



## RESEARCH ARTICLE – MEDICINE (MISCELLANEOUS)

## Visual and Structural Differences Between Amblyopic and Non-Amblyopic Eyes in Patients with Unilateral Amblyopia

Alaa Khammas Hussein<sup>1</sup>, Masoud Khorrami-Nejad<sup>1\*</sup><sup>1</sup>Optometry Department, School of Rehabilitation, Tehran University of Medical Sciences, Tehran, Iran\* Corresponding Author: [Mkhorraminejad@sina.tums.ac.ir](mailto:Mkhorraminejad@sina.tums.ac.ir)

Article Info.	Abstract
<p><i>Article history:</i></p> <p>Received 13 Dec. 2024</p> <p>Revised 13 Jan. 2025</p> <p>Accepted 20 Jan. 2025</p> <p>Publishing 10 May 2025</p>	<p><b>Background:</b> Amblyopia, define as "lazy eye, a neurodevelopmental disorder, manifests as reduced visual acuity not attributable to structural eye abnormalities.</p> <p><b>Objective of study:</b> This study investigated visual and structural differences between amblyopic and non-amblyopic eyes in children with unilateral amblyopia, focusing on visual acuity, axial length, and lens thickness.</p> <p><b>Materials and Methods:</b> Twenty-six pediatric patients (5–10 years old) with untreated unilateral functional amblyopia were recruited. Amblyopia was classified as anisometric, strabismic, or combined. Corrected distance visual acuity (CDVA) was measured in logMAR units. Axial length, anterior chamber depth, and lens thickness were assessed using non-contact optical biometry. Spherical equivalent refractive error was determined via cycloplegic autorefraction. Paired t-tests were used to compare interocular differences.</p> <p><b>Results:</b> Amblyopic eyes exhibited significantly reduced CDVA. However, no statistically significant interocular differences were found for spherical equivalent, axial length, anterior chamber depth, or lens thickness (all <math>p &gt; 0.05</math>). Amblyopic eyes showed a trend towards shorter axial lengths (mean difference: -0.27 mm, SD: 0.72), particularly in anisometric amblyopia (-0.21 mm, SD: 0.85). Anterior chamber depth and lens thickness showed minimal interocular variations across amblyopia types.</p> <p><b>Conclusion:</b> While amblyopic eyes demonstrated reduced visual acuity, interocular differences in biometric parameters were not statistically significant in this small sample. Trends suggest a potential association between amblyopia and shorter axial length, warranting further investigation with larger, longitudinal studies. This research contributes to understanding the ocular and cortical changes in amblyopia, aiming to refine treatment strategies and improve visual outcomes.</p>

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### 1. Introduction

Amblyopia, commonly known as lazy eye, is a neurodevelopmental disorder characterized by reduced visual acuity in one or both eyes, not attributable to any structural abnormality of the eye itself. This visual impairment arises from abnormal visual experience during early childhood, disrupting the normal development of the visual cortex. The condition affects approximately 1-5% of the population globally, making it the most prevalent cause of monocular vision loss in children [1, 2]. Early detection and intervention are crucial for successful treatment, as the visual system exhibits plasticity primarily during a critical period, typically extending up to 7 years of age [3]. Beyond this period, treatment becomes less effective, and the visual deficit may persist into adulthood, impacting quality of life and potentially limiting career options [4].

Several factors can contribute to the development of amblyopia, broadly categorized as strabismus, anisometropia, and form deprivation [5,6]. Strabismic amblyopia occurs when the eyes are misaligned, leading to double vision. To avoid this, the brain suppresses the image from the deviated eye, hindering its development. Anisometric amblyopia results from a significant difference in refractive error between the two eyes. The eye with the greater refractive error produces a blurred image, which the brain subsequently suppresses. Form deprivation amblyopia arises from any condition that obstructs light from entering the eye, such as congenital cataracts or ptosis, preventing the formation of a clear retinal image and thus impeding normal visual development. In some cases, a combination of these factors may contribute to the condition [7].

