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Correlation between High Myopia and Neutrophil to Lymphocyte Ratio and Platelet to Lymphocyte Ratio

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ABSTRACT

Background: Emerging evidence suggests inflammation plays a significant role in the pathogenesis of high myopia, a globally escalating ocular condition. Myopic eye elongation is hypothesized to trigger oxidative stress, activating various inflammatory pathways. **Aim:** This study investigates the clinical correlation between high myopia and systemic inflammation using neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), which are novel, accessible, and cost-effective inflammatory biomarkers. **Patients and Methods:** This prospective, non-randomized, case-control cross-sectional study enrolled 80 participants: 40 with high myopia (axial length >26 mm or refraction >-6.0 D) and 40 normal emmetropic controls. High myopes were rigorously screened to exclude other ocular or systemic diseases that might affect NLR or PLR. All participants underwent comprehensive ocular examinations and peripheral blood tests.

Results: Analysis revealed a significant positive correlation between high myopia and both NLR and PLR ($p<0.001$ for both markers). Axial length (AL) also correlated significantly with NLR ($r=0.40$, $P<0.001$) and PLR ($r=0.349$, $P=0.002$). The Receiver operating characteristic (ROC) curve analysis identified NLR's optimal cutoff at 1.775 (70% sensitivity, 65% specificity), and PLR's at 99.8 (80% sensitivity, 52.5% specificity).

Conclusion: Our findings strongly suggest that high myopia is associated with systemic inflammation, evidenced by elevated NLR and PLR. This supports the hypothesis of inflammatory processes contributing to myopia's pathophysiology.

Keywords: High myopia, Neutrophil to lymphocyte ratio, Platelet to lymphocyte ratio, Systemic inflammation.

INTRODUCTION

Refractive errors represent the most prevalent ocular disorders encountered across all age groups and continue to pose a substantial global public health challenge, profoundly impacting visual function and quality of life for millions worldwide. These conditions arise when the eye cannot properly focus light on the retina, leading to blurred vision[(1)]. The World Health Organization (WHO) has underscored the critical impact of uncorrected refractive errors, identifying them as the primary global cause of visual impairment and the second leading cause of irreversible vision loss [(2)]. Among these, myopia, or nearsightedness, has emerged as a particularly serious and rapidly escalating health concern worldwide. The global prevalence of myopia is experiencing an alarming increase, with projections indicating that nearly half of the world's population could be myopic by the year 2050. A significant subset of this population, approximately 10%, is anticipated to develop high myopia, carrying far greater risks for severe visual compromise [(3)].

High myopia is clinically defined by an excessive elongation of the eyeball's axial length, resulting in a refractive error that typically exceeds -6.00 diopters (D) or an axial length greater than 26 millimeters. This specific form of myopia is not merely a refractive anomaly but constitutes a critical public health challenge due to its strong association with sight-threatening complications [(4)]. The pronounced axial elongation characteristic of high myopia can precipitate a cascade of degenerative changes within the neuronal retina and choroid. These changes are collectively termed "myopic retinopathy" and encompass several severe conditions. These include peripheral retinal degeneration (PRD), an increased susceptibility to posterior staphyloma (PS) (an outward bulging of the posterior sclera), a heightened risk of rhegmatogenous retinal detachments (RRD) due to retinal breaks, various forms of maculopathy impacting central vision, and the development of choroidal neovascularization (CNV), an aberrant growth of new blood vessels that can lead to hemorrhage and severe vision loss [(5)].

Despite extensive research, the precise fundamental causes of myopia are still not entirely understood. However, its complex etiology is widely recognized to be associated with an intricate interplay of genetic predisposition and various environmental factors, as well as synergistic gene–environment interactions [(3)]. Furthermore, a growing body of evidence implicates inflammation in the pathogenesis and progression of myopia. Patients suffering from autoimmune and inflammatory diseases, such as juvenile chronic arthritis, uveitis, type 1 diabetes mellitus, or systemic lupus erythematosus, consistently demonstrate a higher incidence of myopia compared to the general population. In addition, elevated intraocular levels of specific inflammatory mediators, including interleukin-6 (IL-6), vascular endothelial growth factor (VEGF), and complement proteins, have been detected in eyes diagnosed with myopic retinopathy. This compelling evidence suggests that chronic or acute inflammatory processes may also contribute

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significantly to the complex mechanisms underlying myopia-mediated retinal degeneration [6] .

