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Associations between refraction and ocular biometry in 3-to 6-year-old preschoolers: The Beijing Shunyi Children Eye Study

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Associations between refraction and ocular biometry in 3-to 6-year-old preschoolers: The Beijing Shunyi Children Eye Study

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Abstract

Purpose: To estimate the associations between refraction and ocular biometry of preschool children (3-6 years old) in Shunyi District, Beijing.

Design： Cross-sectional study.

Participants: A total of 1141 Chinese children aged 3-6 years old completed the examination. 555 subjects (48.6%) were boys and 586 subjects (51.4%) were girls.

Methods: Children aged 3-6 years old selected from 11 kindergartens were enrolled in this cross-sectional study. Cycloplegic refraction, axial length (AL), anterior chamber depth (ACD) and corneal radius (CR) were measured for all children. AL-to-CR ratio, lens power (LP) and spherical equivalent (SE) were calculated. Those children were divided according to SE into 3 groups: hyperopia group, pre-myopia group and myopia group.

Results: The prevalence of myopia, pre-myopia, and hyperopia was 2.7%, 27.3%, and 70.0% respectively. The mean SE was (1.15±0.76) D, and the refraction in the pre-myopia group was about 1D lower than in the hyperopic one. The mean CR was 7.74±0.25mm and remained stable. The mean AL, ACD, AL/CR, and LP was 22.28±0.67mm, 3.33±0.67mm, and 2.88±0.06, and 25.62±1.46 D respectively. AL, ACD and AL/CR increased with age, while LP decreased with age. Pre-myopic children had longer eyes, greater anterior chamber depths, and higher AL/CR ratio than hyperopic children.

Conclusion: The most common refractive status of 3-6-year-old children in Shunyi District, Beijing was hyperopia. The prevalence of pre-myopia was by no means low. The refraction remained stable within this age range, suggesting reduction in lens power might have balanced the growth of axial length and anterior chamber depth.

Keywords: preschool children, refractive errors, myopia, axial length

Strengths and limitations of this study:

1.Pre-myopia is a non-myopic refractive status that may progress to myopia. There are fewer large-scale refractive data about pre-myopia in preschoolers.

2.Understanding differences in ocular biological parameters between pre-myopic and hyperopic children helps with early myopia prevention.

3.The lens power was figured out by means of Bennett-Rabbetts formula but the lens thickness was not measured.

Introduction

Individual refractive development is dynamic throughout life. Children are born with a peak of approximately +2.00D hyperopia, and the peak moves toward emmetropia over the first 2 years after birth.[1]However, studies of children refractive development in large populations suggest that emmetropia is not the natural endpoint of this process.[2]The ocular components such as corneal and lens power, anterior chamber depth and axial length are crucial in the refractive development. It is the balance between these ocular components that determines the refractive status.[3]After 3 years of age, AL and ACD increased with limited changes in corneal power but significant decreases in lens power.[4] Studies have shown that one of the main determinants of refractive status is axial length.[5] Myopia may develop when rapid increase in axial length exceeds the compensatory capacity of the lens.

Refractive error in children has been one of the global public health problems nowadays and myopia accounts for a large proportion of refractive error.[6] In recent decades, the onset of myopia among children has displayed a trend of younger age, 10.7% of preschoolers aged 5 to 6 years suffered from myopia in Taiwan,[7] the overall prevalence of pre-myopia was high among preschoolers[8]. Children with an adequate physiologic hyperopia refraction, defined as “hyperopic reserve,” are unlikely to become myopic.[9] In 2019, the International Myopia Institute (IMI) defined “pre-myopia” as “refraction≤0.75D and >-0.50D” in children.[10] Prior to the onset of myopia, rapid changes in refraction and ocular components may provide predictive information.[11] One longitudinal study reported that lens power loss suddenly slowed down one year before the onset of myopia combined with relatively high rate of axial elongation.[12]

For these reasons, there is an urgent need to identify children at high risk of early myopia. The optimal time for myopia prevention should be earlier than elementary school age. However, there are fewer large-scale refractive data available on children aged 3-6 years, not to mention data about pre-myopia in preschoolers. Therefore, this study was conducted to evaluate the refraction and ocular components of preschool children. Understanding the pre-myopic refractive status and identifying the associated factors can provide guidance for early prevention. Further objectives include investigating the relationships between refraction and the ocular biometric parameters involved in refractive development.

Methods

1. Study Design and Subjects. This was the first-year results of the 3-year longitudinal study with evaluation of subjects aged 3-6 years from Shunyi District, Beijing. Based on a previously published myopia prevalence rate in preschool children aged 3-6 years,[13] a sample size of 1107 preschoolers was needed to achieve precision of 0.01 and 95% confidence intervals, taking into account a cluster design effect of 1.5 and assumed dropout rate of 10%. Stratified cluster sampling was employed. Shunyi District is situated in the suburban northeast region of Beijing. Under the support of the preschool section of the Shunyi District Education Commission, a total of 1186 children were randomly selected from 11 kindergartens in Shunyi District. Data for all the participants were collected from October 2020 to June 2021. Children who have any history of Down’s syndrome, epilepsy, history of ophthalmologic surgery, and other psychiatric

disorders were excluded. 1141 children aged 3–6 years who finished all the examinations were carefully analyzed one by one in this study.

2. Ethics Statement. The study received approval from the Ethics Committee of Beijing Shunyi Hospital (No.2020125). The research was conducted in conformity with the Declaration of Helsinki. Before the examination, the parents were all well informed of the study's objectives, the examination procedure, and the possible consequences, and of course, we received written informed consent from each and every parent.

3. Examination. Prior to the examination, all the relevant information such as the patient's age and gender were recorded. Visual acuity at a 5-m distance was measured using an international standard E chart (Guangdong Yuehua Medical Instrument Factory) in a well-illuminated room. Anterior Segments were examined with a slit lamp. Auto refraction and corneal radius were checked using a desktop autorefractor (model number: KR-8800; Topcon Corporation, Tokyo, Japan). Biometric examination was performed with the Lenstar LS 900 (Haag-Streit, Switzerland) prior to cycloplegia. Ocular biometric parameters including axial length (AL) and anterior chamber depth (ACD) were checked three times, with an automatic calculation of the average in each eye. A concentration of 1% cyclopentolate (Alcon, USA) was used to carry out the examination of cycloplegia. After 30 minutes, if the pupil diameter was ≥6 mm and there was no light reflex, three successive measurements of refraction were taken. Fundus photography was applied and no abnormality was found in the fundus examination. All examinations were carried out by ophthalmologists and optometrists who had undergone uniform training.

4. Definition. Both spherical power and cylindrical power were measured following cycloplegia. The average of three measurements was taken to calculate the equivalent spherical (SE) refraction. SE is equal to half the cylindrical power plus the spherical power. The Bennett-Rabbetts formula[14] was used to figure out the lens power(LP). Since the high correlation between the right and left eyes, data from the right eyes were chosen in the present study. The mean of the longest and shortest corneal radius (CR) of curvature was used to figure out the CR. The definition of the axial length/corneal radius (AL/CR) ratio was the axial length divided by the mean corneal radius. Based on IMI definition,[10]myopia was defined as SE ≤ −0.50 D, pre-myopia as −0.50 D < SE ≤0.75 D, and hyperopia as +0.75 D< SE.

