Original Article

Peripapillary retinal nerve fiber layer thickness and central macular thickness in children with anisometropia

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ABSTRACT

Background: Anisometropia is associated with asymmetric ocular growth and may influence retinal structure, yet its impact on retinal nerve fiber layer thickness (RNFLT) remains incompletely understood. RNFLT is influenced by axial length (AL) and refractive status, and anisometropia is frequently associated with amblyopia. This study aimed to evaluate RNFLT and central macular thickness (CMT) in children with anisometropia and to examine their relationships with refractive error and ocular biometric parameters.

Methods: This cross-sectional study included children aged 5–16 years with anisometropia and was conducted at Port Said Ophthalmology Hospital, Egypt, between January and June 2025. Children were eligible if they showed an interocular difference in spherical equivalent refraction (SER) greater than 2.0 diopters. Comprehensive ophthalmic evaluation included visual acuity assessment, cycloplegic refraction, intraocular pressure (IOP) measurement, ocular biometry, and spectral-domain optical coherence tomography. Peripapillary RNFLT and CMT were measured and compared descriptively between worse and fellow eyes and according to amblyopia status. RNFLT was assessed across the superior, nasal, inferior, and temporal quadrants. Correlations between SER and AL, IOP, CMT, and RNFLT were summarized using Spearman's rank correlation coefficients.

Results: Among 46 children (median age 14 years; range, 5–16 years), 45.7% (n = 21) had anisometropic amblyopia. Compound anisometropia was observed in 42 children (91.3%), mixed anisometropia in three (6.5%), and simple anisometropia in one (2.2%). Nasal RNFLT was numerically greater in worse eyes compared with fellow eyes (median, 84.0 versus 78.0 μm), while the remaining quadrants and CMT showed relatively small interocular differences. RNFLT values were numerically higher in amblyopic eyes than in non-amblyopic eyes across all quadrants, whereas CMT values were similar between the two groups. SER showed a strong negative correlation with AL (r = −0.91) and positive correlations with inferior (r = +0.56), superior (r = +0.67), temporal (r = +0.59), and nasal (r = +0.37) RNFLT. Correlations with CMT (r = −0.22) and IOP (r = +0.19) were weak.

Conclusions: Children with anisometropia showed regional differences in RNFLT, particularly involving the nasal quadrant, while macular thickness remained largely similar between comparison groups. The observed associations between refractive error, AL, and RNFLT suggest a relationship between refractive status and retinal structure. Given the exploratory nature of the comparisons, these findings warrant cautious, primarily descriptive interpretation. Longitudinal studies are warranted to clarify the temporal relationship and clinical relevance of these localized differences.

KEYWORDS

anisometropia, anisometropic amblyopia, optical coherence tomography, peripapillary retinal nerve fiber layer thickness, macula luteas, eye axial length, ocular tonometry, intraocular pressures

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INTRODUCTION

Anisometropia is defined as a condition where the two eyes have different refractive errors, typically quantified as a difference in spherical equivalent refraction (SER) of at least 1.00 diopter (D) [1]. This is a unique presentation of ocular development where the eyes grow asymmetrically despite a shared genetic background and environment [2]. Anisometropia can be due to a difference in axial length (axial anisometropia) or differences in the optical power of the ocular media (refractive anisometropia) [3]. The condition is also frequently associated with high levels of astigmatism and differences in corneal toricity. Its prevalence varies with age [4, 5] and ethnicity [6].

Retinal nerve fiber layer thickness (RNFLT) is a key structural indicator for various ocular and central nervous system diseases, including glaucoma and myopic changes [7]. RNFLT is known to be thicker in the inferior and superior quadrants and thinner in the nasal and temporal quadrants [8]. Furthermore, factors like age, axial length (AL), and refractive status significantly influence RNFLT – for example, RNFLT increases with shorter AL and hyperopia, and decreases with increasing age, axial elongation, and myopia [9].

Anisometropia is frequently, though not invariably, associated with amblyopia. Both conditions are commonly detected during school vision screenings [5, 10]. While anisometropia is generally believed to contribute to amblyopia in the persistently defocused eye, definitive evidence supporting this causal relationship is lacking and has been questioned by several researchers [5, 10]. Additionally, multiple studies show that monocular deprivation can lead to the development of both anisometropia and amblyopia by disrupting ocular growth as well as synaptic and cortical development [5, 10, 11].

Given the possibility of structural asymmetry caused by anisometropia and the importance of RNFL integrity for vision, investigating RNFLT interocular symmetry is critical. There has been little detailed research into RNFLT and central macular thickness (CMT) in anisometropic amblyopia [12–14]. We aimed to assess RNFLT and CMT using optical coherence tomography (OCT) imaging to determine whether differences exist between the two eyes in children with anisometropia; we also aimed to determine possible correlation of SER in anisometropia with RNFLT, CMT, AL, or intraocular pressure (IOP).

