42.5±14.4 years in the ANLDO group and 37.8±12.3 years in the volunteer control group. There was no significant difference in age between the groups (p=0.064). Platelet value (295.9±70.9→254.7±43.9), PLR value (143.8±77.7→119.0±36.1), and SII value (534.7±192.0→442.6±212.2) in the ANLDO group were significantly higher compared to the Control group (p=0.000, p=0.023, p=0.020, respectively). Neutrophil, lymphocyte, monocyte, NLR, MLR, and WBC values did not exhibit significant differences between the case and control groups (p=0.299, p=0.469, p=0.125, p=0.419, p=0.143, and p=0.465, respectively).

Conclusion: The study revealed elevated systemic platelet counts in ANLDO patients, resulting in higher PLR and SII values. The authors suggest that a histopathological examination to assess the local impact of platelets or other inflammatory processes in nasolacrimal duct obstruction could offer valuable insights into the etiopathology of ANLDO.

Keywords: ANLDO,Nasolacrimal duct obstruction, PLR, SII

Introduction

Acquired nasolacrimal duct obstruction (ANLDO) is a condition characterized by persistent epiphora and eye irritation that can develop at any stage of life (1). Although its precise etiology remains unclear, numerous factors have been implicated in its pathogenesis (2). Among these, sex hormones, environmental influences, and local inflammation have been identified as the primary contributors (3). While ANLDO is more prevalent in women, suggesting a potential role for sex hormones in its development, (3) studies also exist suggesting a lack of effect from sex hormones.(4) In addition, tear film osmolarity and the content of tear film proteins and lipids have been recognized as influential factors in ANLDO (5,6). Analyses of tear composition have

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Address for correspondence: Yasar Dag, MD. Department of Ophthalmology, Başakşehir Çam and Sakura City Hospital, İstanbul, Türkiye
Phone: +90 533 018 82 47 **E-mail:** dryasardag@gmail.com

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demonstrated significantly elevated levels of pro-inflammatory cytokines in ANLDO patients, contributing to inflammation (7). Furthermore, ANLDO can stem from various origins, including tumors, (8) trauma, (9) radiotherapy, (10) and systemic inflammatory conditions (11).

In the pathogenesis of ANLDO, it is hypothesized that obstruction arises due to gradual inflammation within the nasolacrimal duct followed by subsequent fibrosis (12). Nevertheless, the precise initiation of this inflammatory process remains unclear (13).

In recent years, numerous studies investigating systemic inflammatory markers have emerged. These studies have highlighted the significance of parameters such as the platelet/lymphocyte ratio (PLR), neutrophil/lymphocyte ratio (NLR), monocyte/lymphocyte ratio (MLR), and systemic inflammatory index (SII) (calculated as platelet × (neutrophil/lymphocyte)) in discerning levels of inflammation (14-17).

Neutrophils and platelets are central players in the inflammatory process, while lymphocytes exert an anti-inflammatory role (17). The SII, calculated by multiplying plateletand neutrophil counts and then dividing by lymphocyte count, has exhibited notably elevated values across various ocular conditions (14,17,24,25). Newly identified inflammatory biomarkers including SII, NLR, and PLR have shown pronounced elevation in the dry eye (14) and keratoconus, (18)both associated with the ocular surface disease. In addition, elevated NLR and PLR have been observed in cases of retinal vascular occlusions (19). PLR has demonstrated significant elevation in patients with both primary open-angle and primary angle-closure glaucoma (20). Further investigations have revealed high SII and NLR values in primary open-angle glaucoma (15).

In our study, our objective was to explore the impact of systemic inflammation on the initiation of local inflammation, a pivotal factor in the pathogenesis of ANLDO, by employing inflammatory biomarkers.