5. Statistical Analysis. The chi-square test was performed to compare the prevalence of refractive error among different age groups. The mean values of SE refraction, AL, ACD, CR, AL/CR and LP between boys and girls were compared respectively using an independent sample t-test. To find out the differences of ocular biometric components across different age groups and refractive error groups, analysis of variance (ANOVA) was employed. The multiple linear regression model was used to figure out the correlations between SE refraction and ocular biometric components. Statistical significance was defined as P values < 0.05. SPSS 26.0 (IBM SPSS Inc., USA) was used to carry out statistical analyses.

Results

Among the 1186 sampled children who planned to undergo examinations, 1141 completed the cycloplegic refraction and ocular biometric examination after exclusions. The mean age of these subjects was 4.52± 0.87 years. 555 subjects (48.6%) were boys and 586 subjects (51.4%) were girls. It can be summarized from the data in Table 1 that the prevalence of myopia, pre-myopia, and hyperopia was 2.7%(95%CI,1.8-3.7), 27.3%(95%CI,24.7-29.8), and 70.0%(95%CI,67.4-72.7) respectively.

Table 1. Prevalence of refractive errors in 3-to 6-year-old children

N(%)	Myopia(≤-0.5D)	Pre-myopia(>-0.5D and ≤0.75D)	Hyperopia(>0.75D)	P value
Total	31(2.7)	311(27.3)	799(70.0)	0.735
3y	5(4.2)	27(22.7)	87(73.1)	
4y	10(2.1)	140(28.9)	335(69.1)	
5y	11(3.0)	96(26.5)	255(70.4)	
6y	5(2.9)	48(27.4)	122(69.7)	

Table 2 displayed the mean, standard deviation of the SE refraction, AL, ACD, CR, AL/CR and LP of all participants. The mean SE refraction was 1.15±0.76D, and it remained stable during this age range. No significant gender differences were found among different age groups.

AL, ACD and AL/CR increased while LP decreased with age. The mean AL was 22.28±0.67mm, which increased from 22.07 to 22.49mm. The mean ACD was 3.31±0.25mm, which ranged from 3.21 to 3.36mm. Both AL and ACD increased with age, when the data was split by gender, we found out the same trend. The mean value of CR was 7.74±0.25mm. CR did not change with age, but it was higher in boys at 4 to 6 years (p<0.001). AL/CR increased with age and the mean value was 2.88±0.06, which increased from 2.85 to 2.91. The AL/CR in boys were higher than in girls at age 3 to 5 years (p<0.01). The mean LP was 25.62±1.46D, which decreased from 26.50 to 24.96D. It was also lower in boys in all age groups (p<0.001). Compared with girls, boys had 0.51mm longer AL, 0.13mm greater ACD and 1.02D lower LP.

Table 2. Distribution of the ocular biometric parameters in different age groups

	Age(yrs)				Total	P Value
Parameters	3	4	5	6		
Spherical equivalent refraction (D)						
Total	1.15±0.85	1.17±0.75	1.15±0.76	1.08±0.71	1.15±0.76	0.608
Boys	0.97±0.96	1.16±0.73	1.12±0.78	1.07±0.78	1.11±0.78	0.411
Girls	1.32±0.68	1.18±0.78	1.19±0.73	1.08±0.65	1.18±0.74	0.267
P value	0.025	0.750	0.375	0.944	0.143	
Axial length (mm)						
Total	22.07±0.55	22.20±0.65	22.35±0.67	22.49±0.68	22.28±0.67	<0.001
Boys	22.30±0.5	22.46±0.6	22.63±0.6	22.78±0.5	22.54±0.64	<0.00

	9	4	5	9		1
Girls	21.85±0.47	21.93±0.56	22.09±0.57	22.26±0.66	22.03±0.59	<0.001
P value	<0.001	<0.001	<0.001	<0.001	<0.001	
Anterior chamber depth (mm)						
Total	3.21±0.25	3.29±0.25	3.35±0.24	3.36±0.24	3.31±0.25	<0.001
Boys	3.30±0.22	3.36±0.25	3.41±0.23	3.44±0.24	3.38±0.24	0.003
Girls	3.12±0.24	3.22±0.23	3.30±0.24	3.30±0.22	3.25±0.24	<0.001
P value	<0.001	<0.001	<0.001	<0.001	<0.001	
Corneal radius (mm)						
Total	7.75±0.25	7.74±0.26	7.73±0.24	7.74±0.27	7.74±0.25	0.854
Boys	7.77±0.26	7.81±0.26	7.79±0.24	7.82±0.25	7.80±0.25	0.724
Girls	7.73±0.24	7.66±0.24	7.67±0.21	7.68±0.27	7.67±0.24	0.258
P value	0.354	<0.001	<0.001	<0.001	<0.001	
Axial length-to-corneal radius ratio						
Total	2.85±0.07	2.87±0.06	2.89±0.06	2.91±0.06	2.88±0.06	<0.001
Boys	2.87±0.07	2.88±0.06	2.90±0.06	2.91±0.06	2.89±0.06	<0.001
Girls	2.83±0.06	2.86±0.06	2.88±0.05	2.90±0.05	2.87±0.06	<0.001
P value	<0.001	<0.001	<0.001	0.073	<0.001	
Lens power (D)						
Total	26.50±1.34	25.90±1.42	25.30±1.37	24.96±1.38	25.62±1.46	<0.001
Boys	25.99±1.31	25.37±1.32	24.72±1.31	24.40±1.12	25.08±1.37	<0.001
Girls	27.00±1.18	26.41±1.32	25.82±1.21	25.38±1.42	26.10±1.38	<0.001
P value	<0.001	<0.001	<0.001	<0.001	<0.001	

As is shown in Figure 1, similar trends with age were detected in pre-myopia and hyperopia group. SE and CR remained stable from 3 to 6 years in both groups. AL, ACD, AL/CR increased with age while LP decreased with age. The difference in mean SE refraction between the two groups was about 1.06D. Pre-myopic children were approximately 0.28mm longer in AL, 0.12mm greater in ACD, 0.41D higher in LP compared to their hyperopic peers ($P<0.05$). The difference in AL/CR ratio between the two groups was about 0.04 unit, which was higher in pre-myopia group. The AL in myopia group at age 4 was shorter along with steeper CR than in pre-myopia group. However, when the data was calculated with AL divided by CR, a different result was obtained. Myopic children had higher ratio of AL/CR than children from pre-myopic and hyperopic groups. No statistical differences were observed in CR for different refractive groups.

As can be seen from Figure 2, SE was negatively correlated with AL, ACD, and LP. There was a significant negative correlation between SE and AL/CR, (r=-0.56,p<0.001). A strong positive correlation was found between AL and CR. There was a significant positive correlation between AL and ACD, and a negative correlation between AL and LP.

Multiple linear regression models were established to indicate the associations between SE and ocular biometric parameters (Table 3). After being adjusted for age and gender, SE decreased linearly with increasing AL, with a -0.455D change in SE for a 1mm increase in AL. SE decreased linearly with increasing AL/CR, with a 0.1 unit increase in AL/CR associated with -0.72D change in SE. AL variable only explained 13.3% of the variance of SE, while the AL/CR variable accounted for 31.3% of the variance of SE, which was better than AL variable. The model explained 39.9% of the variance in SE when both AL and CR were included. Model 4 explained 84.5% of the variance in the SE when the model took into consideration AL, CR and LP. The results suggested that SE was associated negatively with AL and LP but positively associated with CR.