Much of the contemporary research exploring the role of inflammation in ocular diseases has increasingly focused on readily accessible and cost-effective systemic hematological biomarkers. Among these, the neutrophil to lymphocyte ratio (NLR) and the platelet to lymphocyte ratio (PLR) have gained prominence due to their low cost and broad accessibility in routine clinical laboratories. NLR, in particular, serves as a dynamic indicator reflecting the intricate balance between the innate immune response (primarily mediated by neutrophils) and the adaptive cellular immune response (governed by lymphocytes). This ratio provides a simple, yet powerful, insight into systemic inflammatory status[7].

The diagnostic and prognostic utility of NLR, as an affordable, novel, and increasingly accepted systemic inflammatory marker, has been extensively explored across a diverse range of ocular diseases. Its value has been discussed in conditions such as glaucoma, dry eye disease (DED), idiopathic epiretinal membrane (iERM), retinal vein occlusion, keratoconus (KC), pterygium, and diabetic retinopathy. The significance of this ratio is particularly critical for early detection, especially given that many patients presenting with various eye diseases may have been previously healthy and asymptomatic, making accessible biomarkers like NLR crucial for timely intervention and improved patient outcomes [8].

AIM OF THE WORK

The primary objective of this investigation is to rigorously evaluate the potential relationship between high myopia and systemic inflammatory status, as indicated by the neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR), serving as circulating inflammatory biomarkers. The comprehensive evaluation of high myopia within this study will specifically include quantitative assessment of choroidal thickness and precise measurement of the axial length of the eye, both critical parameters in characterizing myopic ocular morphology.

PATIENTS AND METHODS

This study was a non-randomized cross sectional study case control study. It was carried out from January 2024 until November 2024. It was held at both the Ophthalmology and Clinical Pathology Departments of Al-Zahraa University Hospital of Al-Azhar University.

The study included 80 eyes divided into two groups: group (A): (myopic patients): 40 eyes of patients aged between 20 and 50 years diagnosed as high myopes (according to Ref > -6.00 D and AL > 26.00 mm) and attended ophthalmology clinic for regular follow up of vision and asking for glasses, group (B): Healthy (control group): 40 eyes of healthy persons of the same age group without myopia or any other systemic or ocular diseases.

Inclusion Criteria:

- Patients aging from 20 to 50 years with high myopia determined according to refraction more than -6.00 diopter and AL higher than 26.00 mm with or without myopic degenerations and with no medication or systemic diseases.
- Good candidates for OCT, optical biometry and colored fundus photo, with no media opacity (in cornea, lens and vitreous).

Exclusion Criteria:

- Any systemic diseases affecting blood NLR or PLR such as DM, malignancy, rheumatologic diseases, inflammations, liver diseases, kidney failure, respiratory diseases and coronary artery disease.
- Other ocular diseases like glaucoma and cataract.
- Intraocular inflammations.
- Ocular traumas or history of ocular surgery.
- Other anomalies of ocular surface.

All study participants underwent a comprehensive assessment protocol, commencing with a thorough elicitation of their full medical history. This initial step was critical for gathering pertinent background information that may influence ocular health and disease progression.

Subsequently, each participant underwent a complete ophthalmological examination. This detailed assessment encompassed several key components:

a) Uncorrected and best-corrected visual acuity (BCVA) was meticulously quantified utilizing a Landolt's C chart positioned at a distance of 6 meters. For subsequent rigorous statistical analysis, these raw visual acuity measurements were precisely converted into LogMAR units. This conversion ensured a standardized and linear scale for acuity, facilitating robust comparative studies.

b) Anterior segment evaluation was performed using a TOPCON Slit lamp (Japan). This examination allowed for a detailed stereoscopic view of the conjunctiva, cornea, iris, lens, and anterior chamber, enabling the detection of any anatomical abnormalities or pathological signs.

c) Intraocular pressure (IOP) was precisely measured using Goldmann's applanation Tonometry (KEELER UK). This method is considered the gold standard for IOP measurement, providing a crucial indicator for conditions such as glaucoma.