Methods

This retrospective and case–control study was conducted in adherence to the principles set forth in the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee on January 25, 2023, under decision number 30. The study was carried out at BaşakşehirÇamve Sakura City Hospital (İstanbul, Türkiye). Peripheral venous blood analysis was conducted on adult patients who underwent dacryocystorhinostomy (DCR) for ANLDO between June 2020 and December 2022, during their remission period just before the surgery. Platelet, neutrophil, lymphocyte, monocyte, white blood cell (WBC) count, PLR, NLR, MLR, and SII were compared with a volunteer control group. Patients with a history of previous ocular surgery, diabetes, hypertension, systemic and chronic diseases, acute dacryocystitis attacks, and those who had received blood or blood product transfusions were excluded from the study.

Individuals who had previously undergone surgery in any area, including the nasal region, as well as those with a recent or ongoing history of systemic or topical drug usage, were also excluded from the study. Specifically, patients with nasolacrimal sac and subsequent obstruction were primarily included in the study. Only patients who were in complete systemic or local remission were considered for the study. Patients with obstructions occurring before the nasolacrimal sac were not eligible for inclusion. Blood samples were collected from the peripheral venous blood of all patients, drawn from the antecubital region, and analyzed using a hematology device. All blood samples were assessed using the same device (Archem h3000 fully automated hematology analysis –Türkiye).

Descriptive statistics of the data encompassed mean, standard deviation, median, minimum, maximum, frequency, and ratio values. The distribution of variables was assessed using the Kolmogorov–Smirnov test. For the analysis of independent quantitative data, the independent sample t-test and Mann—Whitney U-test were employed. In the analysis of independent qualitative data, the Chi-square test was utilized, and the Fischer's exact test was employed when the conditions for the Chi-square test were not met. The receiver operating characteristic curve was employed to determine the effect level and cutoff value. The effect level was examined through both univariate and multivariate logistic regression analyses. The statistical analysis was conducted using the SPSS Ver. 28.0 program (SPSS, Chicago, Illinois, USA).

Results

Fifty-four ANLDO patients and 54 healthy volunteers were enrolled in the study. The ANLDO group consisted of 43 females and 11 males. The number of females in both the case and control groups exceeded the number of males. There was no significant difference in age between the case and control groups (p=0.064). Similarly, the gender distribution did not exhibit a significant difference (p=0.267) between the case and control groups.

Values such as platelet count (254.7±43.9×10^3/μL), PLR value (119.0±36.1), and SII value (442.6±212.2) were significantly higher in the case group compared to the control group (p=0.000, p=0.023, and p=0.020, respectively). On the other hand, neutrophil, lymphocyte, monocyte, NLR, MLR, and WBC values did not exhibit significant differences between the case and control groups (p>0.05) (Table 1).

In the univariate model, we observed a significant (p<0.05)

Table 1. Demographic data and numerical values of study

	Control group		ANLDO group		p
	Mean±SD/n-%	Median	Mean±SD/n-%	Median	
Age	37.8±12.3	34.0	42.5±14.4	41.0	0.064[m]
Sex					
Female	38-70.4%		43-79.6%		0.267[X²]
Male	16-29.6%	11-20.4%			
Platelet (10^3/ml)	254.7±43.9	257.0	295.9±70.9	293.5	0.000[t]
Neutrophil (10^3/mL)	4.21±1.02	4.11	4.02±0.94	4.16	0.299[t]
Lymphocyte (10^3/mL)	2.24±0.45	2.27	2.32±0.63	2.32	0.469[t]
Monocyte (10^3/mL)	0.53±0.12	0.51	0.49±0.12	0.50	0.125[t]
PLR	119.0±36.1	109.4	143.8±77.7	130.8	0.023[m]
NLR	1.96±0.68	1.84	1.83±0.58	1.77	0.419[m]
MLR	0.24±0.07	0.24	0.22±0.08	0.21	0.143[m]
SII	442.6±212.2	430.4	534.7±192.0	524.6	0.020[t]
WBC (10^3/mL)	7.16±1.15	7.18	6.98±1.37	7.00	0.465[t]

[t]Independent sample t-test/[m]Mann–whitney u test/[X²]Ki-kare test (Fischer test), WBC: White blood cell count, PLR: Platelet/lymphocyte ratio, NLR: Neutrophil/Lymphocyte ratio, MLR: Monocyte/Lymphocyte ratio, SII: Systemic inflammatory index ((platelet x(neutrophil/lymphocyte)), ANLDO: Acquired nasolacrimal duct obstruction.

discriminatory efficacy of platelet count, PLR value, and SII value in distinguishing between the case and control groups. In the multivariate reduced model, significant independent ($p<0.05$) discriminatory efficacy of platelet count and SII value in differentiating the case and control groups was observed (Table 2 and Figs. 1-3).