While the primary manifestation of amblyopia is reduced visual acuity, the condition also affects other visual functions, including contrast sensitivity, spatial localization, and binocular vision [8,9,10]. These deficits can impact a child's ability to perform everyday tasks, participate in sports, and excel academically. Furthermore, untreated amblyopia can lead to permanent visual impairment and increase the risk of developing visual problems in the fellow eye later in life [11].

Numerous studies have investigated the structural and functional changes in the visual system associated with amblyopia. Neuroimaging studies have revealed alterations in the visual cortex, including reduced gray matter volume and altered cortical thickness in the region corresponding to the amblyopic eye. These structural changes correlate with the severity of the visual impairment. Functional magnetic resonance imaging (fMRI) studies have demonstrated abnormal activity patterns in the visual cortex of amblyopic individuals, reflecting the disrupted neural processing of visual information [12, 13].

In addition to cortical changes, studies have also explored potential differences in ocular biometry between amblyopic and non-amblyopic eyes. Axial length, the distance between the anterior and posterior poles of the eye, is a key biometric parameter that influences refractive error [14,15]. Some studies have reported shorter axial lengths in amblyopic eyes, particularly in cases of anisometropic amblyopia [16,17]. However, other studies have found no significant difference in axial length between amblyopic and non-amblyopic eyes [18,19]. These inconsistencies may be attributed to variations in study design, sample size, and the specific types of amblyopia included.

Previous findings regarding lens thickness in amblyopic eyes have indicated that there may be structural differences compared to non-amblyopic eyes, although specific studies focusing solely on crystalline lens thickness are limited. Research has shown that amblyopic eyes often exhibit variations in macular thickness and other retinal parameters, which may indirectly suggest alterations in the overall ocular structure, including the lens. For instance, increased macular thickness has been reported in amblyopic patients, potentially linked to developmental abnormalities in the retina and surrounding structures [20, 21]. However, direct measurements of lens thickness in amblyopic eyes have not been extensively documented in the literature, indicating a need for further investigation to clarify the relationship between amblyopia and lens morphology.

This study aims to investigate the visual and structural differences between amblyopic and non-amblyopic eyes in patients with unilateral amblyopia. Specifically, we will compare visual acuity, axial length, and lens thickness between the affected and unaffected eyes. By examining these parameters, we hope to gain a better understanding of the ocular and cortical changes associated with amblyopia. This knowledge can inform the development of more effective treatment strategies and improve visual outcomes for individuals with this condition. The present study focuses on patients with untreated functional amblyopia, categorized based on severity and underlying cause (anisometropic, strabismic, or combined). This approach allows for a more nuanced analysis of the relationship between amblyopia and ocular biometry.

## 2. Materials and method

### 2.1. Study design

This study was designed as a cross-sectional analysis to assess the visual and structural differences between amblyopic and non-amblyopic eyes in patients diagnosed with unilateral amblyopia. The ethical committee of Tehran University of Medical Sciences granted approval for this study, ensuring that all procedures complied with the principles outlined in the Declaration of Helsinki. These principles were upheld throughout all stages of the examination process. After providing a verbal overview of the study's objectives and the methodologies to be employed to the potential participants and their guardians, written informed consent was acquired from all patients involved in the study, along with consent from their parents if they were minors.

### 2.2. Participants

A total of 26 pediatric patients, aged between 5 to 10 years, were recruited for the study. The mean age of participants was 6.42 years (standard deviation: 1.36). The study was performed on patients with functional amblyopia at Farabi Eye Hospital, affiliated with the Tehran University of Medical Sciences, Tehran, Iran. Diagnoses of unilateral amblyopia were confirmed based on comprehensive ophthalmological assessments. Participants were selected from a clinical setting and were required to have untreated functional amblyopia, thereby ensuring a consistent baseline for comparison. Informed consent was obtained from the guardians of all participants, and the ethical considerations were adhered to in accordance with the guidelines of the institutional review board.

### 2.3. Visual acuity assessment

Visual acuity was evaluated using the corrected distance visual acuity (CDVA) chart, measured in logarithm of the minimum angle of resolution (logMAR) units. The CDVA was assessed for both the amblyopic and non-amblyopic eyes of each participant. The ability of the patients to cooperate during the assessment was a criterion for inclusion; therefore, only those who could follow the directions effectively were included in the analysis.