d) Fundus examination was conducted after achieving full pupillary dilation through the instillation of 1.0% tropicamide. This critical step enables an expansive view of the posterior segment of the eye. The examination was performed using two complementary techniques: slit-lamp biomicroscopy in conjunction with a +90 D aspheric lens, providing high-magnification stereoscopic views of the optic nerve, macula, and retinal vasculature, and indirect ophthalmoscopy, offering a wider field of view for assessing the peripheral retina and detecting any signs of peripheral retinal degeneration or detachment.

e) Refraction: using Shin-Nippon Accuref R-800. Japan autorefractometer.
f) Axial length: using AL-Scan optical biometry (NIDEK CO.1 TO, TOKYO Japan)
g) OCT: OCT of macula, to assess choroidal thickness using (RTVue X RAvent Optovue- Angiovue, Inc, Fremont, USA) software version (2016-2)
h) Colored fundus photo using Topcon TRC-50 EX fundus camera.
i) Complete blood count (CBC): to calculate neutrophil to lymphocyte ratio and platelet to lymphocyte ratio.

Ethical approval:

All procedures in this study adhered strictly to the ethical regulations set forth by Al-Azhar University's Ethical Committee. We obtained informed consent from every participant after thoroughly explaining the potential benefits and risks of their involvement. Any unforeseen risks that emerged during the research were promptly communicated to both the participants and the Ethical Committee.

To ensure patient privacy and confidentiality, each participant was assigned a unique code number, and all results were used solely for research purposes, not for media dissemination. The study protocol was in full accordance with the tenets of the Declaration of Helsinki.

Statistical analysis

Data were analyzed using SPSS version 25. Qualitative variables were expressed as frequencies and percentages, while continuous quantitative data were presented as means ± standard deviations, median, and range and were compared using independent sample *t*-test or Mann-Whitney Z-test. Pearson's correlation coefficient (*r*) was used to assess relationships between continuous variables. Diagnostic performance was evaluated using receiver operating characteristic (ROC) curve analysis, which provided cutoff values, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area under the curve (AUC). A *p*-value < 0.05 was considered statistically significant, and < 0.001 highly significant. This statistical framework enabled the identification of significant group differences and diagnostic accuracy across variables studied. We used Spearman's correlation test.

RESULTS

This table (1) shows that, there was no statistically significant difference between studied groups regarding age.

Table (1): Comparison between studied groups regarding age.

	Group A (High myopia group) N=40 eyes	**Group B (Normal group) N =40 eyes**	**U test**	**P value**
Age (Year) Mean± SD	31.15± 9.3	33.85± 8.2	641	0.12

SD: standard deviation.

This table (2) shows that, there was highly statistically significant difference between the studied groups regarding VA, BCVA, Refraction, AL while, there was no statistically significant difference between the studied groups regarding CMT.

Table (2): Comparison between studied groups regarding ophthalmological data.

	Group A (High myopia group) N=40 eyes	**Group B (Normal group) N =40 eyes**	**Z-test**	**P value**
VA				
Mean± SD	1.3±0.29	0.03±0.07	7.693	**<0.001**
Median (range)	1.3 (1: 1.78)	0 (0:0.18)		
BCVA				
Mean± SD	0.34±0.23	0.0± 0.0	6.346	**<0.001**
Median (range)	0.3 (0: 0.78)	0 (0:0)		
Refraction				
Mean± SD	-10.2±3.6	-0.1±0.21	-7.693	**<0.001**
Median (range)	-8.75 (-18.50: -6.25)	0 (-0.50: 0.50)		
AL (mm)			**T-test**	
Mean± SD	27.79±1.5	23.2±0.74	17.356	**<0.001**
Median (range)	27.44 (26.04: 30.99)	23.18 (21.02: 24.32)		
CMT (µm)				
Mean± SD	230.27± 18.5	232.2± 16.3	0.495	0.62
Median (range)	230.5 (189:261)	234 (197:261)		

SD: standard deviation, AL: axial length, Z: Mann-Whitney test, VA: visual acuity, BCVA: Best corrected visual acuity

This table (3) shows that, there was statistically significant difference between studied groups regarding choroidal thickness with high myopia group having thinner choroid than normal population.

Table (3): Comparison between studied groups regarding choroidal thickness.