A notable effectiveness of platelet count was observed in differentiating patients between the case and control groups, with a significant area under the curve of 0.693 (0.591–0.794). Moreover, a significant efficacy of platelet count with a cutoff value of 270 was observed in the differentiation of patients between the case and control groups, with an area under the curve of 0.648 (0.544–0.753) (Table 3 and Fig. 4).

Discussion

The pathogenesis of ANLDO is theorized to involve the gradual development of local inflammation within the nasolacrimal ducts, followed by its progression into chronic inflammation leading to fibrosis (4). Our study indicates that systemic inflammation may act as the catalyst for this localized inflammatory process. Acetand Sarikaya similarly concluded that inflammation might contribute to meibomian gland loss in individuals with Polycystic Ovary Syndrome (PCOS). Contrarily, they found no significant impact of inflammation on tear film instability parameters in the same study (21). Another recent Turkish study demonstrated that inflammatory parameters in acne patients did not significantly affect tear film stability and meibomian gland

Table 2. Logistic regression analysis in univariate model and multivariate model

	Univariate model			Multivariate model		
	OR	% 95 GA	p	OR	% 95 GA	p
Platelet (10^3/mL)	1.013	1.005-1.021	**0.001**	1.013	1.005-1.021	**0.001**
PLR	1.011	1.001-1.022	**0.039**			
SII	1.002	1.000-1.004	**0.025**			

Logistic regression (Forward LR); PLR: Platelet/lymphocyte ratio; SII: Systemic inflammatory index ((platelet x(neutrophil/lymphocyte)).

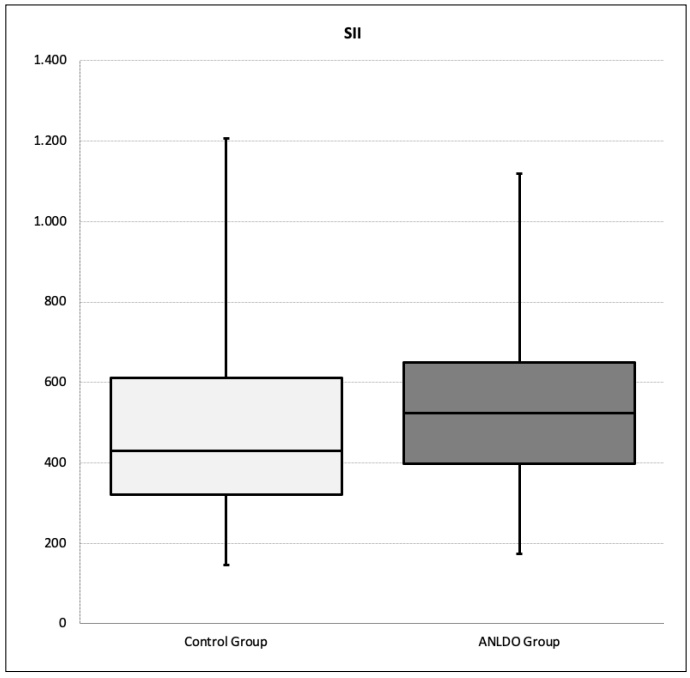

Figure 1. Systemic Inflammatory Index (SII) Ratio in Control and Acquired Nasolacrimal Duct Obstruction Group.