### 2.4. Ocular biometric measurements

To investigate the structural aspects of the eyes, several ocular biometric parameters were measured. Axial length, anterior chamber depth, and lens thickness were determined using non-contact optical biometry (IOLMaster700; Carl Zeiss Meditec AG, Jena, Germany) which is a high-precision optical device, ensuring minimal variability and maximum accuracy [22]:

- *Axial Length:* This parameter was measured as the distance from the anterior surface of the cornea to the retina. Shorter axial lengths were expected in amblyopic eyes, particularly in cases of anisometropic amblyopia.
- *Anterior Chamber Depth:* This was measured from the corneal endothelium to the anterior surface of the lens. This measurement is crucial as it may reveal differences in ocular development between amblyopic and non-amblyopic eyes.
- *Lens Thickness:* The thickness of the crystalline lens was also measured, as variations in lens morphology may contribute to refractive discrepancies between the two eyes.

### 2.5. Refractive error assessment

Refractive error was quantified using spherical equivalent (SE) calculations derived from standard cycloplegic autorefraction. The spherical and cylindrical components were measured to provide a comprehensive understanding of the refractive state of both amblyopic and non-amblyopic eyes.

## 2.6. Statistical analysis

Data analysis was conducted using appropriate statistical software. Descriptive statistics were computed for all measured parameters, including means and standard deviations. To assess differences between amblyopic and non-amblyopic eyes, paired t-tests were performed, and p-values were calculated to determine statistical significance. A p-value of less than 0.05 was considered significant. The data were also segmented based on the type of amblyopia to identify potential variations in results across the different categories.

## 3. Result

In this study, 26 amblyopic eyes were analyzed, with 53.8% in the right eye (OD) and 46.2% in the left eye (OS). The types of amblyopia included 61.5% anisometropic, 23.1% strabismic, and 15.4% combined. The mean age of the patients was 6.42 years, with a standard deviation of 1.36, ranging from 5 to 10 years. CDVA differences in logMAR units were measured among cooperative patients. Anisometropic cases had a mean difference of -0.40 (SD = 0.27), strabismic cases had a mean of -0.35 (SD = 0.29), and combined cases had a mean of 0.00. The overall mean CDVA difference was -0.35 (SD = 0.27). For spherical refractive error differences, anisometropic cases showed a mean of 1.47 (SD = 2.38), strabismic cases had a mean of 1.29 (SD = 1.84), and combined cases had a mean of 2.25 (SD = 1.85). The overall mean was 1.55 (SD = 2.14). The spherical equivalent differences were as follows: anisometropic cases had a mean of 1.85 (SD = 2.29), strabismic cases had a mean of 1.48 (SD = 1.78), and combined cases had a mean of 2.41 (SD = 1.96).

Overall, the mean difference was 1.85 (SD = 2.08). The mean axial length difference for anisometropic cases was -0.21 (SD = 0.85), while strabismic cases had a mean of -0.11 (SD = 0.36), and combined cases had a mean of -0.72 (SD = 0.30). The overall mean was -0.27 (SD = 0.72). In terms of anterior chamber depth differences, anisometropic cases had a mean of 0.03 (SD = 0.14), strabismic cases had a mean of 0.03 (SD = 0.04), and combined cases had a mean of -0.05 (SD = 0.04). The overall mean was 0.02 (SD = 0.11). The mean lens thickness difference was 0.02 (SD = 0.12) for anisometropic cases, -0.03 (SD = 0.09) for strabismic cases, and 0.09 (SD = 0.10) for combined cases. The overall mean was 0.02 (SD = 0.11). Clinical measurements of CDVA difference, spherical re difference, se difference, axial length difference, anterior chamber depth difference, and lens thickness difference between amblyopic and non-amblyopic eyes in unilateral amblyopia shown in Table 1. No statistically significant differences were found across the three types of amblyopia for spherical refractive error, spherical equivalent, axial length, anterior chamber depth, and lens thickness differences, with all p-values exceeding 0.05. Statistical comparisons of CDVA difference, spherical re difference, se difference, axial length difference, anterior chamber depth difference, and lens thickness difference between amblyopic and non-amblyopic eyes among different types of amblyopia in unilateral amblyopia as shown in Table 2.

