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## Research Article

**Keywords:** spherical equivalent refraction, corneal radius of curvature, adjusted, axial length, preschoolers.

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# The Correlation of Cycloplegic Refraction with Corneal Radius of Curvature-Adjusted Axial Length in Chinese Preschoolers

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## **Abstract**

**Background:** In order to master the refractive status and detect severe refractive errors quickly and effectively, this study aimed to investigate the association of axial length after adjusting for corneal radius of curvature with refraction in a group of Chinese preschoolers.

**Methods:** Retrospective review of 716 Chinese children aged from 3 to 6 years, who underwent cycloplegic optometry with 1% atropine eye gel in the ophthalmology department of Children's Hospital of Fudan University, National Children's Medical Center in Shanghai. Meanwhile axial length,

corneal radius of curvature and cycloplegic autorefractometry were obtained and axial length/corneal radius of curvature (AL/CR) ratio was calculated. The correlations of spherical equivalent refraction (SER) with axial length, corneal radius of curvature, AL/CR ratio and corneal radius of curvature-adjusted axial length were analyzed.

**Results:** Only data from the right eye were included in this analysis. Among 716 eyes of 716 Chinese preschoolers, the mean ( $\pm$ SD) SER was  $2.28\pm 2.41$  diopters (D), of which hyperopia, emmetropia, myopia were 84.64%, 8.54%, 6.84%, respectively. The mean( $\pm$ SD) axial length, corneal radius of curvature and AL/CR ratio were  $21.89\pm 1.01$ mm,  $7.76\pm 0.27$  mm, and  $2.82\pm 0.13$ , respectively. The SER was highly negative correlated with both axial length (coefficient  $-0.722$ ) and AL/CR ratio (coefficient  $-0.814$ ), and weakly correlated with corneal radius of curvature (coefficient  $0.090$ ) and gender(coefficient  $0.093$ ). Axial length was weakly correlated with age and gender(coefficient  $0.232$  and  $0.268$ , respectively), but moderately correlated with corneal radius of curvature (coefficient  $0.424$ ). After adjusting for corneal radius of curvature, the correlation coefficient between SER and axial length significantly increased to  $-0.918$ .

**Conclusion:** In the samples of 716 3- to 6-year-old Chinese children, axial length was moderately correlated with corneal radius of curvature. After adjusting for corneal radius of curvature, refraction was closely

correlated with axial length than axial length alone and AL/CR ratio. Therefore, corneal radius of curvature-adjusted axial length might be a useful tool for pediatric ophthalmologists to detect refractive errors.

**Key Words:** spherical equivalent refraction; corneal radius of curvature; adjusted; axial length; preschoolers.

## **Background**

The ocular refractive system is an important part of the normal visual function of human eyes, and constantly changes throughout the whole life. During the preschool age, severe refractive errors can lead to amblyopia. Amblyopia is a public health problem worldwide and its detection is the main target of vision screening programs [1]. Because it is the easiest to go unnoticed, the most difficult to be detected, and the most straightforward to be corrected in early childhood, The United States Preventive Services Task Force( USPSTF ) as well as the American Association for Pediatric Ophthalmology and Strabismus(AAPOS) recommend vision screening for all children at least once between the ages of 3 and 5 years, to detect the presence of amblyopia or its risk factors [2], of which severe refractive error is the leading one.

Cycloplegic refraction is considered to be the gold standard in determining refraction status in children [3-6]. However, accurate technical requirement for environment and examiners, lack of

cooperation with children especially in the instillation of cycloplegic drops and unavailability of technical staff sometimes make it challenging to perform cycloplegic refraction in preschoolers. Therefore, how to detect refractive error efficiently and effectively has always been challenging for pediatric ophthalmologists. Many researchers tried to find the correlations between refraction and other ocular biometric parameters. The refractive status of human eyes is a complex variable, determined by the balance of the optical power of the cornea and the lens, and the axial length of the eye [7–10]. During the first 1 to 2 years after birth, there is an active process shaping the distribution of refraction, known as emmetropization [11], which marked with increases in axial length and decreases in corneal and lens power [12-14]. After that period, the cornea is relatively stable until much later in adult life [15], while axial length increases and lens power decreases. Many cross-sectional population based studies [16-20] showed that corneal radius of curvature remained stable after 3 years old. Several studies have investigated the correlation between spherical equivalent refraction (SER) and other ocular biometry. Ip et al [21] showed lower correlation between SER and corneal radius of curvature ( $r \leq 0.09$ ) and with lens power ( $r \leq 0.13$ ). Iribarren's study [22] suggested that SER was strongly correlated with axial length, and even more strongly with the AL/CR ratio. In contrast, the positive correlation of SER with lens power

