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RESEARCH

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Association between myopia and relative peripheral refraction in children with monocular Tilted disc syndrome

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Abstract

Background This study aimed to investigate the refractive error and relative peripheral refraction in pediatric patients with monocular tilted disc syndrome.

Methods This single-center, prospective, cross-sectional, observational study included 49 patients from the Pediatric Ophthalmology Department of the Second Hospital of Hebei Medical University aged 5–17 years with monocular tilted disc syndrome. Eyes with tilted optic discs formed the study group, and contralateral eyes with normal discs served as controls, with mean spherical equivalents of −3.24 D and −0.47 D, respectively. Best-corrected visual acuity, spherical equivalent, axial length, tilt ratio, defined as the ratio of maximum to minimum disc diameters, and relative peripheral refraction, assessing myopia-related defocus were compared between groups. Pearson's correlation analysis assessed associations between optic disc tilt and spherical equivalent, axial length, and the total refraction difference value.

Results Tilted optic discs were associated with significantly greater myopia (−3.24 ± 1.83 D in tilted eyes and −0.47 ± 0.72 D in non-tilted eyes, P <.001), longer axial length (24.59 ± 1.04 mm in tilted eyes and 23.45 ± 0.78 mm in non-tilted eyes, P <.001), and a higher tilt ratio (1.43 ± 0.05 in tilted eyes and 1.14 ± 0.04 in non-tilted eyes, P <.001). Discrepancies between tilted and non-tilted eyes were observed in the superior, inferior, and nasal quadrants, and the total refraction difference value (P <.001). In eyes with tilted disc syndrome, a negative correlation was found between the total refraction difference value and the spherical equivalent (P <.001). The tilt ratio of optic disc eyes was significantly greater than that of contralateral eyes and was negatively correlated with the spherical equivalent. There was a positive correlation between the tilt ratio and axial length (P <.001).

Conclusions Pediatric patients with monocular tilted disc syndrome exhibited longer axial lengths, more myopic spherical equivalent, and more positive relative peripheral refraction. A greater tilt ratio is associated with larger relative peripheral refraction and axial length, corresponding to more severe myopia.

Keywords Myopia, Optic disc, Pediatric patients, Refractive error, Visual acuity

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Background

Myopia has garnered significant public attention and growing concern. According to Holden et al., by 2050, the global population afflicted with myopia and high myopia will reach 5 billion and 1 billion, respectively [1]. Young individuals in East Asia are particularly impacted by the effects of myopia [2]. High myopia can potentially lead to various ocular complications associated with irreversible vision impairment. These complications include maculopathy, choroidal neovascularization, foveoschisis, macular holes, and retinal detachment [3, 4]. Additionally, high myopia is linked to a higher risk of visual defects and conditions such as glaucoma and cataracts [5]. The rapid increase in the prevalence of myopia necessitates an urgent exploration of the potential mechanisms and factors influencing its emergence and progression.

Tilted disc syndrome (TDS) is a congenital optic nerve anomaly characterized by optic disc tilt, segmental development of the optic nerve, situs inversus of the optic disc, hypoplasia of the retina and choroid, ectasia of the fundus (particularly in the inferonasal quadrant), and thinning of the retinal pigment epithelium [6–9]. Clinically, TDS is associated with vision deficits and refractive errors, particularly astigmatism and anisometropia [10, 11]. In a Chinese population, the prevalence of TDS was reported to be 3.5% among individuals with astigmatism or anisometropia, indicating a relatively notable occurrence within this subgroup [12]. Due to its clinical appearance, TDS is often misdiagnosed as other optic disc anomalies, including papilledema, optic neuritis, or optic pits [10]. Accurate identification is therefore essential to avoid unnecessary intervention.

Although TDS and progressive myopic disc changes are distinct in etiology, they may share similar fundoscopic features [13]. TDS typically presents with a stable, congenital configuration, while myopic disc changes tend to progress over time. Two clinical features that help differentiate TDS from acquired myopic anomalies are the presence of an inferior or inferonasal crescent and a stationary fundus appearance [9].

Previous studies have demonstrated a strong association between TDS and mild to moderate myopia, increased axial length, thickening of the temporal retinal nerve fiber layer, and visual field defects [13–17]. However, the mechanisms by which TDS influences refractive development remain poorly understood. Notably, experimental studies in animal models have highlighted the importance of relative peripheral refraction in the onset and progression of myopia [18].