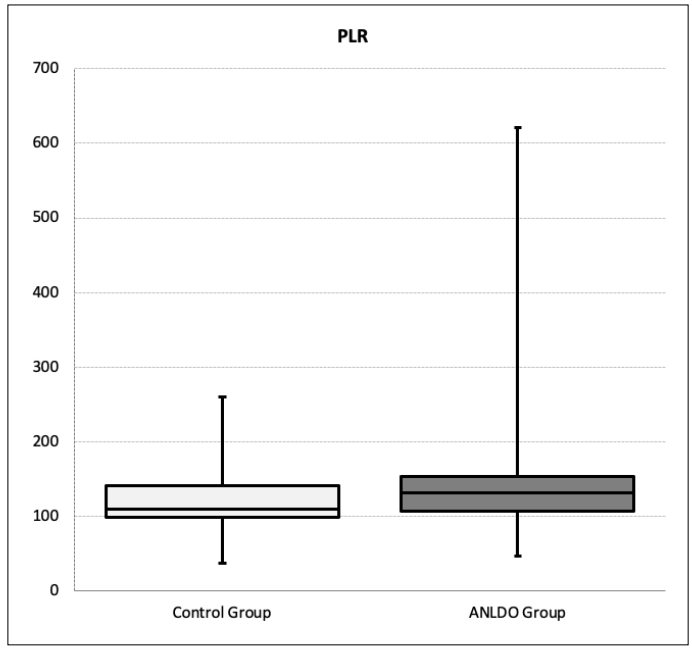

Figure 3. PLR (Platelet/Lymphocyte Ratio) in Control and Acquired Nasolacrimal Duct Obstruction Group.

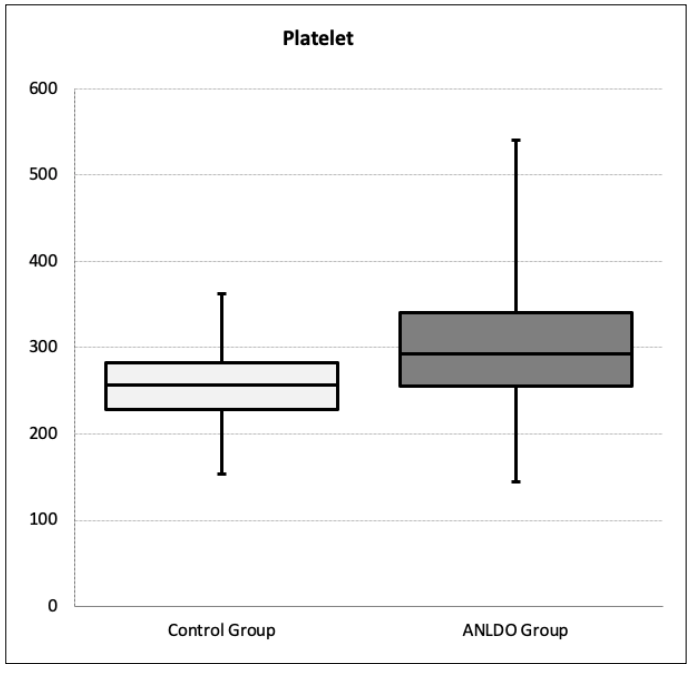

Figure 2. Platelet Count in Control and Acquired Nasolacrimal Duct Obstruction Group.

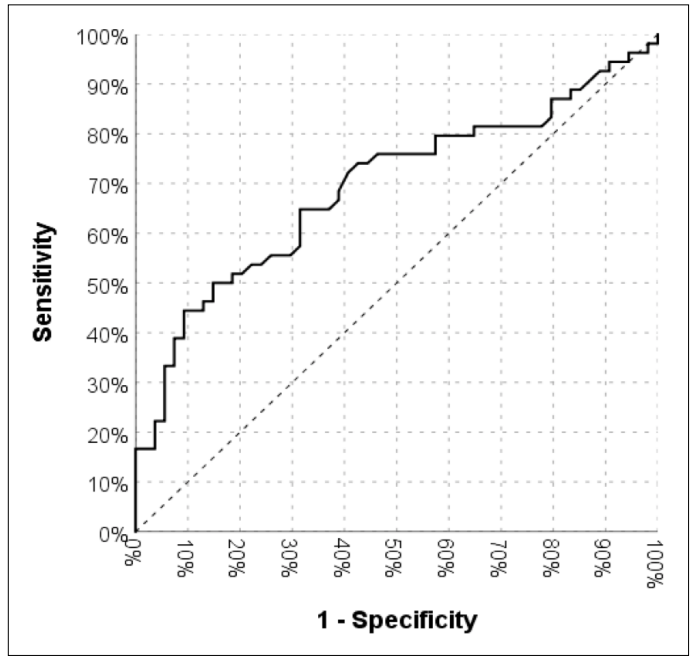

Figure 4. ROC Curve illustrating Sensitivity and Specificity in Acquired Nasolacrimal Duct Obstruction Group.

