• Investigation •

Distribution and correlation of refractive parameters in children with different corneal curvatures in southeast China

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Abstract

● **AIM:** To analyze the distribution of refractive status in school-age children with different corneal curvatures (CC) and the correlation between CC and refractive status.

● **METHODS:** A total of 2214 school-aged children of grade 4 in Hangzhou who were screened for school myopia were included. Uncorrected distance visual acuity (UCDVA), non-cycloplegic refraction, axial length (AL), horizontal and vertical corneal curvature (K_1, K_2) were measured and spherical equivalent (SE), corneal curvature radius (CCR) and axial length/corneal radius of curvature ratio (AL/CR) were calculated. UCDVA<5.0 and SE≤-0.50 D were classified as school-screening myopia. According to the different CCRs, the patients were divided into the lower corneal curvature (LCC) group (CCR≥7.92) and the higher corneal curvature (HCC) group (CCR<7.92). Each group was further divided into the normal AL subgroup and the long AL subgroup. The refractive parameters were compared to identify any differences between the two groups.

● **RESULTS:** Both SE and AL were greater in the LCC group (P=0.013, P<0.001). The prevalence of myopia was 38% in the LCC group and 44% in the HCC group (P<0.001). The proportion of children without screening myopia was higher in the LCC group (62%) than in the HCC group (56%). Among these children without screening myopia, the proportion of long AL in the LCC group (24%) was significantly higher than that in the HCC group (0.012%; P<0.001). The change of SE in the LCC group was less affected by the increase of AL than that in the HCC group.

● **CONCLUSION:** School-aged children in the LCC group have a lower incidence of screening myopia and longer AL. Low CC can mask SE reduction and AL growth to some extent, and the change of AL growth change more in children with low CC than high CC. Before the onset of myopia, its growth rate is even faster than that after the onset of myopia.

● **KEYWORDS:** school-aged children; corneal curvature; axial length; spherical equivalent; myopia screening
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INTRODUCTION

Worldwide, the incidence of myopia is high and increasing, especially in East Asian countries[1]. According to the survey data of the National Health Commission of the People's Republic of China, the prevalence of myopia in China remained at a high level, with a rising trend[2]. At the same time, the phenomenon of myopia prevalence at a younger age was worth people's attention. The characteristics of early onset and rapid progress of myopia in children have raised key concerns about vision health. In 2020, the overall myopia rate of Chinese children and adolescents reached 52.7%[3]. Gao *et al*[4] showed that the current global prevalence of myopia is about 28.3%, and it is estimated that by 2050, half of the world's population will suffer from myopia. While high myopia is estimated to account for 10% of the global population[5]. To effectively prevent and treat myopia before it occurs in children and adolescents, a system of regular vision screening for primary and secondary school students should be established, and myopia prevention guidance or referral recommendations should be made for effective prevention[6-7]. The visual acuity and refractive status of children and adolescents were preliminary judged by basic examinations such as uncorrected distance visual acuity (UCDVA), best corrected visual acuity, and non-cycloplegic refraction. In clinical practice, we often encounter children with a low spherical equivalent (SE), and further examination reveals that most of them exhibit a corneal curvatures (CC) lower than average and an axial length (AL) that is far beyond the reference range for that age group, and some even have high myopic fundus changes, such as tessellated retina[8]. During the myopia screening and treatment process, this type of myopia is often overlooked and can progress into high myopia. Early diagnosis, treatment, and detection are necessary for high myopia. It can result in irreversible damage to the fundus of the eye, such as retinal detachment, macular hemorrhage, choroidal neovascularization, and eventually blindness if prompt treatment is not received[9]. The majority of recent research has concentrated on the connection between SE, AL, and accommodation factors. Nevertheless, it did not contrast the refractive characteristics and status of children with various CCs. According to reports, the age group in which myopia progresses fastest in Chinese children is 9-11 years old[10]. In this paper, subjective and objective eye examinations were performed on school-age children aged 9 to 10y. To enhance the screening system for myopia prevention and control, we aim to analyze the distribution and correlation of refractive status and various refractive parameters in children with different CCs.

SUBJECTS AND METHODS

Ethical Approval This cross-sectional study was approved by the Ethics Committee of Zhejiang Provincial People's Hospital, Hangzhou, Zhejiang Province, China (No.QT2022439). All studies were performed following the Declaration of Helsinki and informed consent was obtained from the parents of the participants.