Multispectral refraction topography (MRT) is a novel imaging technology that allows the quantification of central and peripheral refraction across different retinal regions [19]. This tool provides an opportunity to examine whether eyes with TDS exhibit abnormal peripheral refraction patterns that may contribute to axial elongation and refractive error.

This study aimed to investigate the associations between TDS and key ocular parameters including axial length, spherical equivalent, and relative peripheral refraction in children with monocular TDS. The goal was to determine whether TDS is a potential structural risk factor for myopia development and to explore the role of peripheral defocus in this process.

Methods

Participants

This study included 49 pediatric patients (98 eyes) diagnosed with congenital monocular TDS at the Pediatric Ophthalmology Department of the Second Hospital of Hebei Medical University between June 2021 and December 2023. Each participant had one eye with TDS and one contralateral eye with a normal optic disc. TDS is characterized by several key features [9], including the oblique orientation of the optic disc axis, the presence of an inferonasal crescent, situs inversus of the retinal vessels, posterior staphyloma, and congenital conus. These structural characteristics were utilized to identify pediatric patients with congenital monocular TDS for inclusion in the study.

Participants with a history of congenital optic anomalies other than TDS, such as optic disc coloboma, optic disc pits, or morning glory syndrome, as well as those with previous ocular surgery, ocular trauma, or any pathological conditions affecting the optic nerve, were excluded. Eyes with evidence of progressive myopic disc changes, defined as temporal optic disc stretching, increasing peripapillary atrophy, or documented axial elongation over time were also excluded in order to isolate the effects of congenital disc tilt from those associated with acquired myopia. Children with a confirmed diagnosis of congenital myopia were not included, and patients with high myopia or anisometropia exceeding 3.0 diopters were carefully evaluated to rule out congenital or progressive myopic pathology. None of the included participants had documented myopia progression during the study period. To further minimize the influence of natural myopia progression, only patients with stable refractive error within the past year were included, as verified by medical records and parental report. A total of 23 males and 26 females were included in the final analysis. For each participant, the contralateral eye with a normal optic disc served as a self-controlled comparator, enabling matched intra-subject analysis between tilted and non-tilted eyes.

Study design

We conducted a matched case-control study within a cross-sectional framework at a single medical center to explore the correlation between refractive error, AL, disc tilt ratio, and RPR in pediatric patients presenting with unilateral TDS. This study strictly adhered to the principles outlined in the Declaration of Helsinki and was approved by the Ethics Committee of the Second Hospital of Hebei Medical University (Approval No. 2022-R693; Date of Approval: Aug 16, 2022). Written informed consent was obtained from the patients' guardians before participation in the study.

Study procedures

Eligible individuals underwent a comprehensive ophthalmologic assessment during the initial examination. This included the assessment of best-corrected visual acuity (BCVA), cover test, cycloplegic refraction, spherical equivalent, AL, fundus examination, color fundus photography, tilt ratio (ratio of maximum to minimum disc diameter), and MRT for all eyes. BCVA was assessed using the 5 m Standard Logarithm Visual Acuity chart following the correction of refractive error. Participants were recruited consecutively from children who visited the Pediatric Ophthalmology Department for routine eye examinations or visual complaints during the study period. Cycloplegic refractions were conducted using retinoscopy, followed by subjective refinement after the application of 1% cyclopentolate for children aged < 8 years and 0.5% tropicamide for those aged ≥ 8 years. The spherical equivalent (SE), defined as the sum of a sphere and half of a cylinder, was compared between each patient's eyes to assess the refractive errors, with myopia defined as SE ≤ – 0.50 D.