Table 3. Linear regression models for SE refraction and ocular biometric parameters (adjusted for age and gender, boys as reference)

	Model 1 (n=1141)		Model2 (n=1130)		Model3 (n=1130)		Model4 (n=1019)	
Variables	β	P value	β	P value	β	P value	β	P value
Age(yrs)	0.043	0.079	0.114	<0.001	0.164	<0.001	0.041	<0.001
Gender	-0.169	<0.001	-0.085	0.025	-0.273	<0.001	-0.110	<0.001
AL(mm)	-0.455	<0.001			-1.246	<0.001	-2.263	<0.001
CR(mm)					2.499	<0.001	4.006	<0.001
AL/CR ratio			-7.203	<0.001				
Lens power(D)							-0.492	
R^2	0.133		0.313		0.399		0.845	

Discussion

In this study, the overall refraction remained hyperopic but the ocular biometric parameters including AL, ACD and LP changed significantly from 3 to 6 years old, suggesting reduction in lens power might have balanced the growth of axial length and anterior chamber depth. The refraction in the pre-myopic group was about 1D lower than in the hyperopic group. Compared to hyperopic children, pre-myopic children had longer eyes, greater anterior chamber depths, higher AL/CR ratio but similar CR.

The increase in myopia is widely believed to be driven by environmental factors such as fewer outdoor activities and more near-work activities. Genetic susceptibility also plays a role in myopia.[15] Pre-myopia is a non-myopic refractive status that may progress to myopia. By realizing the relevant risk factors and taking appropriate intervention measures, we can achieve the goal of preventing or at least delaying the onset of myopia. In this study, the overall prevalence of pre-myopia was 27.3%, which was slightly higher than in Shanghai (21.9%).[16] An analysis of the data from children aged 4-6 years who were screened between 2005 and 2021 showed a significant increase in the prevalence of pre-myopia (19.0% vs. 26.5%).[17]

In the present study, the mean SE refraction was 1.15D, which was slightly lower than that of Guangzhou (1.42±0.79D)[18] and Shenzhen (1.37±0.63D),[19] but which was similar to that of Shanghai (1.20±1.05D).[20] The results suggest that the refractive development of 3-to 6-year-old children remained mildly hyperopic in Shunyi District, Beijing. The refraction in the pre-myopic group was 0.44±0.32D, which was about 1D lower than that in the hyperopic group. The study on the prevalence of pre-myopia in preschoolers in Taiwan suggested that the mean SE in the pre-myopia group was 0.35 ± 0.33D.[8] The Taiwan study did not use 1% cyclopentolate for cycloplegic auto-refraction, which may have contributed to the difference in SE refraction. Early educational pressure, such as assignments for preschoolers and extensive tutorial classes after school hours,[21] lead to early depletion of hyperopia reserve. Therefore, investigation of hyperopia reserve as well as regular monitoring of refraction are significant for myopia prevention.

During the rapid development of infant eyes in the first few years, lower mean levels of hyperopia and early refractive error changes, axial elongation and deepening of the anterior chamber are synchronized with corneal flattening and lens power reduction.[22] Previous studies have suggested that corneal flattens with age to compensate for the growth of axial length.[23] In order to find out the relationship between corneal curvature and refraction, researchers recorded different results. Zhang et al[20] found that the mean CR increased with age in boys but not in girls among preschoolers. No significant difference was found in CR between different ages in this study. This finding is consistent with that of Ma et al[24] who observed 1-year change in CR was 0.00± 0.04mm in 3-5 years old children, indicating very little change in this period. Zadnik et al[25] reported that CR remained stable in different age groups and was higher in boys than in girls. In age groups 4-6, the mean CR was 0.13mm higher in boys than in girls.

Since corneal power was reported to cause small changes after year 2,[26] axial length and lens power were the determinant factors of SE. The axial length in newborns is approximately 16.5mm,[27] which rapidly develops to 20 mm at 9 months and reaches 21.42 mm at 3 years of age.[28] The mean axial length of children in this study was 22.28±0.67mm. AL increases with age in children aged 3-6years, and it is 0.51 mm longer in boys than in girls. Similar finding was reported by He et al[29]. There was negative correlation between AL and SE. Axial length increased while refraction decreased. The axial length in pre-myopia group was significantly longer than that of hyperopia. In accordance with previous findings,[30] a strong positive correlation was found between AL and CR.

The current investigation found that the development of children's eyes was characterized by reduction in LP and the growth of AL and ACD. There was significant difference in ACD in different refractive error groups. Anterior chambers deepen gradually and sequentially among preschoolers from hyperopia group to myopia group. The deepening of ACD may also have something to do with lens thinning. The reduction in lens power can largely counteract the myopic shift caused by the lengthening of the eye.[3] There was no significant difference in SE between different age groups, which indicated that LP reduction associated with AL and ACD growth can counteract the myopic drift. LP was negatively associated with AL, and the change in LP is one of the main factors affecting the early progression of refractive status. Compared with girls, boys had longer axial length, greater anterior chamber depth, and lower lens power. These findings are in line with those of previous studies[19 25 31].

Some children with relatively short eyes might be myopic, such as the myopic children from the 4-year-old group in this study. However, the sound conclusion can be reached after the AL/CR was obtained. This finding confirmed that compared with AL, AL/CR can more accurately reflect the real refractive status.[29] AL/CR≥3 suggests that myopia has occurred.[32] He et al[29] examined 3922 children aged 6-12 years old in Shanghai, analyzed their data by ROC curves and found AL/CR greater than 2.99 was diagnostic of myopia. This study suggested that the mean AL/CR ratio was 2.88±0.06. In myopia group, the mean AL/CR was 2.98±0.06, and it was higher in boys than in girls (3.00±0.06 vs 2.95±0.05). AL/CR increased gradually with age, and elongation of AL also occurred among preschoolers in pre-myopia and hyperopia group. In myopia group, AL/CR increased from 2.95 to as much as 3. Among myopic children, who are younger than 6, the values of AL/CR were less than the reported threshold of 2.99. In pre-myopia group, AL/CR increased from 2.89 to 2.93. In hyperopia group, AL/CR was the lowest, and its ratio was less than 2.90. Therefore, the setting up of the age-specific thresholds of AL/CR will improve accuracy of myopia screening, particularly for preschoolers. Apart from changes with age, significant gender differences were detected in AL/CR. Boys aged 3-5 years had an average 0.02unit higher AL/CR ratios than girls. One recent study reported the age and gender specific percentile growth curves for AL and AL/CR in Chinese children, AL and AL/CR were narrowly distributed in the population at 4 years of age.[33] An Irish study assessing risk factors associated with pre-myopia showed that participants with >2 hours/day of screen time [2.92 (0.09)] had significantly higher AL/CR ratios than those with ≤2 hours/day [2.88 (0.08)].[34] Clinicians and parents should pay more attention to children with relatively high AL/CR ratio and provide more timely, useful lifestyle guidance in the prevention of the onset of myopia.