loss (22). The divergent results observed in PCOS and acne patients in these two studies, despite similar methodologies, underscore the noteworthy variations in the active roles of inflammation parameters across distinct diseases (21,22).

Our study identified significantly elevated platelet count, PLR, and SII values in ANLDO patients. Notably, the literature, particularly in diseases like coronary artery disease, has demonstrated elevated PLR values (23). Elevated platelet count and PLR have also been reported in retinal arterial and venous occlusions (24). In addition, PLR has been shown to be significantly elevated in diseases with implicated ischemia, such as glaucoma. In our study, we observed elevated platelet count and PLR values, consistent with these findings. Apart from their role in hemostasis, literature has indicated that

Table 3. Detailed analysis of platelet count

	Area Under the Curve		% 95 GA	p
Platelet (10^3/ml)	0.693		0.591-0.794	0.000
Platelet 270 cutoff	0.648		0.544-0.753	0.000
	Control	**ANLDO**		
Platelet				
≤270	37	21	Sensitivity	61.1%
>270	17	33	Positive Prediction	66.0%
			Specificity	68.5%
			Negative Prediction	63.8%

ANLDO: Acquired nasolacrimal duct obstruction.

platelets exert an indirect influence on inflammation (24-26).

In a study conducted, the emphasis was placed on the role of platelets in inflammatory processes, as follows;"*While endothelial cells and leucocytes are widely accepted as critical players in the microvascular alterations induced by inflammation, recent attention has focused on the modulatory role of platelets, which act both as effector and target cells in inflamed microvessels. Evidence is presented to demonstrate the capacity for "cross-talk" between platelets and other cells (endothelial cells, leucocytes) that contribute to an inflammatory response, and to illustrate the pathophysiological consequences of these interactions of platelets with other cells within the microvasculature.*" (27)

Our study did not reveal significant variations in the numbers of neutrophils, lymphocytes, and monocytes, as well as the corresponding ratios NLR and MLR. Lymphocytes play a role in inhibiting cell proliferation and migration and are pivotal in activating the immune response (28). Intriguingly, although neutrophil and WBC counts, which are integral to inflammation and the immune response, remained similar in both the ANLDO and control groups, SII exhibited a pronounced increase in the ANLDO group. This observation suggests that platelets might be the contributing factor. Recent studies have highlighted the active role of platelets in inflammation. Specifically, the interaction between platelets and leukocytes triggers the activation of chemokines and growth factors integral to the inflammatory cascade. The elevation of platelet levels in circulation may potentially underlie the progression of the chronic inflammatory process (29).

Our study was structured as a retrospective investigation, which inherently excluded the possibility of histological examinations. Consequently, we lack insights into the distribution of inflammatory processes within local tissues. We acknowledge these limitations as constraints in our study.

Conclusion

ANLDO is a condition characterized by uncertain etiology, involving systemic inflammatory mechanisms that evolve into chronic inflammation within the nasolacrimal duct, ultimately leading to ductal obstruction. Our study identified elevated platelet count, a constituent of systemic inflammation, as a potential contributor to ANLDO. Platelet count, when considered in tandem with PLR and SII, could serve as a systemic inflammatory biomarker for ANLDO. However, further investigations are warranted to establish a definitive link between elevated platelet count and the inflammatory process.

Disclosures

Ethics Committee Approval: This retrospective and case–control study was conducted in adherence to the principles set forth in the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee on January 25, 2023, under decision number 30. The study was carried out at BaşakşehirÇamve Sakura City Hospital (İstanbul, Türkiye).

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