Cover/uncover and alternate cover tests were performed by two experienced orthoptists to confirm the presence of strabismus. An accommodative target was required for both distance and near gazes to fixate and assess binocular alignment. The AL was determined using a Lenstar LS900 optical biometer (Haag-Streit AG, Koeniz, Switzerland). Each patient was properly positioned with the forehead firmly attached to the holder. The measurement was taken three times, and the average value was determined to ensure accuracy. After ruling out other abnormal conditions through direct ophthalmoscopic fundus inspection, color fundus photography was performed using a Topcon TRC.NW300 digital camera (Topcon Co., Tokyo, Japan). This imaging technique was used to observe the morphological features of TDS. The ratio between the longest and shortest diameters of the optic disc was defined as the tilt ratio (Additional file 1) [14, 20–22]. When assessing the ovality of the optic disc, a skilled observer precisely measured the maximum and minimum optic disc margins using ImageJ software (version 6.0) [21], averaged three measurement values, and calculated the ratio of the longest to shortest disc diameter as the tilt ratio [14]. Generally, the maximum and minimum disc diameters correspond to the vertical and horizontal axes of the optic disc, respectively. The tilt ratio was negatively correlated with the smaller disc diameter at the same level of disc tilt severity [23]. We measured the RPR of patients using MRT MSI C2000 (Thondar Technology Co. Ltd, Shenzhen, China). Under various refractive compensation conditions, it is possible to detect the RPR to obtain a series of image sequences. Through the analysis and calculation of these images, the total refraction difference value (TRDV) can be measured and recorded as a numerical value for comparison. The retinal RPR is divided into four quadrants: RPR in the temporal quadrant (RDV-T), RPR in the nasal quadrant (RDV-N), RPR in the upper quadrant (RDV-S), and RPR in the inferior quadrant (RDV-I). To obtain accurate results for further analysis, computer evaluation and measurement of the image quality were used to manage the impact of factors such as iris reflection, blinking, and low lighting (Additional file 2). Low-quality frames were automatically excluded by the built-in quality control algorithm of the MRT system. All images were reviewed independently by two trained examiners, and inconsistent readings were re-evaluated to ensure data reliability.

Statistical analyses

All statistical analyses were performed using SPSS software (version 27.00, SPSS Inc., Chicago, USA). The Shapiro–Wilk test was used to assess the normality of continuous variables. For the differential analysis of SE, AL, optic disc tilt ratio, and RPR, a paired sample t-test was applied to data that followed a normal distribution (normality test, P>.05). If the data did not adhere to a normal distribution, a rank sum test of two related samples was employed. Pearson's correlation analysis was conducted to explore the association between the optic disc tilt ratio and SE, AL, and TRDV. Statistical significance was set at a P value of < 0.05.

Results

Refractive characteristics

The participants were 5 to 17 years old, with a mean age of 10.00 years and a standard deviation of 2.09 years. In eyes with TDS, most patients exhibited myopia, with a mean SE of – 3.24 ± 1.83. Myopic refractive errors ranged from – 0.50 to – 9.25 D in the TDS eye, whereas the non-tilted eye had a mean SE of – 0.47 ± 0.72 D, ranging from + 1.75 to – 4.00 D. The SE in the TDS eye was significantly more negative than that of the non-tilted eye (P<.001). Additionally, the mean AL was 24.59 ± 1.04 mm (range 22.91–27.39 mm) in the TDS eye and 23.45 ± 0.78 mm (range 21.41–26.88 mm) in the non-tilted eye. The AL in the TDS eye was significantly longer than that in the non-tilted eye (P<.001). The tilt ratio of the TDS group demonstrated a statistically significant elevation at 1.43 ± 0.05,

Table 1 Comparison of spherical equivalent, axial length, and optic disc Tilt ratio between eyes with Tilted and contralateral non-tilted optic discs in the same patients

Parameter	Tilted Eyes (n=49)	Non-Tilted Eyes (n=49)	Test Value	P-value (95% CI)
SE (diopters)	−3.24 ± 1.83	−0.47 ± 0.72	Z = −5.765	< 0.001* 95%CI (0.000, 0.059)
AL (mm)	24.59 ± 1.04	23.45 ± 0.78	Z = −5.377	< 0.001* 95%CI (0.000, 0.059)
Tilt ratio	1.43 ± 0.05	1.14 ± 0.04	Z = −6.096	< 0.001* 95%CI (0.000, 0.059)

Tilted and non-tilted eyes represent paired measurements from the same patients; the contralateral normal eye was used as the control. All data are presented as mean ± standard deviation.*Indicates a statistically significant difference (P<.001)

Table 2 Comparison of the total refraction difference value (TRDV) and refraction difference value (RDV) in different quadrants between eyes with and without tilted disc syndrome

	Tilted eye	Non-tilted eye	Value of test	P-value
TRDV	0.35 ± 0.48	−0.04 ± 0.65	Z = −3.520	< 0.001*
RDV-S	0.24 ± 1.18	−0.29 ± 0.99	Z = −2.357	0.018*
RDV-I	0.28 ± 0.86	−0.06 ± 1.00	Z = −2.142	0.032*
RDV-T	0.22 ± 1.00	0.00 ± 0.78	Z = −1.456	0.143
RDV-N	0.88 ± 0.86	0.30 ± 0.88	t = −3.599	< 0.001*

* Indicates a statistically significant difference (P<.001)

surpassing that of the control group at 1.14 ± 0.04, with the difference being statistically significant (P<.001) (Table 1).