Admittedly, there are some limitations in our study. One point is that the lens power was figured out by means of Bennett-Rabbetts formula but the lens thickness was not measured. Another point is that our investigation was a cross-sectional one, two follow-up visits were conducted annually to evaluate the changes in refraction and ocular biometric parameters over time. The first-year data is of great importance because it can well illustrate the baseline distribution of ocular biometrics and lay a firm foundation for more scientific researches in the future.

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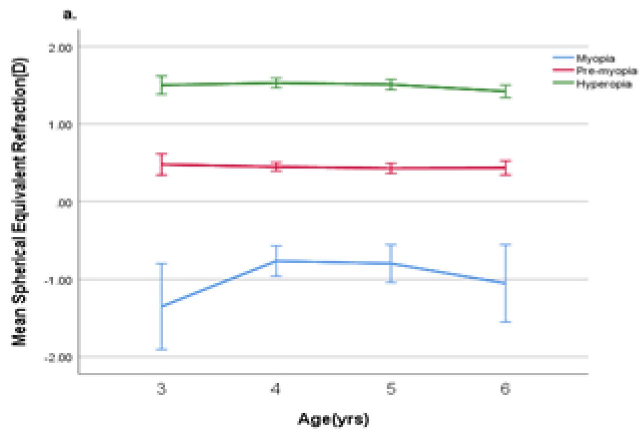

Figure 1. a.Mean values of SE refraction and ocular biometric parameters among different age and refractive error groups. a. Mean values of SE refraction among different age groups.

86x56mm (96 x 96 DPI)

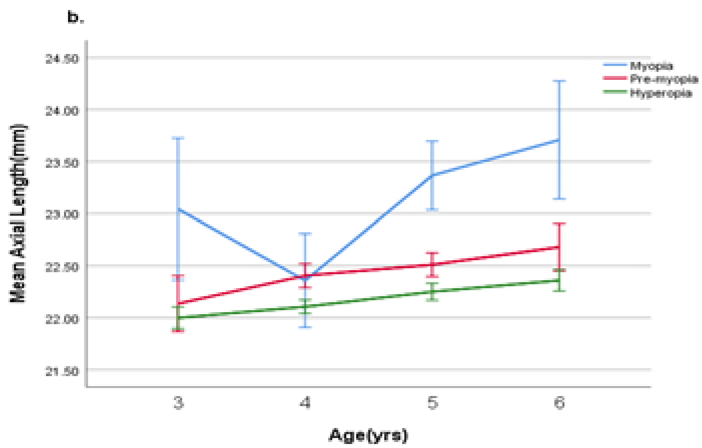

Figure 1.b. Mean values of AL among different age groups.

95x59mm (96 x 96 DPI)

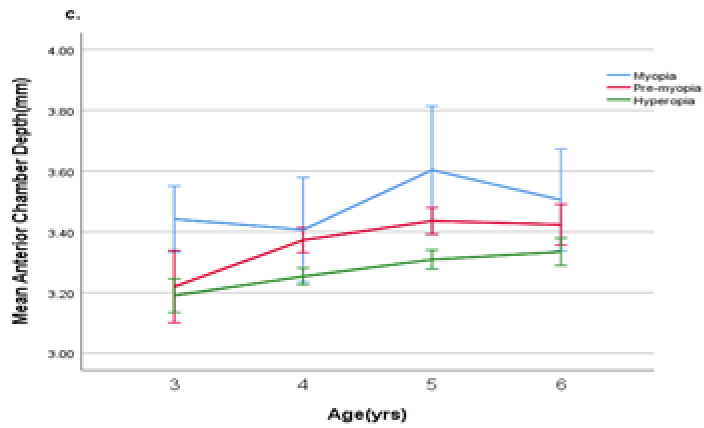

Figure 1.c. Mean values of ACD among different age groups.

93x56mm (96 x 96 DPI)

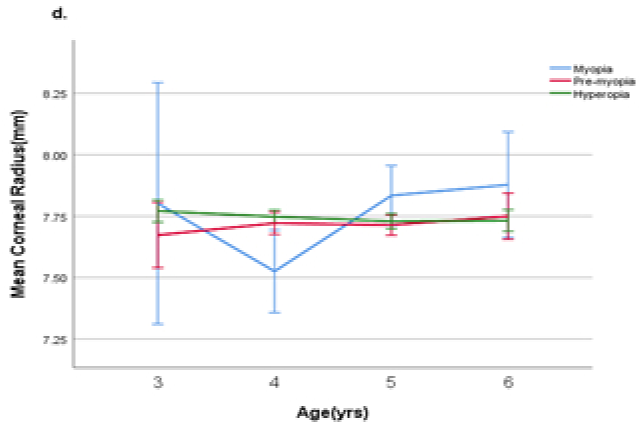

Figure 1.d. Mean values of CR among different age groups.

84x57mm (96 x 96 DPI)

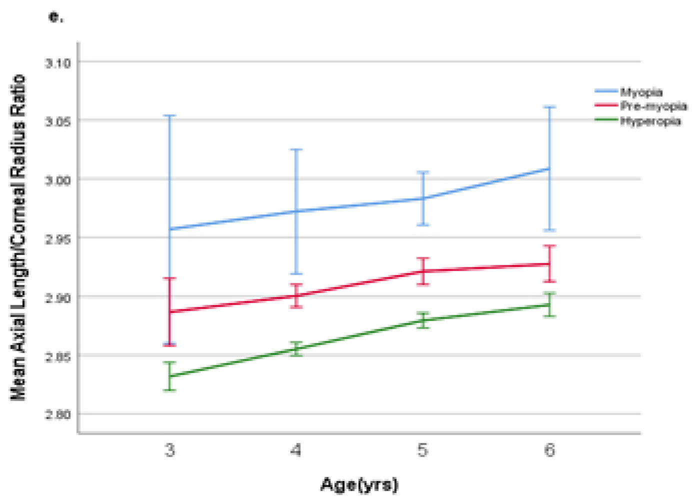

Figure 1.e. Mean values of AL/CR among different age groups.

92x66mm (96 x 96 DPI)

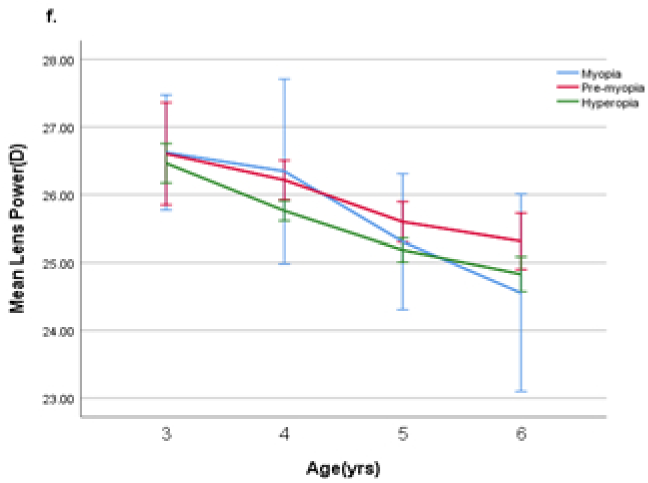

Figure 1.f. Mean values of LP among different age groups.