Study Population Totally 2304 school-age children aged 9 to 10y who underwent myopia screening in four elementary schools in Hangzhou were included in that study, and the screening period was from September to November 2022. The exclusion criteria were: 1) eye diseases affecting visual acuity such as corneal disease, refractive media clouding, and fundus lesions *etc*., 2) a history of major eye trauma and eye surgery, 3) being treated with atropine sulfate eye drops or orthokeratology lenses, 4) missing or obviously erroneous data, no meaningful inclusion in the study. After exclusion criteria, 2214 cases with a total of 4428 eyes were included in the study, including 1146 boys (2292 eyes) and 1068 girls (2136 eyes).

Ocular Examinations All ocular examinations were made by professional ophthalmologists. The non-cycloplegic refraction was obtained using an automated refractometer (Ar-1, NIDEK, Aichi, Japan) and averaged over at least three times. The mean value of the three measurements was recorded as SE. The UCDVA of one eye was examined using the 5 m standard for logarithmic visual acuity charts (ZS-5000E, Mplent, Hunan, China). At a distance of 5 m, line 11 was recognized as standard visual acuity and marked as 5.0. Biometric measurements including AL, horizontal and vertical corneal curvature (K_1, K_2), and CC were obtained from partial-coherence laser interferometry (IOL Master 500 Optical Biometry, Carl Zeiss Meditec, Oberkochen, Germany), and the mean value was taken after six measurements of the effective values. Additionally, when using the machine, all subjects were seated in a comfortable position, with the jaw lightly placed on the jaw rest of the instrument and the forehead against the frontal rest, following the operator's instructions.

Definitions The lower corneal curvature (LCC) group was defined as corneal curvature radius (CCR)≥7.92. The higher corneal curvature (HCC) group was defined as CCR<7.92. Each group was further divided into the normal AL subgroup and the long AL subgroup. The normal AL reference range for 9-year-old children was 21.26-24.32 mm, with long AL defined as exceeding 24.32 mm. The normal AL reference range for 10-year-old children was 21.52-24.50 mm, with long AL defined as exceeding 24.50 mm[11]. The mean SE refractive error was calculated as the sphere power plus half of the cylinder power (the greater the negative value, the deeper myopia). The CCR was calculated, $CCR=1000\times(n_2-n_1)/K_m$ [n_1 was air refractive index (1.000) and n_2 was corneal refractive index (1.3375), $K_m=(K_1+K_2)/2$]. In this study, screening myopia was determined as UCDVA<5.0 and SE≤ -0.50 D[12].

Statistical Analysis Kolmogorov-Smirnov (K-S) test was used to check the normality of the data distribution. The Chi-square test was used to compare the difference between the group of LCC and HCC in sex, myopia, and AL range. UCDVA, SE, corneal astigmatism, AL/CR, K_1, K_2, and so on by Mann-Whitney test compared the difference. Additionally, we employed Pearson correlation analysis to assess the correlation. Analyses were performed using R version 4.1.3, and charts were processed with R studio version 2022.02.1-461. Two-sided P-values of less than 0.05 were considered statistical significance.

RESULTS

Basic Characteristics and Distribution of Refractive Parameters of Examinees The mean value of the CCR (7.92)[11] in school-age children aged 9 to 10y was used as the threshold. A total of 1568 eyes were classified into the LCC group, while 2860 eyes were classified into the HCC group. Totally 835 eyes with lower CC and 2394 eyes with higher CC were included in the Normal AL group. Totally 733 eyes with lower CC and 466 eyes with higher CC were included in the long AL group.

A total of 2214 school-age children (4428 eyes) between the ages of 9 and 10 were included in this study. Table 1 displays their basic characteristics and the distribution of refractive parameters. The proportion of boys in the LCC group (65%) was significantly higher than that in the HCC group (45%; *P*=0.001). All corneal parameters, including CCR, Km, K_1, and K_2, were found to be statistically significantly different between the children in the LCC group and those in the HCC group (*P*=0.001). Additionally, children in the LCC group exhibited greater SE (*P*=0.013), and a lower prevalence of myopia (38%; *P*=0.001). However, the mean AL of children in the LCC group (24.33±0.81 mm) was significantly longer than that of the HCC group (23.50±0.83 mm; *P*=0.001).