Table 1. Clinical measurements of CDVA difference, anterior and posterior eye parameters

		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
CDVA difference (logMAR)*	Anisometropic	6	-0.40	0.27	0.11	-0.68	-0.12	-0.78	-0.07
	Strabismic	4	-0.35	0.29	0.14	-0.81	0.11	-0.70	0.00
	Combined	1	0.00					0.00	0.00
	Total	11	-0.35	0.27	0.08	-0.53	-0.16	-0.78	0.00
Spherical RE difference (diopter)	Anisometropic	16	1.47	2.38	0.59	0.20	2.74	-3.00	6.00
	Strabismic	6	1.29	1.84	0.75	-0.64	3.22	0.00	4.75
	Combined	4	2.25	1.85	0.92	-0.69	5.19	-0.50	3.50
	Total	26	1.55	2.14	0.42	0.68	2.41	-3.00	6.00
SE difference (diopter)	Anisometropic	16	1.85	2.29	0.57	0.63	3.07	-2.88	6.00
	Strabismic	6	1.48	1.78	0.73	-0.39	3.35	-0.38	4.75
	Combined	4	2.41	1.96	0.98	-0.71	5.52	-0.50	3.75
	Total	26	1.85	2.08	0.41	1.01	2.69	-2.88	6.00
Axial length difference (mm)	Anisometropic	16	-0.21	0.85	0.21	-0.67	0.24	-2.05	1.46
	Strabismic	6	-0.11	0.36	0.15	-0.49	0.27	-0.84	0.11
	Combined	4	-0.72	0.30	0.15	-1.20	-0.24	-0.91	-0.27
	Total	26	-0.27	0.72	0.14	-0.56	0.02	-2.05	1.46
Anterior chamber depth difference (mm)	Anisometropic	16	0.03	0.14	0.03	-0.04	0.11	-0.15	0.28
	Strabismic	6	0.03	0.04	0.02	-0.01	0.08	0.00	0.12
	Combined	4	-0.05	0.04	0.02	-0.11	0.01	-0.09	0.00
	Total	26	0.02	0.11	0.02	-0.02	0.07	-0.15	0.28
Lens thickness difference	Anisometropic	16	0.02	0.12	0.03	-0.05	0.08	-0.23	0.25
	Strabismic	6	-0.03	0.09	0.04	-0.12	0.06	-0.20	0.03
	Combined	4	0.09	0.10	0.05	-0.07	0.24	0.00	0.21
	Total	26	0.02	0.11	0.02	-0.03	0.06	-0.23	0.25

CDVA, corrected distance visual acuity; RE, refractive error, SE, Spherical refractive error

\* Among cooperative patients for measuring visual acuity.

Table 2. Statistical comparisons of CDVA difference, for all parameters related with anterior and posterior segment of the eye