Relative peripheral refraction differences

In addition, the total refraction difference value and refraction difference values across the four quadrants of relative peripheral refraction were analyzed (Table 2). The total refraction difference value was significantly higher in tilted eyes (mean 0.35 ± 0.48) than in non-tilted eyes (mean − 0.04 ± 0.65; P<.001). Among the four quadrants, significant differences were observed in the superior quadrant (0.24 ± 1.18 in tilted eyes compared to − 0.29 ± 0.99 in non-tilted eyes; P=.018), inferior quadrant (0.28 ± 0.86 compared to − 0.06 ± 1.00; P=.032), and nasal quadrant (0.88 ± 0.86 compared to 0.30 ± 0.88; P<.001), with the nasal quadrant showing the most pronounced difference. In contrast, no statistically significant difference was found in the temporal quadrant (0.22 ± 1.00 in tilted eyes and 0.00 ± 0.78 in non-tilted eyes; P=.143). These findings indicate a localized pattern of peripheral refraction changes in eyes with tilted optic discs, particularly in the nasal field.

Correlation analysis

Significant differences were observed in TRDV, RDV-S, RDV-I, and RDV-N levels between eyes with TDS and the contralateral eyes. Among these, TRDV (95%CI [0.000, 0.066], P<.001) and RDV-N (95%CI [0.849, 0.857], P<.001) exhibited the most significant variances (P<.001), whereas there was no statistically significant difference in RDV-T (P>.05) (Table 2, Fig. 1). In eyes with TDS, a negative correlation was observed between TRDV and SE (r = −.289, P=.044, Table 3), indicating that larger TRDV values were associated with more negative SE values (Fig. 2). However, no significant correlation was observed between TRDV and AL or the tilt ratio in the eyes with TDS.

Pearson's correlation analysis revealed a significant association between the optic disc tilt ratio and AL, with a higher ovality associated with a longer AL (r=.517; P<.001, 95%CI [0.276, 0.697]; Table 3, Fig. 3). Additionally, a higher tilt ratio was correlated with a more negative SE (r = −.801, P<.001, 95%CI [-0.883, -0.670]); Table 3, Fig. 4). However, no significant correlation was observed between the optic tilt ratio and TRDV (r=.228; P=.132; Table 3.

Discussion

Previous animal and clinical studies have reported that hyperopic defocus can lead to increased axial elongation and vice versa [18, 24, 25]. In our study, the eye with TDS showed significantly more myopic spherical equivalent and longer axial length than the contralateral non-tilted eye, indicating relatively higher myopic severity. The RPR in eyes with optic disc tilt was greater than that in normal eyes, and RPR showed relative hyperopic defocus in children with TDS. This pattern may be associated with myopia development, although it remains unclear whether peripheral defocus precedes or results from axial elongation. However, it is essential to validate these findings in a prospective study involving a larger sample size and follow-up assessments. Our comparison of RPR differences between the TDS group and matched groups revealed significant differences in peripheral refraction, with the most pronounced variance observed in the nasal quadrant (RDV-N) (P<.001). This may reflect a relatively consistent inferonasal tilting orientation among patients, resulting in greater nasal field defocus. The difference in the RDV-T, however, was not statistically significant. This result is consistent with findings from other studies on relative defocus in myopia [25]. However, despite the alterations in peripheral refraction, we did not observe a significant correlation between tilt ratio and TRDV. This may be due to inter-individual anatomical variation, the limited sample size, or the sensitivity of the measurement technique. Further studies are needed to confirm the relationship between these two parameters. To the best of our knowledge, this is the first investigation of RPR in children with tilted optic discs.