86x64mm (96 x 96 DPI)

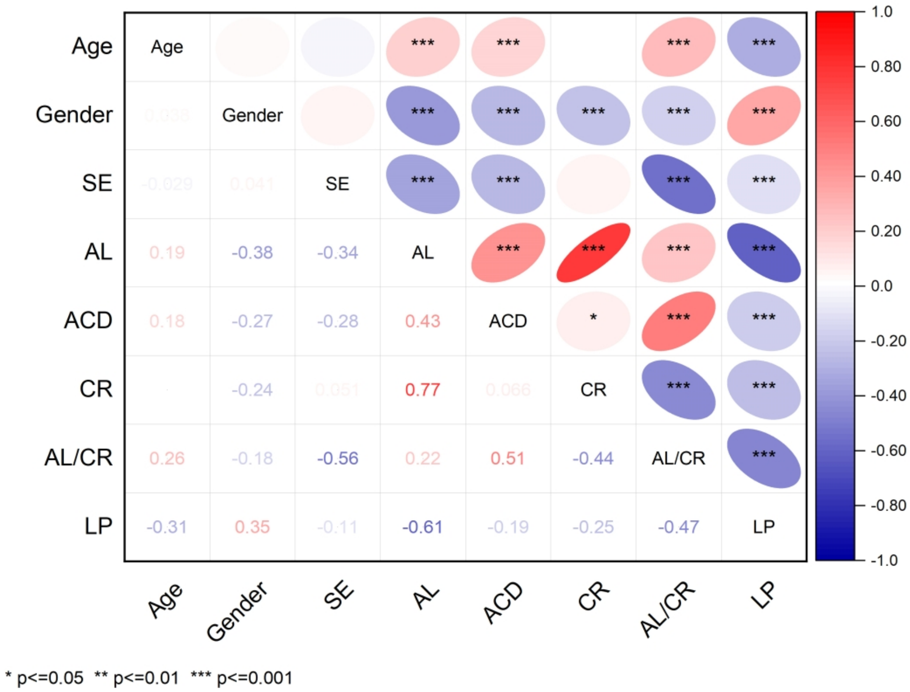

Figure 2.Correlation between SE refraction and ocular biometric parameters. Correlation values shown in lower Triangular.

850x651mm (96 x 96 DPI)

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Associations between refraction and ocular biometry in Chinese preschoolers aged 3-6 years: a cross-sectional study in Shunyi, Beijing

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Associations between refraction and ocular biometry in Chinese preschoolers aged 3-6 years: a cross-sectional study in Shunyi, Beijing

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ABSTRACT

Objective To estimate the associations between refraction and ocular biometry of preschool children (3-6 years old) in Shunyi District, Beijing.

Design Cross-sectional study.

Setting This study was conducted in 11 kindergartens in Shunyi District,Beijing.

Participants A total of 1186 Chinese children aged 3-6 years old without any history of Down’s syndrome,epilepsy,history of ophthalmologic surgery and other psychiatric disorders disorders were selected.Exclusions: Children who were unable to coorperate with the examination.1141 preschoolers completed the examination. 555 subjects (48.6%) were boys and 586 subjects (51.4%) were girls. Cycloplegic refraction, axial length (AL), anterior chamber depth (ACD) and corneal radius (CR) were measured for all children. AL-to-CR ratio, lens power (LP) and spherical equivalent (SE) were calculated.Those children were divided according to SE into 3 groups: hyperopia group, pre-myopia group and myopia group.

Interventions None.

Primary and secondary outcome measures Refraction and ocular biometric parameters.

Results The prevalence of myopia, pre-myopia, and hyperopia was 2.7%, 27.3%, and 70.0% respectively. The mean SE was (1.15±0.76) D, and the refraction in the pre-myopia group was about 1D lower than in the hyperopic one. The mean AL, ACD, CR, AL/CR, and LP was 22.28±0.67mm, 3.33±0.67mm, 7.74±0.25mm, 2.88±0.06, and 25.62±1.46 D respectively. Differences in AL, ACD ,AL/CR and LP among different age groups were statistically significant.. Pre-myopic children had longer eyes, greater anterior chamber depths, and higher AL/CR ratio than hyperopic children.SE was negatively correlated with AL, ACD, AL/CR and LP.

Conclusions The most common refractive status of 3-6-year-old children in Shunyi District, Beijing was hyperopia. The prevalence of pre-myopia was by no means low. Understanding refractive status of preschoolers and associations between ocular biometric parameters and refraction might be helpful in providing more effective prevention before the onset of myopia.

Strengths and limitations of this study:

1.This study utilized a random sample of preschool children in a suburb of Beijing,China..

2.The study participants were children aged 3- 6 years, generally considered to be the period before the onset of myopia.

3.The study participants included students exclusively from kindergartens and may not be representative of children not enrolled in these educational settings.

4.The cross-sectional design limits the ability to establish causality.

Introduction

Individual refractive development is dynamic throughout life. Children are born with a peak of approximately +2.00D hyperopia, and the peak moves toward emmetropia over the first 2 years after birth.[1]However, studies of children refractive development in large populations suggest that emmetropia is not the natural endpoint of this process.[2]The ocular components such as corneal and lens power, anterior chamber depth and axial length are crucial in the refractive development. It is the balance between these ocular components that determines the refractive status.[3]After 3 years of age, AL and ACD increased with limited changes in corneal power but significant decreases in lens power.[4] Studies have shown that one of the main determinants of refractive status is axial length.[5] Myopia may develop when rapid increase in axial length exceeds the compensatory capacity of the lens.

Refractive error in children has been one of the global public health problems nowadays and myopia accounts for a large proportion of refractive error.[6] In recent decades, the onset of myopia among children has displayed a trend of younger age, 10.7% of preschoolers aged 5 to 6 years suffered from myopia in Taiwan,[7] the overall prevalence of pre-myopia was high among preschoolers[8]. Children with an adequate physiologic hyperopia refraction, defined as "hyperopic reserve," are unlikely to become myopic.[9] In 2019, the International Myopia Institute (IMI) defined "pre-myopia" as "refraction≤0.75D and >-0.50D" in children.[10] Prior to the onset of myopia, rapid changes in refraction and ocular components may provide predictive information.[11] One longitudinal study reported that lens power loss suddenly slowed down one year before the onset of myopia combined with relatively high rate of axial elongation.[12]

For these reasons, there is an urgent need to identify children at high risk of early myopia. The optimal time for myopia prevention should be earlier than elementary school age. However, there are fewer large-scale refractive data available on children aged 3-6 years, not to mention data about pre-myopia in preschoolers. Therefore, this study was conducted to evaluate the refraction and ocular components of preschool children. Understanding the pre-myopic refractive status and identifying the associated factors can provide guidance for early prevention. Further objectives include investigating the relationships between refraction and the ocular biometric parameters involved in refractive development.