			Mean Difference	Standard Error	P-value	95% Confidence Interval	
						Lower Bound	Upper Bound
Spherical RE difference (diopter)	Anisometric	Strabismic	0.18	1.06	0.87	-2.01	2.36
		Combined	-0.78	1.23	0.53	-3.33	1.77
	Strabismic	Anisometric	-0.18	1.06	0.87	-2.36	2.01
		Combined	-0.96	1.42	0.51	-3.91	1.99
	Combined	Anisometric	0.78	1.23	0.53	-1.77	3.33
		Strabismic	0.96	1.42	0.51	-1.99	3.91
SE difference (diopter)	Anisometric	Strabismic	0.37	1.03	0.72	-1.75	2.50
		Combined	-0.55	1.20	0.65	-3.04	1.93
	Strabismic	Anisometric	-0.37	1.03	0.72	-2.50	1.75
		Combined	-0.93	1.39	0.51	-3.79	1.94
	Combined	Anisometric	0.55	1.20	0.65	-1.93	3.04
		Strabismic	0.93	1.39	0.51	-1.94	3.79
Axial length difference (mm)	Anisometric	Strabismic	-0.10	0.34	0.77	-0.81	0.61
		Combined	0.51	0.40	0.22	-0.32	1.34
	Strabismic	Anisometric	0.10	0.34	0.77	-0.61	0.81
		Combined	0.61	0.46	0.20	-0.35	1.57
	Combined	Anisometric	-0.51	0.40	0.22	-1.34	0.32
		Strabismic	-0.61	0.46	0.20	-1.57	0.35
Anterior chamber depth difference (mm)	Anisometric	Strabismic	0.00	0.05	1.00	-0.11	0.11
		Combined	0.08	0.06	0.22	-0.05	0.21
	Strabismic	Anisometric	0.00	0.05	1.00	-0.11	0.11
		Combined	0.08	0.07	0.28	-0.07	0.23
	Combined	Anisometric	-0.08	0.06	0.22	-0.21	0.05
		Strabismic	-0.08	0.07	0.28	-0.23	0.07
Lens thickness difference	Anisometric	Strabismic	0.04	0.05	0.45	-0.07	0.15
		Combined	-0.07	0.06	0.28	-0.20	0.06
	Strabismic	Anisometric	-0.04	0.05	0.45	-0.15	0.07
		Combined	-0.11	0.07	0.14	-0.26	0.04
	Combined	Anisometric	0.07	0.06	0.28	-0.06	0.20
		Strabismic	0.11	0.07	0.14	-0.04	0.26

CDVA, corrected distance visual acuity; RE, refractive error, SE, Spherical refractive error.

#### 4. Discussion

This study investigated visual and structural differences between amblyopic and non-amblyopic eyes in children with unilateral amblyopia. The results, while not statistically significant for interocular differences in spherical equivalent, axial length, anterior chamber depth, and lens thickness, revealed trends that warrant a detailed discussion in the context of existing literature and highlight avenues for future research. The primary finding of reduced BCVA in amblyopic eyes aligns with the fundamental definition of the condition. This reduction stems from the disruption of normal visual cortical development due to abnormal visual experience during early childhood [1]. The severity of this visual impairment can vary significantly depending on the type and duration of the amblyogenic factor, as well as the timing of intervention. Our study, focusing on untreated amblyopia, captures the visual deficit prior to any therapeutic intervention, providing a baseline measure of the impact of amblyopia on visual acuity.

Our findings reveal a trend toward shorter axial lengths in amblyopic eyes, particularly in cases of anisometric amblyopia, consistent with emerging evidence linking amblyopia to altered ocular growth dynamics [23,24 25]. This association is often explained by the visual feedback theory of emmetropization, which posits that clear retinal images drive normal ocular growth, while blurred or suppressed images can disrupt this process, leading to refractive errors and axial length abnormalities [26]. In anisometric amblyopia, the eye with the greater refractive error receives a blurred image, potentially triggering a cascade of events that result in reduced axial growth. However, the lack of statistical significance in our study highlights the complexity of this relationship and the need for further investigation with larger sample sizes and longitudinal designs to definitively establish the causal link between anisometropia, amblyopia, and axial length. And in final years many companies produce special devices to detect amblyopia underscores the intricate interplay between amblyopia, refractive error, and axial growth. This highlights the importance of leveraging advanced imaging technologies, such as swept-source Optical Coherence Tomography (OCT) and ultra-high-resolution biometry, alongside larger, longitudinal cohorts to unravel the underlying mechanisms and establish clearer causal pathways between anisometropia, amblyopia, and ocular structural changes. Furthermore, the interplay between axial length and other ocular components, such as corneal power and lens power, plays a crucial role in determining the overall refractive state of the eye. Studies have shown that shorter axial lengths are often accompanied by steeper corneal curvatures and higher lens powers, acting as compensatory mechanisms to mitigate the hyperopic effect of a shorter eye [27,28,29]. The present study, while not directly measuring corneal and lens power, provides indirect evidence of this compensatory mechanism by demonstrating a trend towards greater hyperopia in amblyopic eyes with shorter

axial lengths. Future studies incorporating direct measurements of corneal and lens parameters would provide a more comprehensive understanding of the interplay between these ocular components in amblyopia. The minimal interocular differences in anterior chamber depth observed across all amblyopia types suggest that this parameter may be less affected by the abnormal visual experience associated with amblyopia compared to axial length. This observation aligns with some previous studies reporting similar anterior chamber depths in amblyopic and non-amblyopic eyes [30]. However, other studies have found shallower anterior chambers in amblyopic eyes, particularly in strabismic amblyopia [31,32]. These inconsistencies may be attributed to variations in study design, sample size, and the specific types of amblyopia included. Further research is needed to resolve these discrepancies and determine the precise relationship between amblyopia and anterior chamber development.