METHODS

A cross-sectional study was conducted at Port Said Ophthalmology Hospital, Port Said, Egypt, to evaluate refractive differences among pediatric patients visiting the outpatient ophthalmology clinic. The study was conducted between January and June 2025. The research protocol was prospectively registered in the Pan African Clinical Trial Registry (PACTR; registration number: PACTR202509889401810) and approved by the Ethics Committee of the Faculty of Medicine, Port Said University. All procedures were conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from the parents or legal guardians of all participants prior to enrollment and before initiation of any study-related procedures.

A convenience sampling approach was used. Children aged 5–16 years were eligible for inclusion if they showed an interocular difference in SER greater than 2.0 diopters. Both male and female participants were eligible. Exclusion criteria included age younger than 5 years or older than 16 years, a history of ocular surgery, or the presence of ocular pathology, including glaucoma, cataracts, maculopathy, and corneal opacity.

Sample size planning was informed by previously reported mean peripapillary RNFLT values of 113.9 ± 7.2 μm in amblyopic eyes and 109.2 ± 6.9 μm in normal eyes [12], using the sample-size calculation approach for comparison of two independent means described by Kim [15]. Because the principal interocular comparisons in the present study involved paired eyes from the same participants, this calculation was considered an approximate planning estimate rather than a definitive paired-sample power calculation. Ultimately, 46 children were enrolled.

A detailed medical and ophthalmic history was obtained for all participants. Each child subsequently underwent a comprehensive ophthalmological examination that included assessment of visual acuity, cycloplegic refraction, anterior and posterior segment evaluation, IOP measurement, ocular biometry, and OCT imaging. Uncorrected visual acuity (UCVA) and best-corrected visual acuity (BCVA) were measured monocularly for each eye using a Snellen chart (Topcon ACP-8 automatic chart projector, Topcon Corporation, Tokyo, Japan) and were converted to logarithm of the minimum angle of resolution (logMAR) units for statistical analysis.

Cycloplegic refraction was performed 30 minutes after instillation of 1% cyclopentolate hydrochloride eye drops (Plegica 1%, Egyptian Group for Pharmaceutical Industries [EGPI], Hikma Co., Egypt). Refractive error measurements were obtained using an automated refractometer (Topcon RM-8000B auto-refractometer, Topcon Co., Tokyo, Japan). Anterior segment evaluation was conducted using a slit-lamp biomicroscope (Topcon Co., Tokyo, Japan), and posterior segment examination was performed using a 90-diopter non-contact aspheric lens (Volk Optical,

Inc., Mentor, OH, USA) under slit-lamp biomicroscopy. Intraocular pressure was measured using a non-contact air-puff tonometer (Topcon Co., Tokyo, Japan).

AL measurements were obtained using an optical biometer (Lenstar LS 900, Haag-Streit AG, Koeniz, Switzerland). CMT and peripapillary RNFLT were assessed using spectral-domain OCT (SD-OCT) with a Topcon 3D OCT system (Topcon Corp., Tokyo, Japan) equipped with ImageNet 6 software (version R6 or later). OCT imaging was performed approximately 30–45 min following cycloplegic refraction. Peripapillary RNFLT measurements were analyzed across four quadrants: superior, nasal, inferior, and temporal.

Anisometropia was classified into three categories. Simple anisometropia was defined as a condition in which one eye was emmetropic while the fellow eye exhibited a refractive error, either myopia or hyperopia. Compound anisometropia was defined as the presence of refractive error in both eyes of the same type but differing in magnitude; this included anisomyopia, in which both eyes were myopic but one eye showed a greater degree of myopia, and anisohypermetropia, in which both eyes were hyperopic with differing refractive magnitudes. Mixed anisometropia was defined as the presence of myopia in one eye and hyperopia in the fellow eye [16]. For the present study, anisometropic amblyopia was defined clinically as reduced BCVA in an anisometropic eye in the absence of other ocular pathology.

In cases of simple anisometropia the ametropic eye was designated as the worse eye, whereas the emmetropic eye was considered the fellow eye. In anisomyopia the more myopic eye was classified as the worse eye and the less myopic eye as the fellow eye. In anisohypermetropia the eye with greater hyperopia was considered the worse eye, while the less hypermetropic eye served as the fellow eye. In cases of mixed anisometropia, the eye with the higher absolute refractive error was classified as the worse eye, and the contralateral eye as the fellow eye.