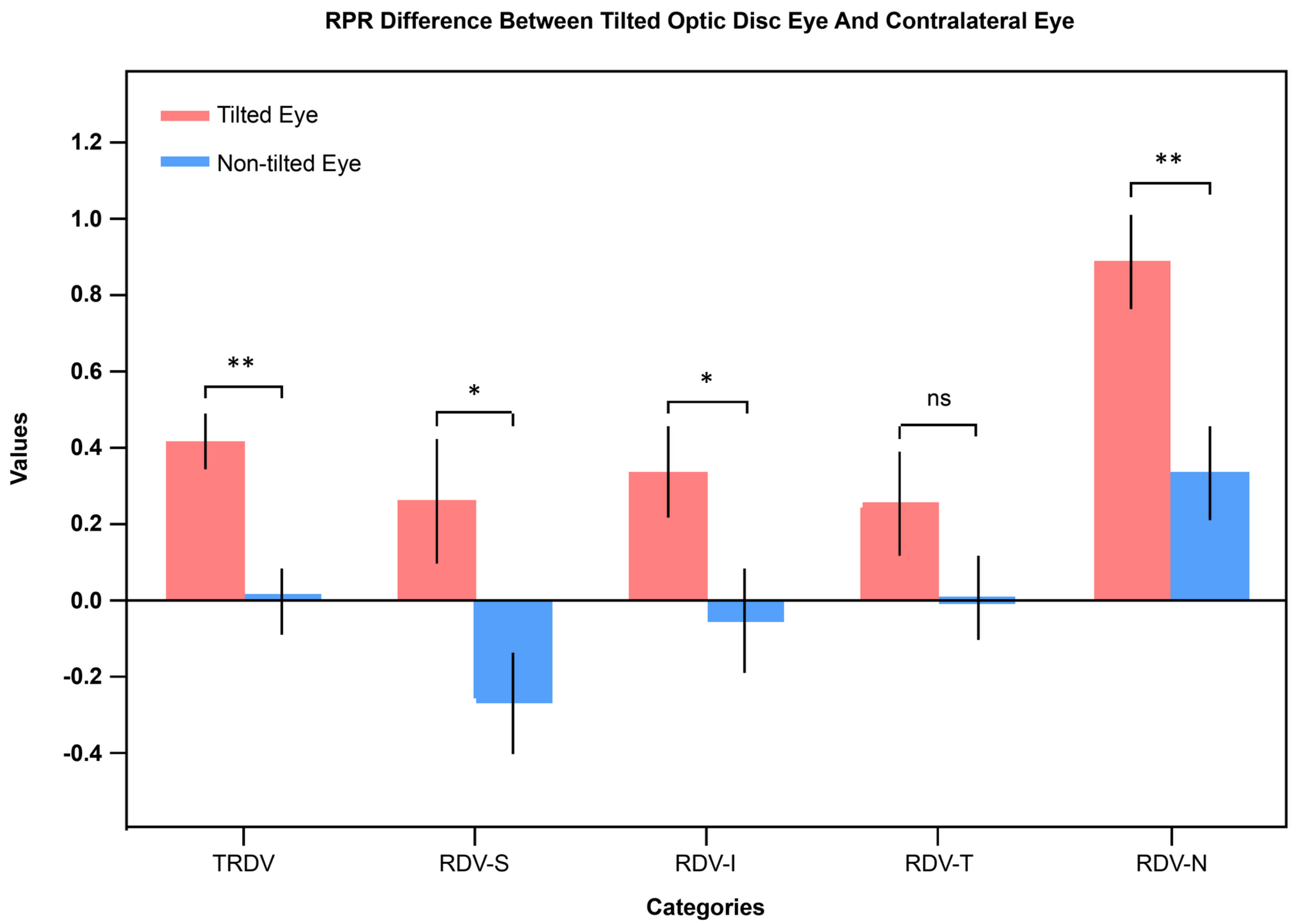

Fig. 1 Relative peripheral refraction (RPR) difference between eyes with tilted disc syndrome and the contralateral eye. Bar chart depicting the RPR discrepancy in the tilted disc syndrome eye and the contralateral eye across four categories: total refractive difference value (TRDV), superior quadrant refractive difference value (RDV-S), inferior quadrant refractive difference value (RDV-I), temporal refractive difference value (RDV-T), and nasal refractive difference value (RDV-N). **Indicates a statistically significant difference ($P<.001$), *Indicates a statistically significant difference ($P<.05$), "ns" indicates the absence of a statistically significant difference

Table 3 Pearson's correlation coefficients between the total refraction difference value (TRDV), the optic disc tilt ratio and the spherical equivalent (SE), axial length (AL) in eyes with tilted disc syndrome

	Tilt Ratio		TRDV	
	t	*P*-value	t	*P*-value
SE	−0.801	< 0.001	−0.289	0.044*
AL	0.517	< 0.001*	0.198	0.240
TRDV	0.228	0.132	-	-
Tilt Ratio	-	-	0.228	0.132

*Indicates a statistically significant difference ($P<.05$)