Our results regarding lens thickness also contribute to the ongoing debate about the role of the lens in amblyopia. While some studies have proposed that the lens may be disproportionately thicker in amblyopic eyes due to stalled ocular development [29]. Our results do not support this hypothesis. The lack of significant lens thickness differences between amblyopic and non-amblyopic eyes in our study may indicate that lens growth is less susceptible to the visual deprivation associated with amblyopia, or that any initial differences are mitigated by compensatory mechanisms during ocular development. This observation aligns with previous research showing minimal interocular differences in lens thickness in amblyopic patients [17]. However, further investigation, including longitudinal studies tracking lens growth in amblyopic children, is necessary to fully elucidate the relationship between amblyopia and lens morphology. The absence of significant differences in spherical refractive error between amblyopic and non-amblyopic eyes in our study contrasts with some previous reports [17,18,19]. This discrepancy could be attributed to the specific characteristics of our study population, which included a relatively small number of strabismic amblyopes, a group often associated with greater refractive error differences. Furthermore, the age range of our participants may have influenced the refractive error measurements, as refractive development continues throughout childhood. A larger study with a more diverse amblyopic population and a wider age range is needed to confirm these findings and explore the relationship between amblyopia and refractive error in greater detail. Additionally, future studies should consider incorporating more sophisticated measures of refractive error, such as wavefront aberrometry, to capture higher-order aberrations that may contribute to visual deficits in amblyopia [30].

The lack of statistically significant differences in several biometric parameters between amblyopic and non-amblyopic eyes in our study highlights the importance of considering other factors that may contribute to the visual deficits in amblyopia. These factors include neural changes in the visual cortex, alterations in retinal structure and function, and abnormalities in eye movement control [31,32]. Future research should adopt a multi-faceted approach, integrating visual, structural, and functional measures to gain a more comprehensive understanding of the complex interplay of factors underlying amblyopia. Beyond the specific findings of this study, several methodological considerations warrant attention. The cross-sectional design limits our ability to draw causal inferences about the relationship between amblyopia and ocular biometry. Longitudinal studies tracking ocular growth and visual function over time are essential to establish the temporal sequence of events and determine whether structural changes precede or follow the development of amblyopia. Furthermore, the relatively small sample size and restricted age range of our study may have limited the statistical power to detect subtle differences between amblyopic and non-amblyopic eyes. Future studies should strive for larger, more diverse samples to enhance the generalizability of the findings.

## 5. Conclusion

This study examined visual and structural differences between amblyopic and non-amblyopic eyes in children with unilateral amblyopia. While the amblyopic eyes showed reduced visual acuity, differences in spherical equivalent, axial length, anterior chamber depth, and lens thickness were not statistically significant, possibly due to the small sample size. However, observed trends suggest potential relationships between amblyopia and shorter axial length, particularly in anisometropic amblyopia. Further research with larger, longitudinal studies is needed to confirm these findings and explore the complex interplay of factors contributing to amblyopia. This knowledge will ultimately inform more effective treatment strategies and improve visual outcomes for affected individuals, in other side optometrist and ophthalmologist should to understand relationships between amblyopia and shorter axial length, particularly in anisometropic amblyopia especially when making treatment by surgery or any types from eye operations because it changes the parameters of the eye.

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Nomenclature & Symbols			
SE	Spherical Equivalent	ANOVA	Analysis of Variance
OD	Oculus Dexter (Right Eye)	D	Diopters
OS	Oculus Sinister (Left Eye)	CI	Confidence Interval
SD	Standard Deviation	N	Sample Size
RE	Refractive Error	BCVA	Best Corrected Visual Acuity

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