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA). Data distribution was assessed using the Shapiro-Wilk test. Quantitative variables were summarized using median values. Comparisons between worse and fellow eyes and between amblyopic and non-amblyopic groups are presented descriptively. Associations between SER and quantitative parameters, including quadrant-specific RNFLT, CMT, AL, and IOP, were summarized using Spearman's rank correlation coefficient. Given the exploratory nature of the analyses, emphasis was placed on the direction and magnitude of the observed differences and associations rather than statistical significance.

RESULTS

A total of 46 children were included with a median age of 14 years (range 5–16 years). Compound anisometropia was the most prevalent subtype among participants—observed in 42 children (91.3%), followed by mixed anisometropia in three children (6.5%) and simple anisometropia in one child (2.2%). With respect to amblyopia status, 21 participants (45.7%) were diagnosed with anisometropic amblyopia, whereas 25 participants (54.3%) were classified as non-amblyopic.

Comparison of quadrant-specific RNFLT and CMT between worse and fellow eyes is presented in Table 1. Overall, most RNFLT parameters were similar between the two eyes. Nasal RNFLT was numerically greater in the worse eye than in the fellow eye (median, 84.0 versus 78.0 μm). The superior and inferior quadrants showed slightly greater median RNFLT values in the fellow eye, whereas temporal quadrant RNFLT values were nearly identical between eyes. CMT values were also nearly identical between worse and fellow eyes.

Table 2 summarizes the descriptive comparison of quadrant-specific RNFLT and CMT according to amblyopia status. RNFLT values across all quadrants were numerically higher in amblyopic eyes compared with non-amblyopic eyes. CMT values were similar between the two groups.

Correlation analyses between SER and other ocular parameters are presented in Table 3. A strong negative correlation was observed between SER and AL (r = −0.91). SER also showed positive correlations with RNFLT in the inferior (r = +0.56), superior (r = +0.67), temporal (r = +0.59), and nasal (r = +0.37) quadrants. In contrast, the correlations of SER with IOP (r = +0.19) and CMT (r = −0.22) were weak.

Table 1. Descriptive comparison of quadrant-specific RNFLT and CMT between worse and fellow eyes

Variable	Worse Eye	Fellow eye
Inferior RNFLT (μm), Median	131.5	136.0
Superior RNFLT (μm), Median	124.0	127.1
Nasal RNFLT (μm), Median	84.0	78.0
Temporal RNFLT (μm), Median	70.0	70.0
CMT (μm), Median	261.1	259.4

Abbreviations: RNFLT, retinal nerve fiber layer thickness; CMT, central macular thickness; μm, micrometers.

Table 2. Descriptive comparison of quadrant-specific RNFLT and CMT according to amblyopia status

Variable	Non-amblyopic	Amblyopic
Inferior RNFLT (μm), Median	130.0	146.0
Superior RNFLT (μm), Median	120.0	124.0
Nasal RNFLT (μm), Median	80.0	86.0
Temporal RNFLT (μm), Median	69.0	71.0
CMT (μm), Median	260.7	261.5

Abbreviations: RNFLT, retinal nerve fiber layer thickness; CMT, central macular thickness; μm, micrometers.

Table 3. Spearman correlation coefficients between SER and ocular parameters

Variables	r-value
Axial Length	- 0.91
IOP	+ 0.19
Inferior RNFLT	+ 0.56
Superior RNFLT	+ 0.67
Nasal RNFLT	+ 0.37
Temporal RNFLT	+ 0.59
CMT	- 0.22

Abbreviations: SER, spherical equivalent refraction; IOP, intraocular pressure; RNFLT, retinal nerve fiber layer thickness; CMT, central macular thickness. Note: Correlation coefficients (r-value) represent Spearman's rank correlations and are presented descriptively.

DISCUSSION

In this study, children with anisometropia showed regional retinal differences, with higher nasal RNFLT values in the worse and amblyopic eyes, while other quadrants and CMT were broadly similar. SER showed strong or moderate correlations with AL and quadrant-specific RNFLT, highlighting the association between refractive status and retinal architecture. These findings suggest that the observed RNFLT differences may be regionally localized rather than diffuse.

Thanks to recent progress in OCT, retinal structures can be measured reliably. OCT is widely used to investigate how the retina and optic nerve are involved in anisometropic amblyopia [12–14]. In contrast to population-based studies by O'Donoghue et al. [17] and Huynh et al. [18], which emphasized refractive and AL asymmetry in anisometropic eyes, and biometric analyses by Kim et al. [19] showing that anisomyopia severity is primarily related to interocular differences in vitreous chamber depth, our study extends these observations by describing greater nasal RNFLT values in anisometropic eyes with and without amblyopia, suggesting retinal structural differences in addition to ocular biometric differences.