was only moderate. Therefore axial length is the main factor that determines the degree of refractive status. However Ip et al [21] found a significant overlap in the distribution of axial length between myopia, hyperopia, and emmetropia in their sample of 12-year-old group, and the AL/CR ratio correlated better with SER than axial length alone. In recent years, many studies about the relationship between refraction and ocular biometry based on school aged population and studies of preschoolers were relatively fewer.

Therefore, our study tried to find a more exact ocular biometric parameter better correlated with refraction than axial length alone in Chinese preschoolers. Since corneal radius of curvature is relative stable after 3 years old, everyone has a different corneal radius of curvature. Our study aims to analyze the correlation between spherical equivalent refraction and axial length after adjustment for corneal radius of curvature in a sample of 3- to 6-year-old Chinese children.

## **Methods**

### **Study Design**

This was a retrospective study that was conducted in the ophthalmology department in Children's Hospital of Fudan University, National Children's Medical Center. All the preschoolers didn't pass the school vision screening and were referred to pediatric ophthalmologists. In the first visit, the examination included uncorrected visual acuity, axial length,

corneal radius of curvature, eye movements, the anterior segment and fundus examination. If uncorrected visual acuity was lower (3- to 4-year old <20/50, 4- to 5-year-old <20/40, 5- to 6-year-old <20/30, respectively) or refractive error was suspected, cycloplegic refraction examination would be done in the second visit after using 1% Atropine Sulfate Eye Gel (Shenyang Xingqi Pharmaceutical Co., Ltd, China). Those aged from 3 to 6 years who underwent cycloplegic refraction examination with 1% Atropine Sulfate Eye Gel, whose axial length, corneal radius of curvature and cycloplegic autorefraction were obtained in both eyes from January 2017 to May 2020 at our ophthalmology department were included in our study and children with strabismus or other ocular diseases except amblyopia were excluded. Their complete medical records were reviewed, including age, gender, axial length, corneal radius of curvature and cycloplegic autorefraction.

### **Ocular Examinations**

Cycloplegia was induced in each eye with 1% Atropine Sulfate Eye Gel three times a day for three days. Before cycloplegia, three consecutive reliable measurements of corneal radius of curvature with autorefractometer (ARK-1, NIDEK, Japan) and axial length with IOL Master (Carl Zeiss, Meditec) were taken and the mean values of the three readings were provided automatically. The anterior segment including the eyelid, conjunctiva, cornea, iris, and pupil, and fundus

including optic and macular examination were evaluated by slit-lamp (SLM-2, Carl Zeiss, German) and retinal digital photography (AFC-210, NIDEK, Japan), respectively. Children could not have strabismus by cover test at far (5.0 m), near (0.33 m), or near with 2.0D (the add power in the PALs) over their distance correction. After cycloplegia, three consecutive reliable cycloplegic autorefractions including sphere, cylinder and axis were obtained with autorefractometer and the mean value was also given automatically.

### **Definitions**

Axial length was defined as the distance from the tear film and retinal pigment epithelium (RPE). Corneal radius of curvature was measured in meridians, the steepest corneal radius of curvature and the flattest corneal radius of curvature and was calculated by the mean of two meridians. The axial length/corneal radius of curvature(AL/CR) ratio was defined as the axial length divided by the mean corneal radius of curvature. The spherical equivalent refraction(SER) was calculated as the sum of spherical diopters(D) plus one-half cylindrical diopters. Myopia was defined as the  $SER \leq -0.5D$ , hyperopia as  $\geq +0.5D$  and emmetropia as between  $-0.5$  and  $+0.5D$ <sup>[20]</sup>.

### **Statistical Analysis**

Data analysis was performed with the program IBM SPSS 25 (SPSS Inc., Chicago, IL). Because there was high correlation between the ocular

biometric parameters in the right and left eyes [20,21], only the data from the right eyes were included in the statistical analyses. The distribution of the samples were analyzed using Kolmogorov-Smirnov tests. Correlations of spherical equivalent refraction with axial length, mean corneal radius of curvature, axial length/corneal radius of curvature(AL/CR) ratio and age were evaluated using Spearman correlation coefficients. Partial correlations were performed to analyze the correlation of spherical equivalent refraction with axial length after adjusting for corneal radius of curvature. A *P* value < 0.05 was considered significant and all confidence intervals (CI) are 95%.