Methods

1. Study Design and Subjects. This was the first-year results of the 3-year longitudinal study with evaluation of subjects aged 3-6 years from Shunyi District, Beijing. Based on a previously published myopia prevalence rate in preschool children aged 3-6 years,[13] a sample size of 1107 preschoolers was needed to achieve precision of 0.01 and 95% confidence intervals, taking into account a cluster design effect of 1.5 and assumed dropout rate of 10%. Stratified cluster sampling was employed. Shunyi District is situated in the suburban northeast region of Beijing. Under the support of the preschool section of the Shunyi District Education Commission, a total of 1186 children were randomly selected from 11 kindergartens in Shunyi District. Data for all

the participants were collected from October 2020 to June 2021. Children who have any history of Down's syndrome, epilepsy, history of ophthalmologic surgery, and other psychiatric disorders were excluded. 1141 children aged 3–6 years who finished all the examinations were carefully analyzed one by one in this study.

2. Ethics Statement. The study received approval from the Ethics Committee of Beijing Shunyi Hospital (No.2020125). The research was conducted in conformity with the Declaration of Helsinki. Before the examination, the parents were all well informed of the study's objectives, the examination procedure, and the possible consequences, and of course, we received written informed consent from each and every parent.

3. Examination. Prior to the examination, all the relevant information such as the patient's age and gender were recorded. Visual acuity at a 5-m distance was measured using an international standard E chart (Guangdong Yuehua Medical Instrument Factory) in a well-illuminated room. Anterior Segments were examined with a slit lamp. Auto refraction and corneal radius were checked using a desktop autorefractor (model number: KR-8800; Topcon Corporation, Tokyo, Japan). Biometric examination was performed with the Lenstar LS 900 (Haag-Streit, Switzerland) prior to cycloplegia. Ocular biometric parameters including axial length (AL) and anterior chamber depth (ACD) were checked three times, with an automatic calculation of the average in each eye. A concentration of 1% cyclopentolate (Alcon, USA) was used to carry out the examination of cycloplegia. After 30 minutes, if the pupil diameter was ≥6 mm and there was no light reflex, three successive measurements of refraction were taken. Fundus photography was applied and no abnormality was found in the fundus examination. All examinations were carried out by ophthalmologists and optometrists who had undergone uniform training.

4. Definition. Both spherical power and cylindrical power were measured following cycloplegia. The average of three measurements was taken to calculate the equivalent spherical (SE) refraction. SE is equal to half the cylindrical power plus the spherical power. The Bennett-Rabbetts formula[14] was used to figure out the lens power(LP). Since the high correlation between the right and left eyes, data from the right eyes were chosen in the present study. The mean of the longest and shortest corneal radius (CR) of curvature was used to figure out the CR. The definition of the axial length/corneal radius (AL/CR) ratio was the axial length divided by the mean corneal radius. Based on IMI definition,[10]myopia was defined as SE ≤ −0.50 D, pre-myopia as −0.50 D < SE ≤0.75 D, and hyperopia as +0.75 D< SE.

5.Patient and public involvement statement

None.

6. Statistical Analysis. The chi-square test was performed to compare the prevalence of refractive error among different age groups. The mean values of SE refraction, AL, ACD, CR, AL/CR and LP between boys and girls were compared respectively using an independent sample t-test. To find out the differences of ocular biometric components across different age groups and refractive error groups, analysis of variance (ANOVA) was employed.Trend analysis was conducted to detect age differences. The multiple linear regression model was

used to figure out the correlations between SE refraction and ocular biometric components. Statistical significance was defined as P values < 0.05. SPSS 26.0 (IBM SPSS Inc., USA) was used to carry out statistical analyses.

Results

Among the 1186 sampled children who planned to undergo examinations, 1141 completed the cycloplegic refraction and ocular biometric examination after exclusions. The mean age of these subjects was 4.52± 0.87 years. 555 subjects (48.6%) were boys and 586 subjects (51.4%) were girls. It can be summarized from the data in Table 1 that the prevalence of myopia, pre-myopia, and hyperopia was 2.7%(95%CI,1.8-3.7), 27.3%(95%CI,24.7-29.8), and 70.0%(95%CI,67.4-72.7) respectively.

Table 1. Prevalence of refractive errors in 3-to 6-year-old children

N(%)	Myopia(≤-0.5D)	Pre-myopia(>-0.5D and ≤0.75D)	Hyperopia(>0.75D)	P value
Total	31(2.7)	311(27.3)	799(70.0)	0.735
3y	5(4.2)	27(22.7)	87(73.1)	
4y	10(2.1)	140(28.9)	335(69.1)	
5y	11(3.0)	96(26.5)	255(70.4)	
6y	5(2.9)	48(27.4)	122(69.7)	

Table 2 displayed the mean, standard deviation of the SE refraction, AL, ACD, CR, AL/CR and LP of all participants. The mean SE refraction was 1.15±0.76D, and it remained stable during this age range. No significant gender differences were found among different age groups.

AL, ACD and AL/CR increased while LP decreased with age. The mean AL was 22.28±0.67mm, which increased from 22.07 to 22.49mm. The mean ACD was 3.31±0.25mm, which ranged from 3.21 to 3.36mm. Both AL and ACD increased with age, when the data was split by gender, we found out the same trend. The mean value of CR was 7.74±0.25mm. CR did not change with age, but it was higher in boys at 4 to 6 years (p<0.001). AL/CR increased with age and the mean value was 2.88±0.06, which increased from 2.85 to 2.91. The AL/CR in boys were higher than in girls at age 3 to 5 years (p<0.01). The mean LP was 25.62±1.46D, which decreased from 26.50 to 24.96D. It was also lower in boys in all age groups (p<0.001). Compared with girls, boys had 0.51mm longer AL, 0.13mm greater ACD and 1.02D lower LP.

Table 2. Distribution of the ocular biometric parameters in different age groups

	Age(yrs)				Total	P_{trend} value
Parameters	3	4	5	6		
Spherical equivalent refraction (D)						
Total	1.15±0.85	1.17±0.75	1.15±0.76	1.08±0.71	1.15±0.76	0.312
Boys	0.97±0.96	1.16±0.73	1.12±0.78	1.07±0.78	1.11±0.78	0.867
Girls	1.32±0.68	1.18±0.78	1.19±0.73	1.08±0.65	1.18±0.74	0.092

P value	0.025	0.750	0.375	0.944	0.143	
Axial length (mm)						
Total	22.07±0.55	22.20±0.65	22.35±0.67	22.49±0.68	22.28±0.67	<0.001
Boys	22.30±0.59	22.46±0.64	22.63±0.65	22.78±0.59	22.54±0.64	<0.001
Girls	21.85±0.47	21.93±0.56	22.09±0.57	22.26±0.66	22.03±0.59	<0.001
P value	<0.001	<0.001	<0.001	<0.001	<0.001	
Anterior chamber depth (mm)						
Total	3.21±0.25	3.29±0.25	3.35±0.24	3.36±0.24	3.31±0.25	<0.001
Boys	3.30±0.22	3.36±0.25	3.41±0.23	3.44±0.24	3.38±0.24	<0.001
Girls	3.12±0.24	3.22±0.23	3.30±0.24	3.30±0.22	3.25±0.24	<0.001
P value	<0.001	<0.001	<0.001	<0.001	<0.001	
Corneal radius (mm)						
Total	7.75±0.25	7.74±0.26	7.73±0.24	7.74±0.27	7.74±0.25	0.750
Boys	7.77±0.26	7.81±0.26	7.79±0.24	7.82±0.25	7.80±0.25	0.512
Girls	7.73±0.24	7.66±0.24	7.67±0.21	7.68±0.27	7.67±0.24	0.529
P value	0.354	<0.001	<0.001	<0.001	<0.001	
Axial length-to-corneal radius ratio						
Total	2.85±0.07	2.87±0.06	2.89±0.06	2.91±0.06	2.88±0.06	<0.001
Boys	2.87±0.07	2.88±0.06	2.90±0.06	2.91±0.06	2.89±0.06	<0.001
Girls	2.83±0.06	2.86±0.06	2.88±0.05	2.90±0.05	2.87±0.06	<0.001
P value	<0.001	<0.001	<0.001	0.073	<0.001	
Lens power (D)						
Total	26.50±1.34	25.90±1.42	25.30±1.37	24.96±1.38	25.62±1.46	<0.001
Boys	25.99±1.31	25.37±1.32	24.72±1.31	24.40±1.12	25.08±1.37	<0.001
Girls	27.00±1.18	26.41±1.32	25.82±1.21	25.38±1.42	26.10±1.38	<0.001
P value	<0.001	<0.001	<0.001	<0.001	<0.001	