	Group A (High myopia group) N=40 eyes	**Group B (Normal group) N =40 eyes**	**U-test**	**P value**
Choroidal Thickness (µm)				
Mean± SD	177.13±69.71	222.25±47.02	491.5	**0.003**
Median (range)	188.5 (76: 307)	221 (120: 302)		

This table (4) shows that, there was statistically significant difference between studied groups regarding neutrophil, lymphocyte, platelet, NLR, and PLR. high myopia group had higher values of neutrophils, platelets, NLR, and PLR and lower value of lymphocytes which is consistent with inflammatory conditions.

Table (4): Comparison between studied groups regarding laboratory data.

	Group A (High myopia group) N=40 eyes	**Group B (Normal group) N =40 eyes**	**T-Test**	**P value**
Neutrophil (×10³/µL)				
Mean± SD	4.01±0.86	3.61± 0.79	2.166	**0.03**
Lymphocyte (×10³/µL)				
Mean± SD	2.02±0.3	2.16±0.3	2.087	**0.04**
Platelet (×10³/µL)				
Mean± SD	234.6±55.72	208.4±50.86	2.196	**0.03**
NLR				
Mean± SD	1.99±0.31	1.69±0.39	3.808	**<0.001**
PLR				
Mean± SD	116.41±22.2	96.4±18.1	4.418	**<0.001**

SD: standard deviation. NLR: neutrophil-to-lymphocyte ratio, PLR platelet-to-lymphocyte ratio.

This table (5) shows that, logMAR VA had significant positive correlation with PLR, NUT, PLT and NLR. LogMAR BCVA had significant positive correlation with PLR, NUT and NLR. Refraction had significant negative correlation with PLR, NUT and NLR. Meaning when refraction value decreases (higher myopia) the NUT, NLR and PLR increase. AL had significant positive correlation with PLR, NUT and NLR. With increasing value of AL (higher myopia) the value of NUT, NLR and PLR increase.

Table (5): Correlation between various clinical parameters and ophthalmic measurements.

		LogMAR VA	**LogMAR BCVA**	**Refraction**	**AL (mm)**	**Choroidal Thickness (µm)**	**CMT (µm)**
PLR	r	0.398**	0.258*	-0.336**	0.349**	-0.115	-0.091
	p-value	**0.000**	**0.021**	**0.002**	**0.002**	0.311	0.420
NUT	r	0.292**	0.263*	-0.289**	0.260*	-0.082	0.108
	p-value	**0.009**	**0.018**	**0.009**	**0.02**	0.472	0.339
LYM	r	-0.176	-0.066	0.160	-0.203	0.133	0.072
	p-value	0.119	0.560	0.155	0.072	0.238	0.524
PLT	r	0.239*	0.199	-0.201	0.189	-0.040	-0.026
	p-value	**0.033**	0.077	0.074	0.094	0.726	0.817
NLR	r	0.417**	0.301**	-0.403**	0.400**	-0.197	0.030
	p-value	**0.000**	**0.007**	**0.000**	**0.000**	0.079	0.793

r: Spearman correlation coefficient, AL: axial length.

NLR had sensitivity of 70% and specificity of 65% with highly significance for the detection of high myopia. PLR had sensitivity of 80% and specificity of 52.5% with highly significance for the detection of high myopia (Table 6).

Table (6): ROC analysis for NLR and PLR for the detection of high myopia.

	Area under the curve (AUC)	Cutoff value	Sensitivity	Specificity	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
							Lower Bound	Upper Bound
NLR	0.732	1.775	70%	65%	0.058	**0.000**	0.618	0.847
PLR	0.776	99.8	80%	52.5%	0.054	**0.000**	0.671	0.882

Case 1

Case NO.1 group (2): 27-year-old male, his Ref.= -0.25 and 0.00 (emmetrope) AL=24.05 and 24.01 mm, CMT=228 and 234µm, choroidal thickness=243 and 212 µm, OD and OS respectively. From CBC result NLR=1.54 and PLR= 86.8 (lower than our cutoff value for high myopia NLR1.775 and PLR 99.8) (Figures 1 and 2).