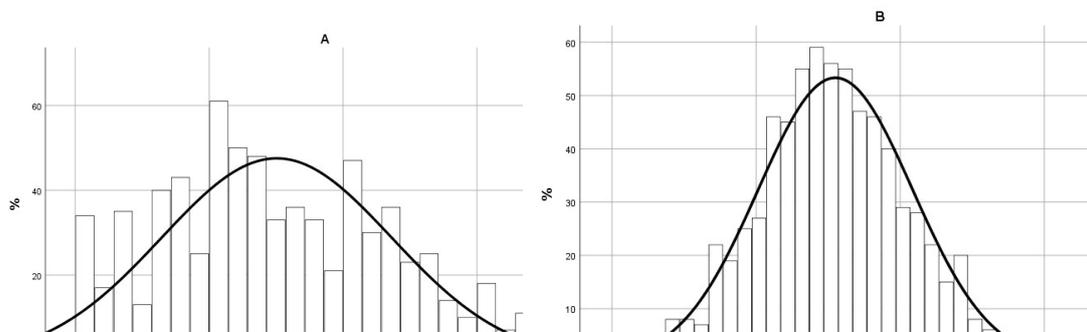
## **Results**

Of 716 Chinese preschoolers, there were 339 males (47%) and 377 females (53%), aged from 3 to 6 years. Overall, 606 (84.64%) participants were hyperopic, 61 (8.52%) were emmetropic, and 49 (6.84%) were myopic. General characteristics of age, SER and other ocular biometric parameters are showed in Table 1. The mean( $\pm$ SD) age of these preschoolers at the time of examination was  $4.50\pm 0.86$  years. The mean ( $\pm$ SD) spherical equivalent refraction was  $+2.28\pm 2.41$ D with mean ( $\pm$ SD) corneal radius of curvature  $7.78\pm 0.27$ mm, mean ( $\pm$ SD) axial length  $21.89\pm 1.01$ mm and mean ( $\pm$ SD) axial length/corneal radius (AL/CR) ratio  $2.82\pm 0.13$ . The mean ( $\pm$ SD) AL/CR ratio was  $2.79\pm 0.11$ ,  $2.91\pm 0.06$  and  $3.01\pm 0.11$  in hyperopia, emmetropia and myopia group, respectively. The

Kolmogorov-Smirnov test indicated that the frequency distributions were nonnormal for SER, AL/CR ratio, corneal radius of curvature and age, only axial length distribution was normal. Figure1(A-E) shows the distributions of age, corneal radius of curvature, axial length, AL/CR ratio and SER, separately.

Table 1 General Characteristics of Age, SER and other Ocular Biometric Parameters of 716 Chinese preschoolers

	Mean	SEM	Median	Range	Kurtosis	Skewness	K-S
Age(y)	4.50	0.86	4.42	3.00-6.83	-0.66	0.27	0.000
spherical equivalent refraction (D)	2.28	2.41	2.00	-9.25-+10.75	2.50	0.41	0.000
Axial length (mm)	21.89	1.01	21.89	18.64-25.71	0.51	0.07	0.056
Mean corneal radius of curvature (mm)	7.78	0.27	7.76	7.06-8.85	0.45	0.30	0.025
Axial length/mean corneal radius ratio	2.82	0.13	2.83	2.33-3.41	1.50	-0.30	0.000
hyperopia	2.79	0.11	2.81	2.33-3.00	0.70	-0.97	0.000
emmetropia	2.91	0.06	2.90	2.78-3.07	0.03	0.21	0.200
myopia	3.02	0.11	3.01	2.81-3.40	1.72	1.04	0.149