Myopia Screening Results Whether they were myopic or not, some children had AL longer than the normal reference range. The 51% of children with myopia had the AL longer than the normal reference range for their age. In the LCC group, 499 out of 595 cases (84%) had AL measurements above the reference range. In the HCC group, 447 out of 1272 cases (35%) had AL measurements above the reference range (Figure 1). However, among non-myopia children in the LCC group, 234 out of 973 cases (24%) had AL measurements above the reference range. In the HCC group, 19 out of 1588 cases (0.012%) had AL measurements above the reference range (Figure 1).

SE with AL Correlation Analysis In both groups, there was an SE inflection point on the AL curves, which was more pronounced in the HCC group. The SE at the turning point was approximately -0.5 D in both groups. However, the AL was approximately 24 mm in the LCC group, which was at the upper limit of the normal reference range for AL. In contrast, the AL was approximately 23 mm in the HCC group, which fell within the normal reference range for AL. Before the turning point, AL growth had less of an impact on SE changes, whereas after the turning point, SE changes were more influenced by AL growth. After the onset of myopia (after the turning point), the change of SE in the LCC group was less affected by the increase in AL compared to the HCC group (Figure 2).

DISCUSSION

This work described the refractive parameters in 2214 school-age children with different CCs in Hangzhou. The results showed that, low CC could partially mask the decrease in SE and the increase in AL. Before the onset of myopia, the AL growth rate was even faster than that after the onset of myopia. Among Chinese school-age children, the prevalence, progression rate, and severity of myopia and high myopia were quite high. In China, the prevalence of myopia rose from 7.8% in grades 1 and 2 to 25.3% in grades 5 and 6, in a study of primary school students. Moreover, from 0.1% to 1.0%, high myopia was more common[13]. Based on our survey, 42% of grade 4 children had myopia, which was in line with the findings of Wang *et al*[14]. In teenagers between the ages of 16 and 18, the prevalence of high myopia rose from 10.5% in 2010–2013 to 19.4% in 2014–2016[15]. Remarkably, the HCC group's myopia rate (44%) was noticeably greater than the LCC group (38%). Studies on the prevalence of myopia in school-age children with various CCs do not yet exist. Several biometric and refractive characteristics, such as CC, lens thickness, and AL, affected the final refractive condition of the human eye[16]. The refractive parameters of children and adolescents constantly change as they grow and develop[17]. During the initial phases of eye development, there was a noticeable increase in the AL of the eye, which was accompanied by significant changes in refraction. Additionally, the curvature of the cornea flattens and the refractive power

Table 1 Demographic and ocular biometric data of Chinese school-age children of two groups

Parameters	Lower corneal curvature (*n*=1568 eyes)	Higher corneal curvature (*n*=2860 eyes)	*P*
Sex			0.001
Boys	1020 (0.65)	1272 (0.44)	
Girls	548 (0.35)	1588 (0.56)	
UCDVA (grade)	4.85±0.28	4.80±0.30	0.065
SE (D)	-0.48±1.46	-0.74±1.62	0.013
Am (D)	-1.16±0.55	-1.42±0.62	0.001
Myopia			0.001
No	973 (0.62)	1588 (0.56)	
Yes	595 (0.38)	1272 (0.44)	
AL (mm)	24.33±0.81	23.50±0.83	0.001
AL range			0.001
Normal AL	835 (0.53)	2394 (0.84)	
Long AL	733 (0.47)	466 (0.16)	
CCR (mm)	8.11±0.16	7.68±0.17	0.001
AL/CR	3.00±0.10	3.06±0.10	0.001
K_1 (D)	41.07±0.80	43.26±0.94	0.001
K_2 (D)	42.23±0.87	44.68±1.10	0.001
K_m (D)	41.65±0.78	43.97±0.97	0.001

UCDVA: Uncorrected distance visual acuity; SE: Spherical equivalent; Am: Corneal astigmatism; Myopia: The myopia referred to in this study was screening myopia with UCDVA<5.0 and SE≤-0.5 D; AL: Axial length; Normal AL: 21.26-24.32 mm was the normal AL reference range for 9-year-old children, and 21.52-24.50 mm was for 10-year-old children; Long AL: Exceeding 24.32 mm was defined as long AL for 9-year-old children, and exceeding 24.50 mm was defined as long AL for 10-year-old children; CCR: Corneal curvature radius; AL/CR: Axial length/corneal radius of curvature ratio; K_1: Horizontal corneal curvature; K_2: Vertical corneal curvature; Km: The mean of K_1 and K_2.