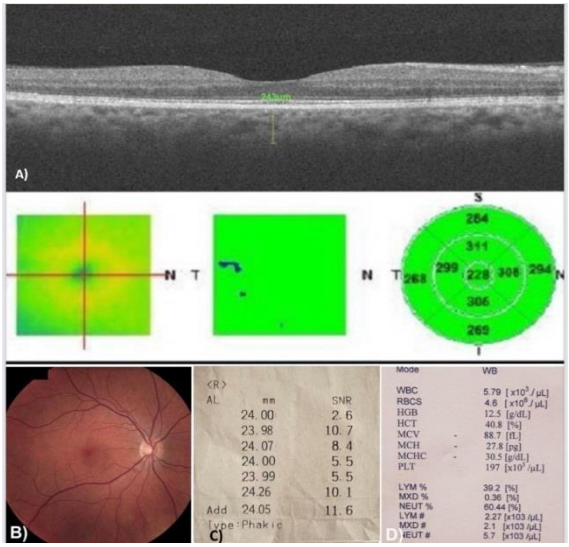

Fig. (1): Composite image of OD investigations of a normal case A) OCT macula showing normal macula with preserved foveal contour and pit. Choroidal thickness=243µm CMT=228 µm. B) Colored photo for the case shows normal fundus. C) AL of this eye = 24.05mm D) CBC results to calculate NLR=1.54 and PLR=86.8.

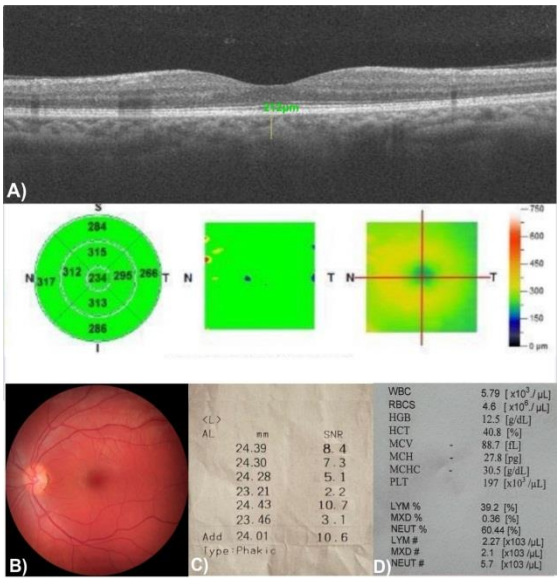

Fig. (2): Composite image of OS investigations of case No. (1). A) OCT image shows normal dry macula with preserved foveal contour and pit. Choroidal thickness=212 µm. CMT= 234µm. B) colored fundus photo normal. C) AL= 24.01 mm. D) CBC results of WBCs to calculate NLR= 1.54 and PLR= 86.8

CASE 2

Case NO.2 group (1): 26-year-old male patient with high myopia his Ref= -15.50, -12.50 D, AL=30.99, 29.42 mm, CMT = 251, 241 µm and choroidal thickness = 190, 203 µm OD and OS respectively. Using his CBC results the NLR= 2.29 and PLR= 142.32. These values of both ratios of a high myope patient are higher than that of normal case 1 and our cutoff values. The result supports our assumption of inflammation being a constitute of the pathogenesis of high myopia (Figures 3 and 4).

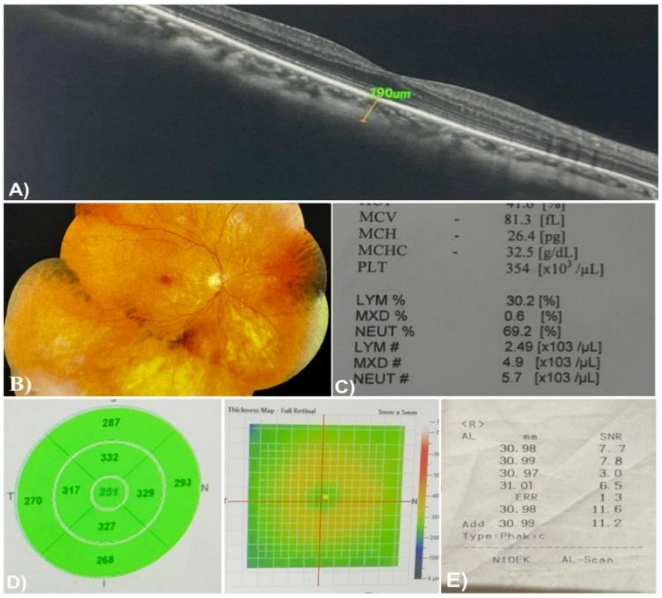

Fig. (3): Composite image of OD investigations of a high myopia patient. A) OCT within normal dry macula with preserved foveal pit. Choroidal thickness= 190 µm. B) colored fundus photo shows tessellated fundus with peripapillary atrophy. C) CBC result to calculate NLR=2.29 PLR=142.32. D) CMT= 251µm. E) AL for this patient's OD = 30.99 mm.