Some studies have confirmed that TDS is commonly associated with an increased prevalence of myopia [11, 15]. In our cohort, 92% of eyes with TDS were myopic, compared to 33% in contralateral eyes, highlighting a higher prevalence within the affected eye rather than at the individual level. However, the prevalence and severity of myopia in individuals with TDS have varied across different studies. For example, the Tanjong Pagar study found myopia in 88.5% of cases with TDS and in 32% of the matched group [12]. Vongphanit et al. reported myopia in 66% of eyes with a tilted optic disc, compared to 12% of eyes with a non-tilted optic disc [14]. Our study demonstrated a particularly high rate of myopia in children with monocular TDS. This may be partly attributed to the morphological similarity between myopic optic discs and tilted discs, which can complicate differentiation and increase the risk of selection bias. Notably, previous studies employed independent control eyes, whereas our study utilized a paired, intra-subject design, which may also account for differences in prevalence estimates. Furthermore, the relatively small sample size in our study could have led to an overestimation of the true prevalence of myopia. In addition, we acknowledge that the use of tropicamide for cycloplegia in children over eight years of age may have allowed residual accommodation, potentially contributing to an overestimation of myopia severity. This methodological limitation should be considered when interpreting the refractive outcomes.

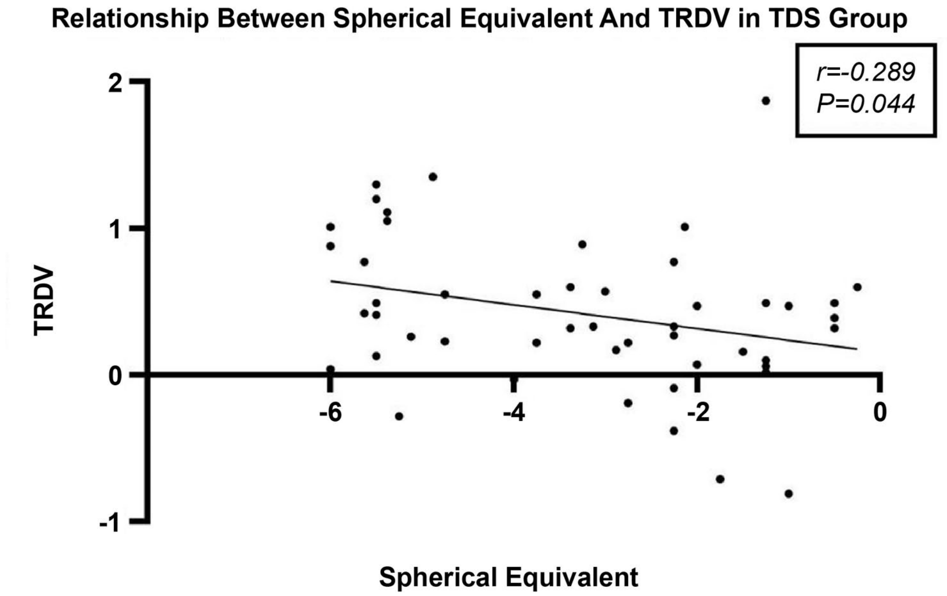

Fig. 2 Scatterplot illustrating the correlation between the spherical equivalent (SE) and total refraction difference value (TRDV) in eyes with tilted disc syndrome (TDS). The scatterplot shows the relationship between the SE and TRDV in eyes with TDS. Each point represents an individual eye within the TDS group. The data indicate a significant negative correlation between the TRDV and SE