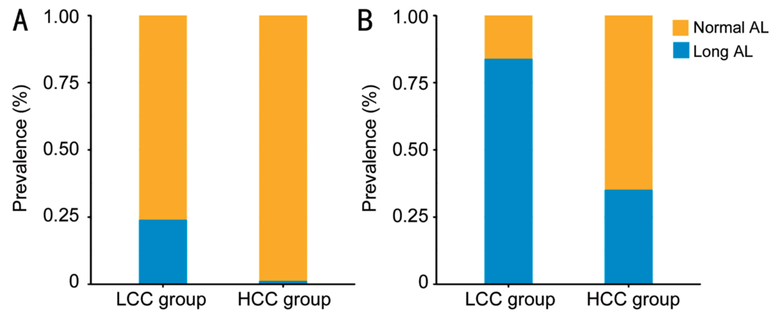

Figure 1 Refractive status and AL of children with different corneal curvatures A: Non-myopia; B: Myopia. Myopia referred to in this study was screening myopia with UCDVA<5.0 and SE≤-0.5 D; Normal AL: 21.26-24.32 mm was the normal AL reference range for 9-year-old children, and 21.52-24.50 mm was for 10-year-old children; Long AL: Exceeding 24.32 mm was defined as long AL for 9-year-old children, and exceeding 24.50 mm was defined as long AL for 10-year-old children. LCC: Lower corneal curvature; HCC: Higher corneal curvature; UCDVA: Uncorrected distance visual acuity; AL: Axial length.

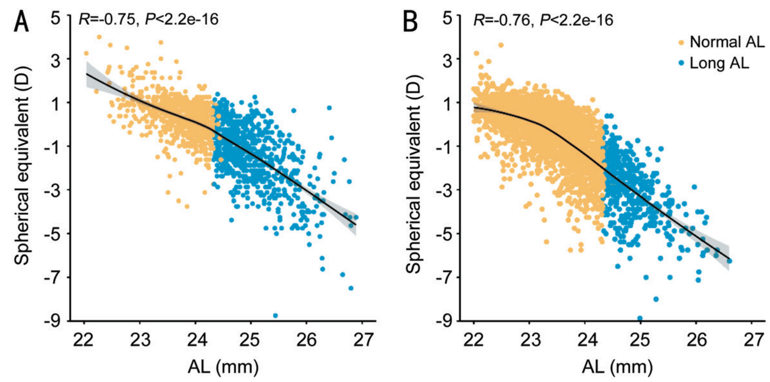

Figure 2 The relationship between AL and spherical equivalent in children with different corneal curvatures A: Lower corneal curvature; B: Higher corneal curvature. The gray area around the lines indicates the 95% confidence interval. Normal AL: 21.26-24.32 mm was the normal AL reference range for 9-year-old children, and 21.52-24.50 mm was for 10-year-old children; Long AL: Exceeding 24.32 mm was defined as long AL for 9-year-old children, and exceeding 24.50 mm was defined as long AL for 10-year-old children. AL: Axial length.