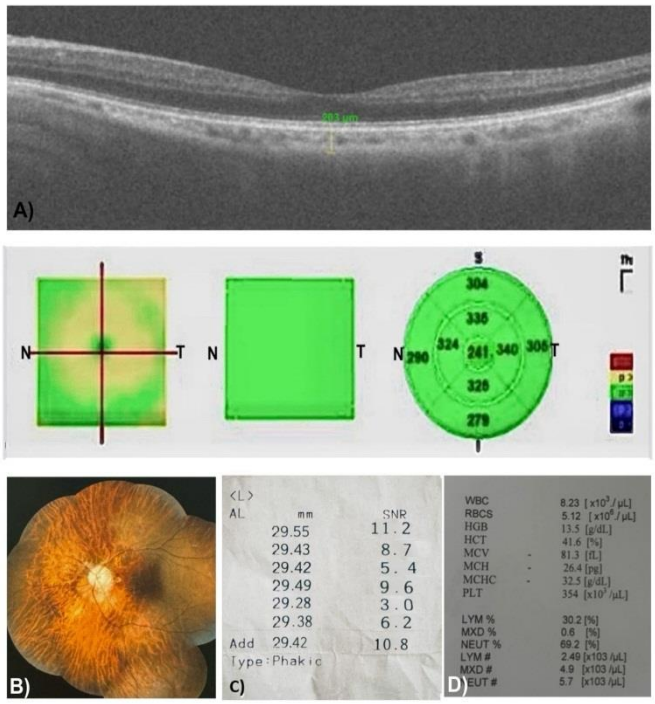

Fig. (4): Composite image of OS investigations of case No. (2). A) OCT image shows normal dry macula with preserved foveal contour and pit. Choroidal thickness=203 µm. CMT= 241 µm. B) colored fundus photo shows tessellated fundus and peripapillary atrophy. C) AL= 29.42 mm. D) CBC results of WBCs for calculation of NLR= 2.29 and PLR= 142.32.

DISCUSSION

The escalating global prevalence of myopia necessitates an intensified focus on elucidating the diverse factors contributing to its development and progression. While a consensus among researchers posits that a complex interplay between genetic predispositions and various environmental influences serves as the primary etiological basis for this condition, the precise molecular and cellular mechanisms underpinning myopia progression remain largely undefined [8]. This gap in understanding highlights the ongoing need for comprehensive research.

In recent years, the potential impact of inflammation on myopia progression has garnered increasing scientific attention. Elevated levels of ocular or systemic inflammation may contribute to the advancement of myopia through various pathways, potentially either directly or indirectly inducing adverse scleral remodeling, which is a critical process in axial elongation. Conversely, the very development of myopia itself might conversely exacerbate ocular inflammation, suggesting a complex bidirectional relationship [9].

As regard age there was no statistically significant difference between studied groups. Mean age of 31.1± 9.3 and 33.8± 8.2 years for group I and group II respectively (P value 0.17).

Our study's demographic characteristics, specifically patient age, align with findings from **Wang *et al.* [10]**, who similarly observed no significant age difference between high myopia and control groups, with mean ages around 63 years in a cohort of 50 patients per group. Regarding visual function, our results demonstrate a highly significant difference in best-corrected visual acuity (BCVA) between high myopia and control groups ($p < 0.001$), with the high myopia group showing poorer visual acuity (mean ± SD: 0.34 ± 0.23 LogMAR) compared to controls (0.0 ± 0.0 LogMAR). This finding is consistent with **Abdellah *et al.* [12]**, who also reported significantly worse BCVA in high myopia (0.63 ± 0.15) versus normal groups (0.95 ± 0.07, $p < 0.001$), and **Wang *et al.* [11]**, noting worse BCVA in pathological myopia (0.18 ± 0.17) than emmetropes (-0.10 ± 0.07, $p < 0.001$).

Refraction measurements also showed a highly significant difference ($p < 0.001$) between our study groups, with the high myopia group averaging -10.2 ± 3.6 D compared to -0.1 ± 0.21 D in controls. This aligns with **Burgoyne *et al.* [13]**, who reported comparable significant differences in refraction between high myopia (-7.61 ± 2.27 D) and normal (-0.14 ± 1.82 D) groups ($p < 0.001$).