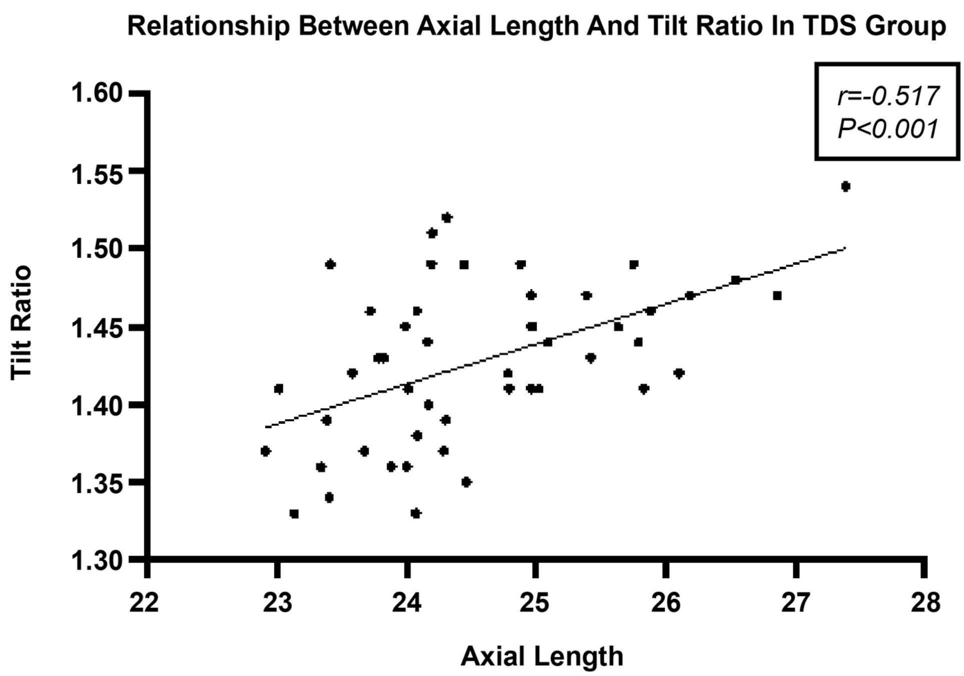

Fig. 3 Scatterplot illustrating the relationship between the axial length and optic disc tilt ratio in eyes with tilted disc syndrome

Most patients with TDS were found to exhibit moderate to severe myopia, with an average SE of − 3.59 ± 2.35 for children with unilateral tilted discs. Some of these cases experienced impaired BCVA, slightly worse than age-matched individuals without this condition. This finding aligns with previous studies. Tong et al. reported that 49% of children with TDS in Singapore had over 3 D of myopia, with a mean SE of − 3.01 D in eyes with tilted discs [26]. Other studies have associated tilted optic discs with mild to moderate myopia [12, 27]. Research on the central corneal thickness of children with TDS reported a mean spherical refraction of − 3.06 ± 1.86 D for eyes with TDS [6]. A survey conducted by You et al. reported a mean myopia of 6.59 ± 0.68 D, which is consistent with our findings. However, studies on poor BCVA are limited [28]. In our analysis, we observed three cases of affected

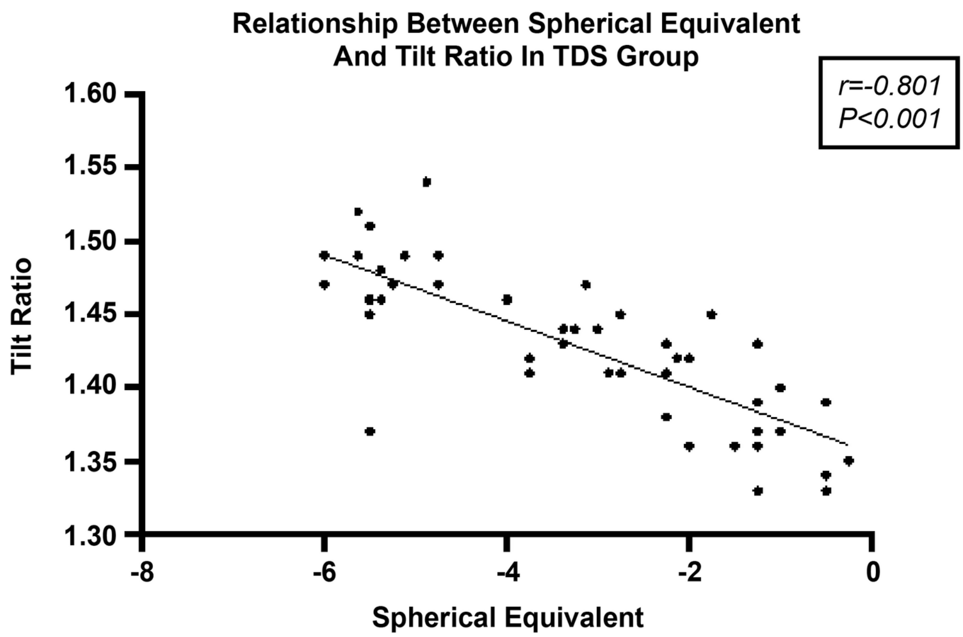

Fig. 4 Scatterplot illustrating the relationship between the spherical equivalent (SE) and optic disc tilt ratio in eyes with tilted disc syndrome (TDS). The scatterplot shows the relationship between the optic disc tilt ratio and SE in eyes diagnosed with TDS. Each point represents an individual eye. The data demonstrate a strong negative correlation between the tilt ratio and SE

eyes with BCVA < 0.8. These cases may reflect anisometropic amblyopia, though no formal diagnosis was documented. This interpretation was based on interocular refractive differences exceeding 2.5 D and reduced acuity despite correction. Additionally, structural changes associated with TDS may reduce retinal sensitivity [15, 29]. Some patients with optic tilt may have pigmentary accumulation [14], contributing to poorer BCVA.