of the lens decreases[18]. By balancing variations in AL with other refractive parameters, such as the CC and lens thickness, the visual system maintains a normal refractive condition[19]. The results of domestic and international scholars showed that corneal dynamics were at a stable level after 2 years of age[20], and there was no significant difference in CC between different ages after that[21]. However, AL increased irreversibly with growth and development[22], reaching the adult level at the age of 13-14y[20]. Both of them, especially AL, played an important role in determining the final refractive status. A disproportionate relationship between refractive parameters is the primary source of most refractive errors. Our study found that both SE and AL were overall greater in the LCC group than in the HCC group. That means corneas were steeper in shorter eyes and flatter in longer eyes, a similar conclusion was made by Bushuyeva and Maliiva[23] and Hoon *et al*[20]. In line with earlier research[24], the LCC group displayed a final refractive state that was nearly emmetropia despite having a somewhat longer AL than the HCC group. This suggests that the lower CC may partially compensate for the longer AL. Despite AL elongation, an emmetropization impact may be the mechanism preventing myopic shift[20]. Higher CC and bigger AL/CR were risk factors for the development of myopia in children[25]. Possibly because the thick, flat cornea protects against myopia during preschool, and the corneas of myopic children were softer and more prone to deformation than those of emmetropia or hypermetropia[26]. Long *et al*[27] found statistical differences in corneal thickness and corneal biomechanical parameters in children with different refractive states. The structure and biomechanics of the cornea and sclera may be altered long before the onset of myopia. The balancing and matching of multiple refractive parameters in the eye so that the final refractive state tended to be emmetropia[28-29]. It could prevent myopia from further deepening. Even high myopia could have some degree of refractive compensation[28]. González Blanco *et al*[30] conducted a study of university students, the growth of the AL was the main morphological change in the eye during myopia progression, AL and CC were not completely independent variables, and both could change simultaneously without affected SE. During the progression of myopia, the radial elongation of the AL caused an increase in the volume of the eye and the transverse diameter of the cornea, causing the CC to flatten[31], and the decrease in CC could compensate for the myopic refractive changes produced by mild AL growth. The present study found that girls have shorter AL and greater CC compared to boys. Other studies have also reported similar findings[32]. When the growth of the AL exceeded a certain limit, such as in high myopia patients, the effect of reduced CC to compensate for the increase in myopia tended to gradually disappear[30]. While the overall morphology of the cornea becomes steeper, and the CC increases due to the elongation of the ocular wall[33]. According to the study of Chinese adults with high myopia by Jin *et al*[28], 28 mm was the AL limit that the changes in corneal (such as reduction of CC, thickness, and volume) parameters provide a refractive compensation effect on myopia. When AL>28 mm, such compensation did not exist. The results of this study indicated that the relationship between SE and AL changes when the AL exceeds 23-24 mm. In other words, while the AL had exceeded the normal range, the refractive compensation caused by the reduction of CC was partially lost.

We defined school screening myopia as school-age children with UCDVA<5.0 and non-cycloplegic refraction SE≤-0.50 D[12]. In our study, we found that the rate of children with non-screening myopia was higher in the LCC group than in the HCC group, and the percentage of their AL exceeded the normal reference range was significantly higher in the LCC group compared to the HCC group. Li *et al*[34] observed that the prevalence rate of high myopia defined by AL was higher than that defined by SE, which was evidence that lower CC could mask to some extent the decrease in SE and increase in AL. According to the study[1], the prevalence rate of myopia in preschool children was low in China as well as in Europe, but increased with age as they entered the school years. Slowing the rate of myopia progression was a central goal of myopia-related research, but preventing the onset of myopia was even more valuable[35]. The vast majority of myopia in adolescent children was axial myopia, and when the magnitude of AL growth could be matched with other refractive parameters during children's growth and development, the myopic refractive changes brought about by AL exceeding the normal reference range were likely to be masked by the lower CC[36], according to the most commonly used myopia screening methods, UCDVA and non-cycloplegic refraction, resulting in the development of myopia not being detected and controlled in a timely and effective manner. Myopia was the result of a combination of genetic and environmental factors, current SE was the best single predictor of future myopia status[34]. The earlier the age of onset of myopia in children, the faster myopia progresses[37] and the more likely it is to progress to high myopia, even with vision-threatening fundus changes[38]. The prevalence rate of high myopia among children in China climbed year by year between 2014 to 2018[34], and children with low CC and long AL were much more likely to develop pathological retina changes and thus jeopardize their visual acuity if they were not effectively prevented and controlled[39]. The ocular biometric measures were not affected by accommodation, so it could be obtained from modern biometers objective and reliable results under noncycloplegic conditions[1]. The measurement process of AL was simple, easy to perform, and highly acceptable to patients. Dynamic monitoring of AL helped to detect myopia promptly[40].

In this study, the analysis of school-age children with different CCs revealed that the correspondence relationship between AL and SE in different ranges was not the same, and was not linearly correlated. When the AL was before the turning point, SE changes were less affected by AL growth. It means that before the onset of myopia, AL showed a rapid growth trend, and its growth rate was even faster than that after the onset of myopia, Rozema *et al*[17] had the same discovery. Whereas after the turning point (after the onset of myopia), there was a linear correlation between SE and AL. The change of SE in the LCC group was less affected by the increase of AL than that in the HCC group. It illustrates that the same magnitude of AL growth exhibits a smaller change in SE, that was, low CC could be able to mask AL growth. Thus, the study of the AL and SE correspondence in myopic patients required different AL nodes according to different CCs. In a study of preschool children aged 3-6y, Guo *et al*[41] found that for every 1 mm increase in AL, there was a 0.45 D increase in myopia. Meng *et al*[42] finding that a 1 mm increase in AL would result in a myopic progression of 2.00 to 2.50 D in the absence of other compensations. Different scholars have different results on the relationship between AL and SE, which might be due to their different research objects. Children aged 3-6y were mostly in the state of hypermetropia or pre-myopia and were in the stage of rapid growth and development, so AL increases rapidly. Itoi *et al*[43] and Yu *et al*[44] suggested that the increase in AL was correlated with age and SE, and there was a decreasing trend of AL increase with age, especially for people over 15 years old[45].