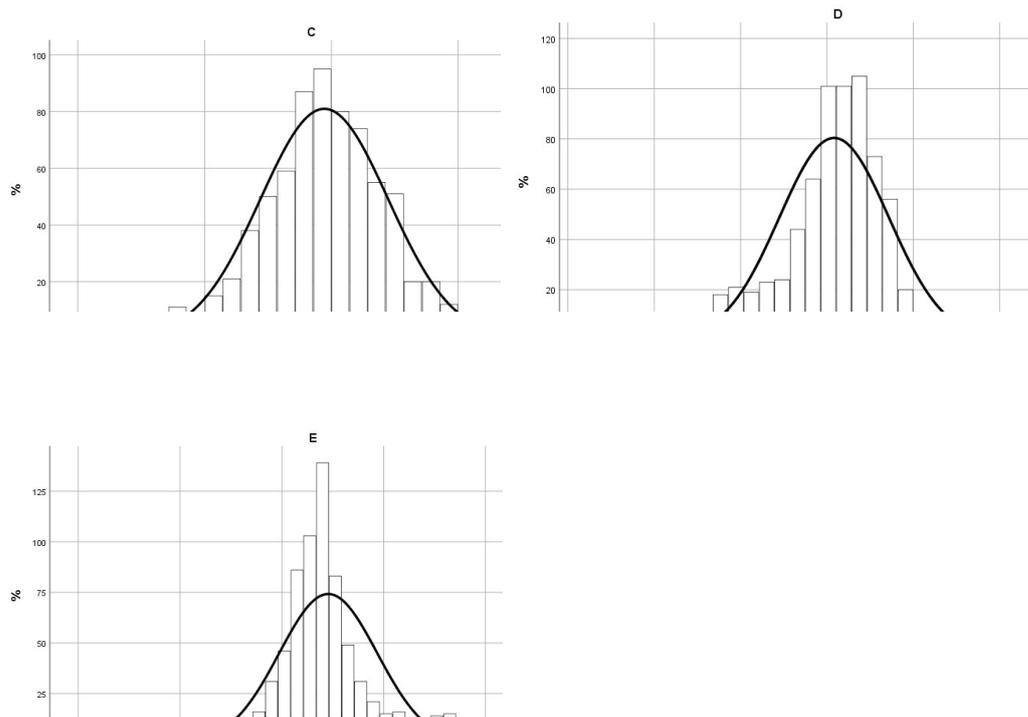


Figure 1 The distribution of age(A), mean corneal radius of curvature(B), axial length(C),AL/CR ratio(D) and spherical equivalent refraction(E), respectively in 3- to 6-year-old Chinese preschoolers.

Table 2 shows the correlations of ocular biometric parameters with age, axial length, corneal radius of curvature and AL/CR ratio, and correlation of SER with corneal radius of curvature-adjusted axial length. It could be seen that axial length was weakly correlated with age and gender (coefficient 0.232 and 0.268, respectively), but moderately correlated with corneal radius of curvature (coefficient 0.424). There were strong correlations between SER and axial length, AL/CR ratio (coefficient -0.722 and -0.814, respectively), but weak correlation between SER and corneal radius of curvature (coefficient 0.09). Analysis of Partial Correlation showed that after adjustment for corneal radius of curvature, the correlation coefficient of SER with axial length increased to -0.918.

Table 2 Correlations of ocular biometric parameters with age, AL, CR and AL/CR ratio and SER with CR-adjusted AL

	Spearman Correlation Coefficient					Partial Correlation Coefficient
	Age	Gender	CR	AL	AL/CR ratio	CR-adjusted AL
CR	0.020	-0.221	-	0.424	-0.347	-
AL	0.232	-0.268	0.424	-	0.639	-
AL/CR ratio	0.242	-0.088	-0.347	0.639	-	-
SER(D)	0.067	0.093	0.090	-0.722	-0.814	-0.918

AL=axial length; CR=corneal radius of curvature; AL/CR ratio=axial length/corneal radius of curvature; SER= spherical equivalent refraction.

Figure 2 shows the distribution of axial length in 3- to 6-year-old Chinese children with hyperopia, emmetropia and myopia. The range of axial length in hyperopia group was 18.64 to 23.77mm, emmetropia group 21.28 to 23.85mm, myopia group 21.76 to 25.71mm.