Previous studies report inconsistent structural findings in anisometropic amblyopia. In concordance with Wu et al. [12], we observed numerically greater RNFLT in amblyopic anisometropic eyes; this pattern was particularly apparent in the nasal quadrant, with relatively similar central macular thickness, suggesting a potentially localized pattern. In contrast to Al-Haddad et al. [20], who reported increased macular thickness with comparable RNFL measurements, our findings showed relatively similar macular thickness alongside greater nasal RNFLT, underscoring regional rather than diffuse retinal structural involvement.

Amblyopic eyes often have thicker retina or RNFL [12, 20, 21]. Yen et al. [21] evaluated RNFLT in unilateral amblyopia and showed significantly increased RNFLT in anisometropic amblyopia, but not in strabismic amblyopia, compared with fellow eyes. The authors hypothesized that this RNFL thickening may reflect arrested postnatal ganglion cell pruning in refractive amblyopia, while acknowledging the absence of histopathologic confirmation. Yoon et al. [22] reported significantly increased peripapillary RNFLT in eyes with hyperopic anisometropic amblyopia compared with fellow eyes, while macular retinal thickness remained unchanged, suggesting selective involvement of the peripapillary RNFLT rather than the macula. Our findings are consistent with previous reports by Yen et al. [21] and Yoon et al. [22] describing greater RNFLT in refractive amblyopia, although the distribution of this finding may vary regionally.

Prior studies report heterogeneous findings regarding retinal structural changes in amblyopia. Choi et al. [23] showed that increasing myopia is associated with peripapillary RNFL thinning and increased foveal thickness, underscoring the influence of refractive status rather than amblyopia per se. In unilateral strabismic amblyopia, Altintas et al. [24] found no significant differences in RNFL or macular parameters between amblyopic and fellow eyes. Similarly, Kee et al. [25] reported no overall significant differences between amblyopic and normal children; however, subgroup analyses revealed significant distinctions between anisometropic and strabismic amblyopia,

where children with anisometropic amblyopia displayed thinner foveal thickness and greater RNFL thickness compared to those with strabismic amblyopia [25]. In this context, our findings of greater nasal RNFLT values in anisometropic eyes suggest that the observed retinal structural differences may be regionally localized rather than diffuse.

Previous studies report variable retinal structural changes in anisometropia and amblyopia. Yalcin and Balci [26] evidenced increased foveal thickness without significant RNFL changes in hypermetropic anisometropic amblyopia, whereas our findings showed broadly similar macular thickness with greater nasal RNFLT, suggesting a potentially regional rather than global pattern. Jiang et al. [27] reported parafoveal thinning with preserved foveal thickness in myopic anisometropia. In our cohort, central macular thickness was broadly similar between worse and fellow eyes and according to amblyopia status, consistent with findings reported by Dickmann et al. [28] in anisometropic amblyopia. The relatively small number of eyes with mixed anisometropia in the present study highlights an area for future investigation.

A major strength of this study is the detailed quadrant-specific OCT analysis combined with comprehensive ocular biometry in children with anisometropia, offering clinically relevant insights for pediatric imaging. Nonetheless, the modest sample size and absence of an age-matched control group limit generalizability. In addition, the exploratory nature of the multiple interocular, between-group, and correlation comparisons warrants cautious, primarily descriptive interpretation of the observed patterns. Future large-scale, population-based and longitudinal studies incorporating control cohorts and additional parameters such as corneal curvature are warranted to refine OCT interpretation in pediatric anisometropia, amblyopia, and glaucoma assessment.

CONCLUSIONS

Higher median nasal quadrant RNFLT values were observed in worse eyes and in amblyopic eyes. In contrast, CMT and RNFLT values in the remaining quadrants were broadly similar between comparison groups. The observed associations between refractive error, AL, and RNFLT suggest a relationship between refractive status and retinal structure. Our findings could indicate that anisometropia is associated with subtle, localized differences in RNFLT rather than diffuse retinal structural differences, while overall macular architecture appears to be largely preserved. Clinically, these results underscore the importance of considering refractive status when interpreting OCT-derived RNFL measurements, particularly in pediatric patients evaluated for amblyopia or glaucoma-related changes. Further longitudinal studies are warranted to elucidate the developmental trajectory and clinical relevance of these localized changes.

ETHICAL DECLARATIONS

Ethical approval: The research protocol was prospectively registered in the Pan African Clinical Trial Registry (PACTR; registration number: PACTR202509889401810) and approved by the Ethics Committee of the Faculty of Medicine, Port Said University. All procedures were conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from the parents or legal guardians of all participants prior to enrollment and before initiation of any study-related procedures.

Conflict of interests: None.

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