As is shown in Figure 1, similar trends with age were detected in pre-myopia and hyperopia group. SE and CR remained stable from 3 to 6 years in both groups. AL, ACD, AL/CR increased with age while LP decreased with age. The difference in mean SE refraction between the two groups was about 1.06D. Pre-myopic children were approximately 0.28mm longer in AL, 0.12mm greater in ACD, 0.41D higher in LP compared to their hyperopic peers (P<0.05). The difference in AL/CR ratio between the two groups was about 0.04 unit, which was higher in pre-myopia group. The AL in myopia group at age 4 was shorter along with steeper CR than in pre-myopia group. However, when the data was calculated with AL divided by CR, a different result was obtained. Myopic children had higher ratio of AL/CR than children from pre-myopic and hyperopic groups. No statistical differences were observed in CR for different refractive groups.

As can be seen from Figure 2, SE was negatively correlated with AL, ACD, and LP. There was a significant negative correlation between SE and AL/CR, (r=-0.56,p<0.001). A strong positive correlation was found between AL and CR. There was a significant positive correlation between AL and ACD, and a negative correlation between AL and LP.

Multiple linear regression models were established to indicate the associations between SE and ocular biometric parameters (Table 3). After being adjusted for age and gender, SE decreased linearly with increasing AL, with a -0.455D change in SE for a 1mm increase in AL. SE decreased linearly with increasing AL/CR, with a 0.1 unit increase in AL/CR associated with -0.72D change in SE. Model1 explained 13.3% of the variance of SE, while Model2 accounted for 31.3% of the variance of SE, which was better than Model1. The results suggested that SE was associated negatively with AL, ACD, AL/CR and LP.

Table 3. Linear regression models for SE refraction and ocular biometric parameters (adjusted for age and gender, boys as reference)

	Model 1 (n=1141)		Model2 (n=1130)	
Variables	β	P value	β	P value
Age(yrs)	0.043	0.079	0.114	<0.001
Gender	-0.169	<0.001	-0.085	0.025
AL(mm)	-0.455	<0.001		
AL/CR ratio			-7.203	<0.001
R^2	0.133		0.313	

Discussion

The increase in myopia is widely believed to be driven by environmental factors such as fewer outdoor activities and more near-work activities. Genetic susceptibility also plays a role in myopia.[15] Pre-myopia is a non-myopic refractive status that may progress to myopia. By realizing the relevant risk factors and taking appropriate intervention measures, we can achieve the goal of preventing or at least delaying the onset of myopia. In this study, the overall prevalence of pre-myopia was 27.3%, which was slightly higher than in Shanghai (21.9%).[16] An analysis of the data from children aged 4-6 years who were screened between 2005 and 2021 showed a significant increase in the prevalence of pre-myopia (19.0% vs. 26.5%).[17]

In the present study, the mean SE refraction was 1.15D, which was slightly lower than that of Guangzhou (1.42±0.79D)[18] and Shenzhen (1.37±0.63D),[19] but which was similar to that of Shanghai (1.20±1.05D).[20] The results suggest that the refractive development of 3-to 6-year-old children remained mildly hyperopic in Shunyi District, Beijing. The refraction in the pre-myopic group was 0.44±0.32D, which was about 1D lower than that in the hyperopic group. The study on the prevalence of pre-myopia in preschoolers in Taiwan suggested that the mean SE in the pre-myopia group was 0.35 ± 0.33D.[8] The Taiwan study did not use 1% cyclopentolate for cycloplegic auto-refraction, which may have contributed to the difference in SE refraction. Early educational pressure, such as assignments for preschoolers and extensive tutorial classes after school hours,[21] lead to early depletion of hyperopia reserve. Therefore, investigation of hyperopia reserve as well as regular monitoring of refraction are significant for myopia prevention.

During the rapid development of infant eyes in the first few years, lower mean levels of hyperopia and early refractive error changes, axial elongation and deepening of the anterior chamber are synchronized with corneal flattening and lens power reduction.[22] Previous studies have suggested that corneal flattens with age to compensate for the growth of axial length.[23] In order to find out the relationship between corneal curvature and refraction, researchers recorded different results. Zhang et al[20] found that the mean CR increased with age in boys but not in girls among preschoolers. No significant difference was found in CR between different ages in this study. This finding is consistent with that of Ma et al[24] who observed 1-year change in CR was 0.00± 0.04mm in 3-5 years old children, indicating very little change in this period. Zadnik et al[25] reported that CR remained stable in different age groups and was higher in boys than in girls. In age groups 4-6, the mean CR was 0.13mm higher in boys than in girls.

Since corneal power was reported to cause small changes after year 2,[26] axial length and lens power were the determinant factors of SE. The axial length in newborns is approximately 16.5mm,[27] which rapidly develops to 20 mm at 9 months and reaches 21.42 mm at 3 years of age.[28] The mean axial length of children in this study was 22.28±0.67mm. AL increases with age in children aged 3-6years, and it is 0.51 mm longer in boys than in girls. Similar finding was reported by He et al[29]. There was negative correlation between AL and SE. Axial length increased while refraction decreased. The axial length in pre-myopia group was significantly longer than that of hyperopia. In accordance with previous findings,[30] a strong positive correlation was found between AL and CR.

The current investigation found that the development of children's eyes was characterized by reduction in LP and the growth of AL and ACD. There was significant difference in ACD in different refractive error groups. Anterior chambers deepen gradually and sequentially among preschoolers from hyperopia group to myopia group. The deepening of ACD may also have something to do with lens thinning. The reduction in lens power can largely counteract the myopic shift caused by the lengthening of the eye.[3] There was no significant difference in SE between different age groups, which indicated that LP reduction associated with AL and ACD growth can counteract the myopic drift. LP was negatively associated with AL, and the change in LP is one of the main factors affecting the early progression of refractive status. Compared with girls, boys had longer axial length, greater anterior chamber depth, and lower lens power. These findings are in line with those of previous studies[19 25 31].