Consistently, axial length (AL) was significantly higher in our high myopia group (27.79 ± 1.5 mm) than in controls (23.2 ± 0.74 mm, $p < 0.001$). This result is supported by multiple studies: **Wang *et al.* [14]** documented significantly larger AL in high myopes (27.21 ± 1.07 and 29.57 ± 1.59 mm) versus normal individuals (23.97 ± 1.23 mm, $p < 0.001$); **Lin *et al.* [15]** found higher average AL in high myopia (27.1 ± 1.12 mm) compared to normal eyes (24.0 ± 1.02 mm, $p < 0.001$); and **Ang *et al.* [16]** also reported highly significant AL differences across myopia severity subgroups ($p < 0.001$).

Regarding central macular thickness (CMT), our study found no significant difference between the high myopia group (230.27 ± 18.5 μm) and the control group (232.2 ± 16.3 μm, $p = 0.04$). This is consistent with **Kim *et al.* [17]** and **Abdellah *et al.* [11]**, who also reported no significant CMT differences between high myopia and control groups. However, **Choudhary *et al.* [18]** observed a statistically significant higher central foveal thickness in high myopes (298.93 ± 38.813 μm) compared to emmetropes (224.63 ± 16.439 μm, $p < 0.001$), potentially due to differences in age range and refractive error severity in their cohort.

Concerning systemic inflammatory markers, our study revealed a significant difference in neutrophil count (high myopia: 4.01 ± 0.86; control: 3.61 ± 0.79; $p = 0.03$), while **Wang *et al.* [11]** reported an insignificant difference ($p = 0.059$). Lymphocyte count showed a significant difference in our study (high myopia: 2.02 ± 0.3; control: 2.16 ± 0.3; $p < 0.04$), consistent with **Wang *et al.* [11]** ($p = 0.015$). Platelet count was significantly different in our groups (high myopia: 234.6 ± 55.7; control: 208.4 ± 50.86; $p = 0.03$), but contrary to **Qi *et al.* [20]** who found lower values in high myopia.

Crucially, neutrophil to lymphocyte ratio (NLR) demonstrated a highly significant difference ($p < 0.001$) between our groups (high myopia: 1.99 ± 0.31; control: 1.69 ± 0.39), consistent with **Qi *et al.* [20]** ($p = 0.02$) and **Wang *et al.* [11]** ($p < 0.001$), all reporting higher NLR in myopia. Similarly, platelet to lymphocyte ratio (PLR) was significantly higher in our high myopia group (116.41 ± 22.2) than controls (96.4 ± 18.1, $p = 0.00$), aligning with **Icel *et al.* [21]** ($p = 0.010$).

Correlation analysis revealed significant negative relationships between refraction and both NLR ($r = -0.289$, $p = 0.009$) and PLR ($r = -0.336$, $p = 0.002$), corroborated by **Icel *et al.* [21].** Furthermore, we found a significant positive correlation between AL and NLR ($r = 0.260$, $p = 0.02$) and PLR ($r = 0.349$, $p = 0.002$), which is consistent with **Wang *et al.* [14]** and **Icel *et al.* [21]**.

Finally, Receiver Operating Characteristic (ROC) analysis was employed to distinguish between the groups. The area under the curve (AUC) for NLR was 0.732 (sensitivity 70%, specificity 65% at cutoff 1.775), and for PLR was 0.776 (sensitivity 80%, specificity 52.5% at cutoff 99.8). These outcomes are reinforced by **Wang *et al.* [11]**, who reported comparable AUC values for NLR (0.728) and PLR (0.650).

CONCLUSION

This study's findings indicate that inflammation constitutes a pivotal pathogenic mechanism in the etiology and progression of high myopia (HM). This observation necessitates a substantive reorientation of future investigative endeavors, specifically advocating

for the focused exploration of anti-inflammatory therapeutic strategies. Such a paradigm shift holds significant promise for the development of innovative and efficacious approaches aimed at both the prophylactic mitigation and therapeutic management of the complex complications intrinsically associated with this debilitating ocular condition. The integration of anti-inflammatory modalities into clinical practice could thus represent a transformative advancement in the overall management of high myopia.

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