According to Tay et al., the tilt ratio is significantly correlated with myopia and AL. In their study of 137 male participants with myopia, individuals with greater optic disc tilt had higher degrees of myopia and a longer AL [15]. Similarly, Terasaki found that eyes with greater optic disc tilt exhibited larger AL and more severe myopia [21]. Li et al. also demonstrated that a larger ovality ratio was associated with more myopic SE and AL [20]. It is hypothesized that optic disc tilting may occur or progress as a result of axial elongation of the eyeball during the myopia progression [30]. Our findings align with these observations [15, 21, 31, 32]. In contrast, some studies have shown no significant correlation between the tilt ratio and myopia or AL.

Although our study revealed several innovative findings, it has some limitations. Primarily, a longitudinal study is required to ascertain the correlation between optic disc morphology and RPR. Patients need to be followed up for least 12 months to observe whether there is a difference in retinal RPR. Furthermore, this study did not investigate the underlying correlations between disc tilt and refractive errors, leaving it unclear why children with optic disc tilt are more susceptible to developing myopia. The etiology of myopia is complex and remains a subject of debate [1, 13], while the functional decompensation factors associated with optic morphological abnormalities are still elusive. Additionally, myopia is influenced by various factors, including genetics, age, near-sighted work, education level, and occupation, making it challenging to ascertain the impact of a single variable [33]. Another limitation is that we did not consider the correlation between the optic disc tilt and astigmatism. Previous studies suggested astigmatism as the most common refractive error related to optic disc tilt, which accounts for up to 93.5% of cases, with more than half as oblique astigmatism [11, 14]. Further verification is needed to ascertain whether this observation is true in our patient cohort.

Conclusion

In conclusion, this study elucidated the correlation between TDS and myopic refractive errors. Eyes with TDS exhibit greater retinal RPR and more negative SE power than contralateral eyes with a normal optic disc. These findings support the hypothesis that TDS may be a structural predisposing factor for the development of myopia. Moreover, the positive correlation between tilt ratio and axial length, along with the negative correlation between tilt ratio and spherical equivalent, further suggests a link between disc morphology and refractive status. However, the lack of a significant association between tilt ratio and peripheral refraction highlights the complexity of this relationship.

While the cross-sectional design limits conclusions regarding myopia progression, the observed structural and refractive asymmetry between paired eyes warrants further investigation. Future studies should incorporate longitudinal follow-up to determine whether TDS is predictive of accelerated myopic progression or differential response to refractive interventions in pediatric populations.

Abbreviations

AL	Axial length
BCVA	Best-corrected visual acuity
MRT	Multispectral refraction topography
RDV-I	Retinal peripheral refraction in the inferior quadrant
RDV-N	Retinal peripheral refraction in the nasal quadrant
RDV-S	Retinal peripheral refraction in the superior quadrant
RDV-T	Retinal peripheral refraction in the temporal quadrant
RPR	Retinal peripheral refraction
SE	Spherical equivalent
TDS	Tilted disc syndrome
TRDV	Refraction difference value

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12886-025-04108-6.

Supplementary Material 1: **Additional file 1 (figure)**: Measurement of the optic disc tilt ratio in tilted disc syndrome using color fundus photography. **Additional file 2 (figure)**: Measurement of retinal peripheral refraction using the multispectral refraction topography system. **Table 1.** Comparison of spherical equivalent, axial length, and optic disc tilt ratio between eyes with tilted and contralateral non-tilted optic discs in the same patients **Table 2. C**omparison of the total refraction difference value (TRDV) and refraction difference value (RDV) in different quadrants between eyes with and without tilted disc syndrome**Table 3.** Pearson's correlation coefficients between the total refraction difference value (TRDV), the optic disc tilt ratio and the spherical equivalent (SE), axial length (AL) in eyes with tilted disc syndrome

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Not applicable.

Author contributions

J.W.: Methodology, Data curation, Project administration, Writing– review & editing; S.Z: Formal analysis, Data curation, Visualization, Writing– original draft; H.J.: Formal analysis, Data curation, Writing– original draft; JD: Conceptualization, visualization; R.X.: Investigation. Data curation; J.W.: Data Curation; SW: Data Curation; S.C.: Conceptualization, Funding Acquisition, Resources, Supervision. All authors read and approved the final manuscript.

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Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study strictly adhered to the principles outlined in the Declaration of Helsinki and was approved by the Ethics Committee of the Second Hospital of Hebei Medical University (Approval No. 2022-R693; Date of Approval: Aug 16, 2022). Written informed consent was obtained from the patient's guardian before participation in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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