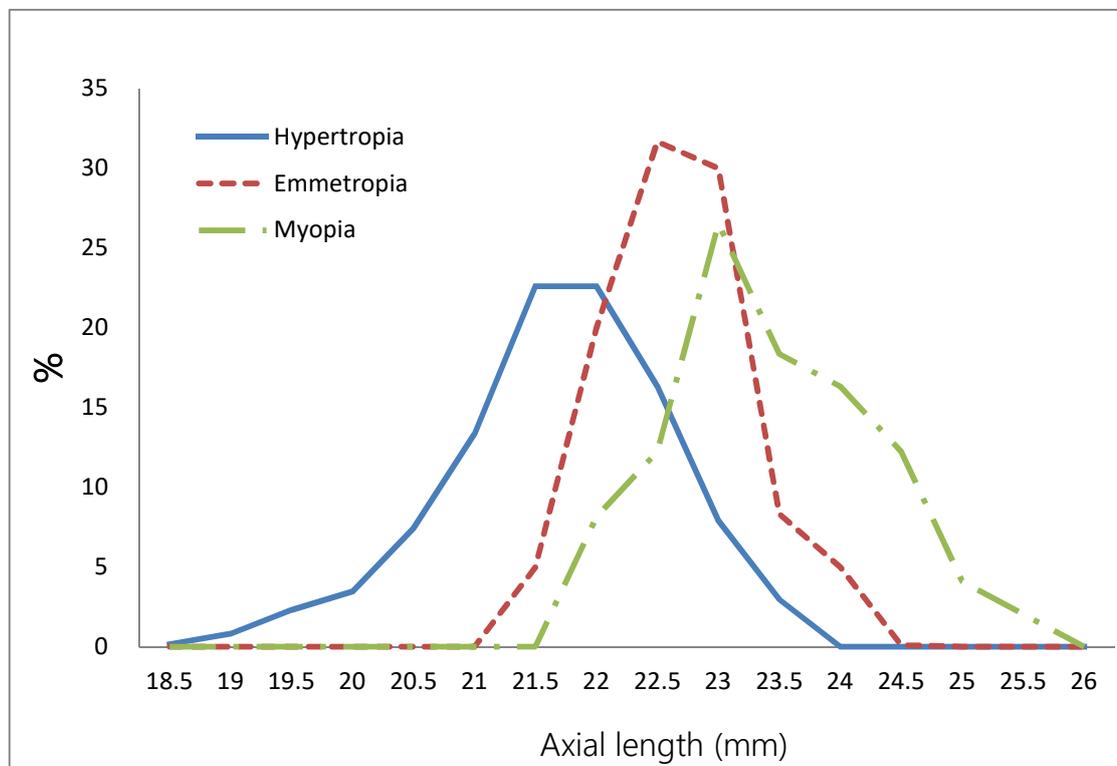


Figure2 The distribution of axial length in 3- to 6-year-old Chinese children with hyperopia, emmetropia and myopia.

There were 103 children in our study with SER between +2.25D and +2.75D, who were divided into two groups stratified by the axial length(Long AL Group and Short AL Group). Table 3 shows the comparison of corneal radius of curvature and corneal curvature in the two groups. In Long AL Group, the mean ( $\pm$ SD) corneal radius of curvature was  $7.88 \pm 0.20$ mm, significantly longer than that in Short AL Group  $7.57 \pm 0.22$ mm and the mean ( $\pm$ SD) of corneal curvature was  $42.85 \pm 1.12$ D, significantly lower than that in Short AL Group  $44.61 \pm 1.30$ D. There was no difference in the SER of the two groups.

Table 3 The comparison of CR and CC in two groups stratified by AL with the same SER (+2.25D -2.75D)

	AL(mm)	CR(mm)	CC(D)	SER(D)
	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD
Long AL Group(n=50) (21.76 $\leq$ AL<23.24)	22.21 $\pm$ 0.37	7.88 $\pm$ 0.20	42.85 $\pm$ 1.12	2.49 $\pm$ 0.20
Short AL Group (n=53) (20.21 $\leq$ AL<21.76)	21.28 $\pm$ 0.38	7.57 $\pm$ 0.22	44.61 $\pm$ 1.30	2.50 $\pm$ 0.20
<i>P</i> value	0.000	0.000	0.000	0.992

Statistical significance was tested using Kolmogorov-Smirnov Z test.

CR=corneal radius of curvature; CC=corneal curvature; SER=Spherical equivalent refraction; AL=axial length; SD=standard deviation.

## Discussion

### Distribution

In our study, only axial length was normally distributed and other biometric parameters including corneal radius of curvature, AL/CR ratio and SER were all not normally distributed. This result is consistent with Foo's report [23], which was a 3-Year-Old study, but not consistent with other population-based studies [16,21]. Our study was based on 3- to 6-Year-Old clinical data including a number of severe refractive errors but not population-based random samples, therefore it did not represent the distribution of the population in 3- to 6-year-old Chinese children.