Also, this study found the SE corresponding to the turning point was about -0.5 D in both groups, while the corresponding AL was about 24 mm in the LCC group and 23 mm in the HCC group. This seems to indicate that the turning point was the point at which myopia occurs. Interestingly, this was very similar to the mean AL at onset reported by the Rozema *et al*[17]. The turning point in the HCC group was within the normal AL range, that was, myopia had occurred or was about to occur while AL was still in the normal range. But for the LCC group, the turning point was at the upper limit of the normal reference range, that was, myopia would occur when

AL was about to exceed the normal reference range. Some researchers speculated that the flattened CC may compensate for the rapid elongation of the AL during the preschool period[46]. In children who were still growing and developing, the biological parameters of the eye were in a dynamic process of change during the emmetropization[19]. It was also because of the emmetropization effect, that the growth of AL would slow down after myopia, the same change in SE was accompanied by less AL growth. The initial AL of children with lower CC was longer, so the AL was also larger when myopia occurred. Therefore, children with lower CC may have longer AL than those with higher CC when they enter school age.

While cycloplegic refraction was the gold standard for the diagnosis of myopia because children were more capable of adjusting[47]. However, it was more difficult to collect cycloplegic refraction data than collect ocular biometric parameter values in children, suggesting that ocular biometric parameter values may be a more realistic alternative data source[46]. Some studies have shown that the AL/CR was an objective measure, and had high sensitivity and specificity in the evaluation of ametropia[33]. The changes of AL and CC could be expressed through the AL/CR, which could effectively reflect the current refractive state of the subject[48], the AL/CR had a higher diagnostic value for myopia than non-cycloplegic refraction alone or AL and CC alone[49]. If the cut-off values for AL/CR were broken down by age group, the sensitivity and specificity in diagnosing myopia would be further enhanced[1]. Jong *et al*[25] believed that the AL/CR was of some value in differentiating different grades of myopia (high myopia or low myopia).

These results suggested the importance of preventing myopia at the pre-myopia stage, AL and AL/CR screening might helped prospectively identify children at risk of myopia[19]. Monitoring changes in AL/CR could help identify children at risk for myopia. Prevention advice should be given to children at high risk and the onset of myopia should be closely monitored so that myopia prevention and control can be applied on time. Myopia prevention and control should also be highly focused on the growth of AL. In the case of the rapid growth of AL, stronger controls needed to be switched or overlaid to minimize the possibility of high myopia and reduce the risk of complications of high myopia. We recommend that CC and AL be included as indicators for myopia screening in young children.

The innovation of this study was to group children according to their different CC and compare each refractive parameter, as well as the correlation between them. There were significant differences in refractive parameters among children with varying CC, and the relationship between each parameter was also distinct. Our study also had several limitations. First, it was important to note that the current study was cross-sectional. Therefore, it was not possible to establish a causal relationship between the development of myopia and changes in ocular refractive parameters, such as CC. Second, due to the limitation in the study conditions, sufficient cycloplegia was not performed, which may have led to an increased incidence of myopia. Third, the lens power also plays an essential role in the final refractive state[46]. However, this study did not consider these factors.

In conclusion, for individuals, it is important to conduct a comprehensive evaluation of CC in conjunction with their own AL, as AL/CR may serve as an indicator of potential cognitive concerns. A lower CC may partially mask a decrease in SE and an increase in AL, and the patterns of AL growth tend to be more variable in children with lower CC than in those with higher CC. Meanwhile, the rate of AL growth should be closely monitored before the onset of myopia. The AL has been shown to exhibit a rapid growth trend before the onset of myopia, with a growth rate even faster than that observed after the onset of myopia. Emphasis was placed on managing the eye health of preschool children, detecting early signs of myopia, and developing interventions to reduce the occurrence and progression of myopia, especially high myopia.

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