Some children with relatively short eyes might be myopic, such as the myopic children from the 4-year-old group in this study. However, the sound conclusion can be reached after the AL/CR was obtained. This finding confirmed that compared with AL, AL/CR can more accurately reflect the real refractive status.[29] AL/CR≥3 suggests that myopia has occurred.[32] He et al[29] examined 3922 children aged 6-12 years old in Shanghai, analyzed their data by

ROC curves and found AL/CR greater than 2.99 was diagnostic of myopia. This study suggested that the mean AL/CR ratio was 2.88±0.06. In myopia group, the mean AL/CR was 2.98±0.06, and it was higher in boys than in girls (3.00±0.06 vs 2.95±0.05). AL/CR increased gradually with age, and elongation of AL also occurred among preschoolers in pre-myopia and hyperopia group. In myopia group, AL/CR increased from 2.95 to as much as 3. Among myopic children, who are younger than 6, the values of AL/CR were less than the reported threshold of 2.99. In pre-myopia group, AL/CR increased from 2.89 to 2.93. In hyperopia group, AL/CR was the lowest, and its ratio was less than 2.90. Therefore, the setting up of the age-specific thresholds of AL/CR will improve accuracy of myopia screening, particularly for preschoolers. Apart from changes with age, significant gender differences were detected in AL/CR. Boys aged 3-5 years had an average 0.02unit higher AL/CR ratios than girls. One recent study reported the age and gender specific percentile growth curves for AL and AL/CR in Chinese children, AL and AL/CR were narrowly distributed in the population at 4 years of age.[33] An Irish study assessing risk factors associated with pre-myopia showed that participants with >2 hours/day of screen time [2.92 (0.09)] had significantly higher AL/CR ratios than those with ≤2 hours/day [2.88 (0.08)].[34] Clinicians and parents should pay more attention to children with relatively high AL/CR ratio and provide more timely, useful lifestyle guidance in the prevention of the onset of myopia.

Admittedly, there were several limitations in our study. First, the lens power was figured out by means of Bennett-Rabbetts formula but the lens thickness was not measured,which could affect the accuracy of lens power measurements. This limitation may lead to complications in interpreting the role of lens in refractive error. Second,the differences we observed across age groups cannot be explained by age alone, but by multiple factors such as environmental and behavioral factors,socio-economic factors and other unmeasured confounders.Third, our investigation was a cross-sectional one, it was not possible to assess changes in ocular biometrics before the onset of myopia. Therefore, two follow-up visits were conducted every six months to evaluate the changes in refraction and ocular biometric parameters over time. The first-year data of 2-year longitudinal study is of great importance because it can well illustrate the baseline distribution of ocular biometrics and lay a firm foundation for more scientific researches in the future.

In conclusion, the overall refraction was hyperopic but the ocular biometric parameters including AL, ACD and LP changed significantly from 3 to 6 years old, associations between ocular biometry and refraction were observed. The refraction in the pre-myopic group was about 1D lower than in the hyperopic group. Compared to hyperopic children, pre-myopic children had longer eyes, greater anterior chamber depths, higher AL/CR ratio but similar CR. Whether specific ocular biometric parameters actively attribute to myopia development or merely correlate with refractive status need longitudinal studies to clarify.

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Patient and public involvement: Patients and/or the public were ont involved in the design, or conduct, or reporting, or dissemination plans of this research.

Data availability statement: All data relevant to the study are included in the article or upload as supplementary information.

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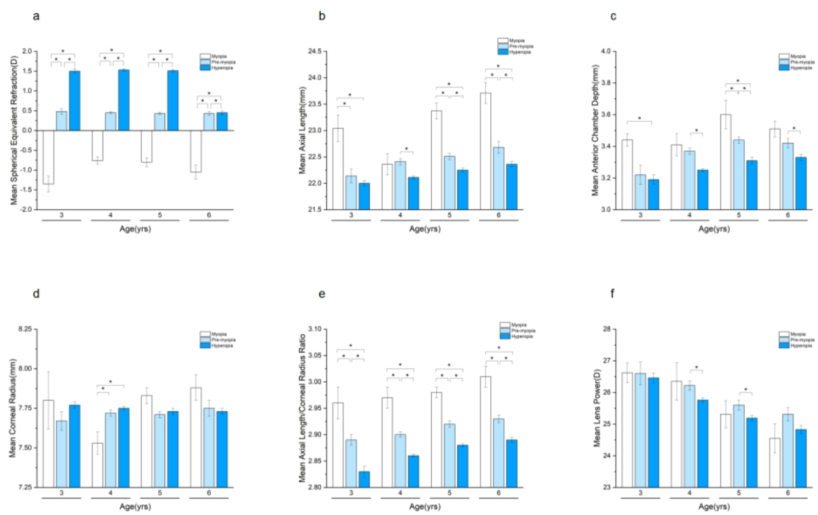
Figure legends: Figure 1. Mean values of SE refraction and ocular biometric parameters among different age and refractive error groups.The error bars represent standard error of the mean(SEM), *statistically significant.

a. Mean values of SE refraction among different age groups. b. Mean values of AL among different age groups. c. Mean values of ACD among different age groups. d. Mean values of CR among different age groups. e. Mean values of AL/CR among different age groups. f. Mean values of LP among different age groups.

Figure 2. Correlation between SE refraction and ocular biometric parameters. Correlation values shown in lower Triangular.



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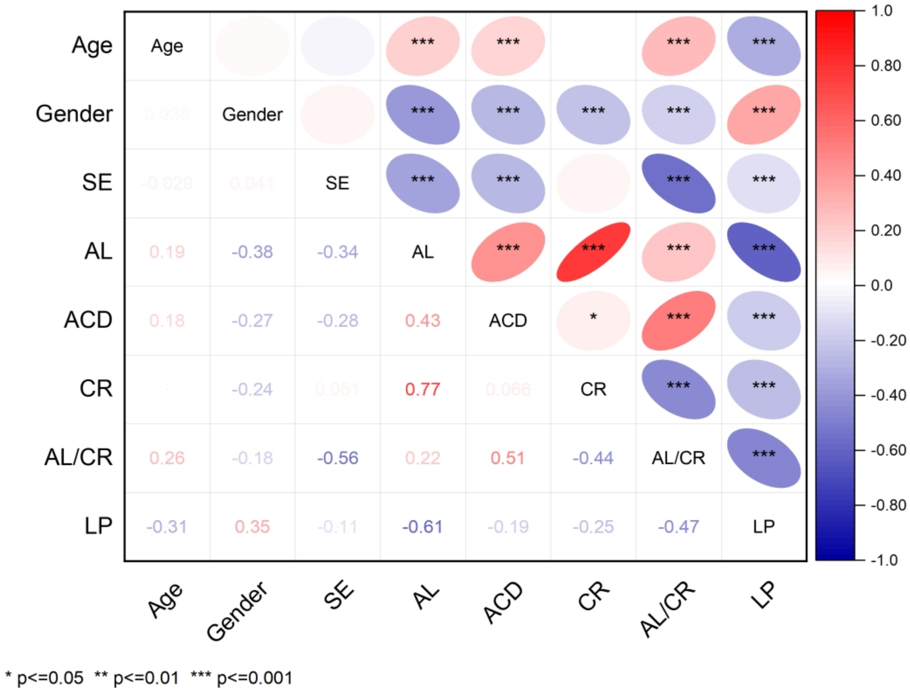

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850x651mm (96 x 96 DPI)