### **Axial length and Corneal radius of curvature**

In our study, we find that axial length was better correlated with corneal radius of curvature ( $r=0.40$ ) at mean age 4.5 years Chinese preschoolers. Scheiman et al [16] also reported a high correlation between axial length and corneal curvature ( $r=-0.70$ ) at mean age 9.3 years and decreased to  $-0.53$  at mean age 24.1 years. Other previous studies [21,24-26] found there was no relationship between axial length and corneal curvature in any category of myopia. In order to verify the relationship between axial length and corneal radius of curvature or corneal curvature in Chinese preschoolers, our study also analyzed 103 eyes with SER between  $+2.25D$  and  $+2.75D$ . The conclusion was that the eyes with longer axial length had lower corneal curvature and longer corneal radius of curvature in 3- to 6-year-old Chinese children.

### **SER and AL/CR ratio**

Axial length is considered to be correlated with corneal radius of curvature and everyone has a different corneal radius of curvature. Therefore in recent researches AL/CR ratio has been proposed to be the most significant determinant of the refractive status and correlated better with refraction than axial length alone [21,27,28], because it minimizes issues with respect to variability in axial length and corneal radius of curvature [23,28-30]. Grosvenor et al [27] reported the correlation between AL/CR ratio and refractive error was high to -0.915. In our study of 3- to 6-year-old children the correlation was -0.814, which was consistent with the report ( $r=-0.81$ ) by Ip in the 12-year-old group [21] and also higher than axial length alone -0.722. AL/CR ratio had also been shown to be a more useful predictor in detecting myopia development [21] but not myopia progression[12,13]. Our data showed that the mean AL/CR ratio in myopia is 3.02, and 3.0 is the cutoff value of AL/CR ratio which was considered to be associated with the development of myopia [14]. Foo et al [23] reported the AL/CR ratio was correlated with cycloplegic refraction in myopes, but not in emmetropes and hyperopes.

### **SER and Corneal radius of curvature-adjusted axial length**

Axial length was considered to be the main determinant of SER in all of the ophthalmometric parameters. Ip et al [21] reported that axial length showed high correlation ( $r$ ) with SER in the 6-( $r=-0.44$ ) and 12-year-old ( $r=-0.61$ ) children. Foo's study [23] also showed a better correlation ( $r=-0.36$ ) between axial length and SER in 3-year-old children. In our study, the correlation coefficient of SER with axial length was  $-0.722$ , which is similar to  $-0.762$  reported by Grosvenor [27] and  $-0.76$  reported by Stenstrom [7]. While we could also see that there was a significant overlap in the distribution of axial length among hyperopia, emmetropia and myopia group in 3- to 6-year-old Chinese children, which is consistent with Ip's report in the sample of 12-year-old group<sup>[21]</sup>. According to our study, axial length was moderately associated with corneal radius of curvature, therefore after adjusting for corneal radius of curvature, the correlation coefficient of SER with axial length increased to  $-0.918$ , also higher than that with AL/CR ratio  $-0.814$ . Corneal radius of curvature -adjusted axial length seems to be a more useful predictor of the refraction.

## **Conclusion**

In our study of 3- to 6-year-old Chinese children, SER was lower correlated with corneal radius of curvature and better correlated with axial length and AL/CR ratio. Axial length was moderately correlated with

corneal radius of curvature. After adjusting for corneal radius of curvature, the correlation between SER and axial length was significantly improved. Although corneal radius of curvature-adjusted axial length can not replace full cycloplegic refraction-the gold standard in diagnosis of refractive errors and amblyopia, it could possibly be used as the best reference of refraction for pediatric ophthalmologists to detect severe refractive errors than axial length alone and AL/CR ratio, when cycloplegic refraction is unavailable in preschoolers.

### **Limitation**

Due to relatively small sample size of data in our study, we didn't further give the detail predictor for SER using corneal radius of curvature-adjusted axial length. The small size of data was mainly because the uncooperation of children in preschool age made it not easy to get all the ocular biometric parameters in one child. However our report still reminds pediatric ophthalmologists that corneal radius of curvature should be stratified when evaluating the relationship between axial length and refraction.

### **Abbreviations**

SER: Spherical equivalent refraction; CR: corneal radius of curvature; CC: corneal curvature; AL: axial length; AL/CR ratio: axial length/corneal radius of curvature ratio; SD: standard deviation.

### **Availability of data and materials**

All data generated or analysed during this study are included in this published article and its supplementary information files.

### **Authors' contributions**

XZ performed the data analyses and wrote the first draft of the manuscript. YL performed acquisition of data. WW, CY contributed to the conception and designed the study. Both of them should be considered as corresponding authors. All authors (XZ, YL, WW, CY) read the manuscript drafts for intellectual content, suggested revisions and approved the final draft for submission.

### **Ethics approval and consent to participate**

This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Children's Hospital of Fudan University, National Children's Medical Center. The guardian of each preschooler provided verbal consent before any examination and written informed consent for data to be used.

### **Competing interests**

The authors report no conflicts of interest and have no proprietary interest in any of the materials mentioned in this article.

### **Consent to publish**

All authors read and approved the final manuscript and agreed for publication.

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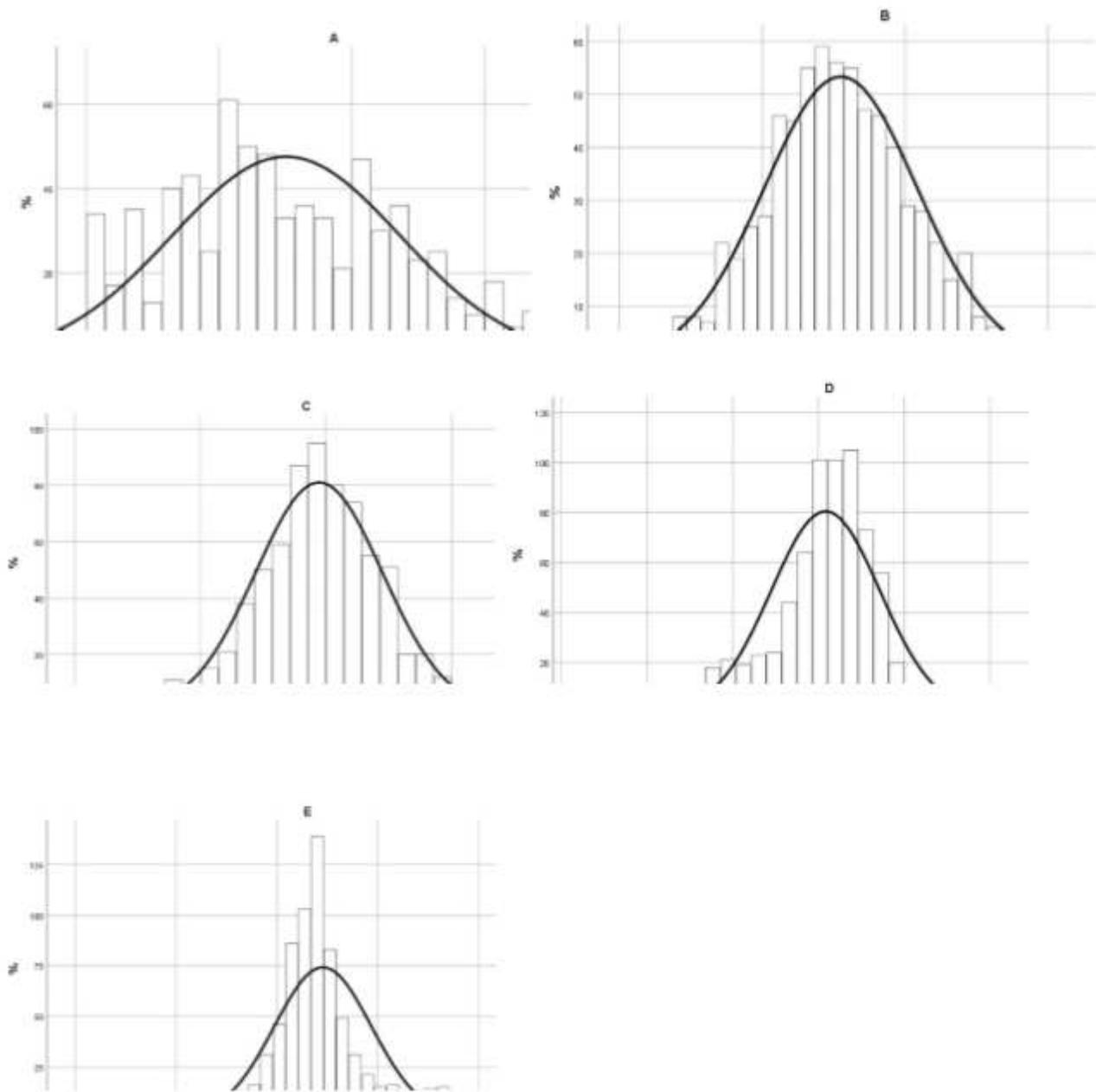
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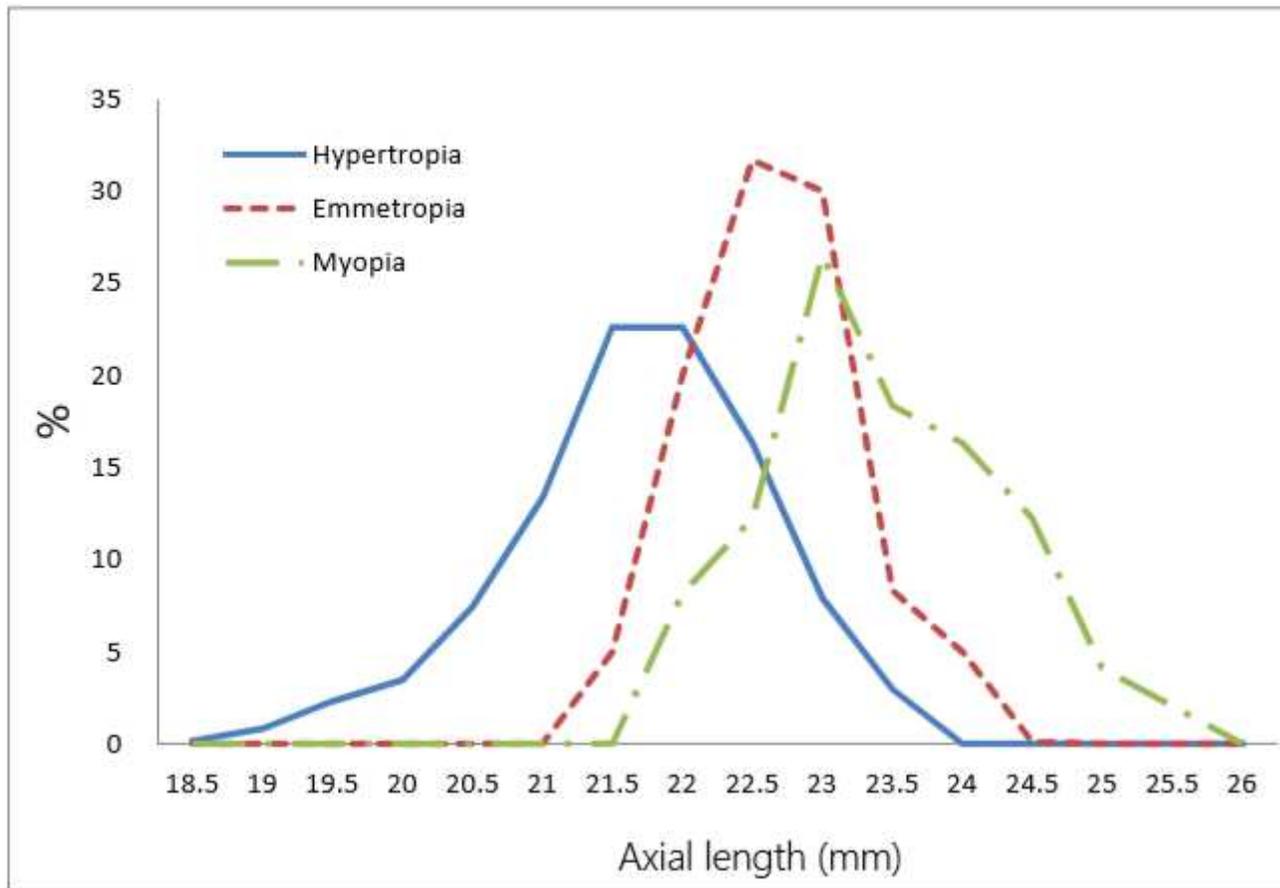
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# Figures



**Figure 1**

The distribution of age(A), mean corneal radius of curvature(B), axial length(C),AL/CR ratio(D) and spherical equivalent refraction(E), respectively in 3- to 6-year-old Chinese preschoolers.



**Figure 2**

The distribution of axial length in 3- to 6-year-old Chinese children with hyperopia, emmetropia and myopia