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· Investigation ·

Axial length/corneal radius of curvature ratio and refractive development evaluation in 3- to 4-year-old children: the Shanghai Pudong Eye Study

Ke-Ke Zhao[1], Yuan Yang[2,3], Hong Wang[1], Lu Li[1], Zhao-Yang Wang[2,3], Fan Jiang[1], Ji-Fang Qu[1]

[1]Shanghai Children's Medical Center, Shanghai Jiao Tong University School of Medicine, Shanghai 200127, China
[2]Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200011, China
[3]Shanghai Key Laboratory of Orbital Diseases and Ocular Oncology, Shanghai 200011, China

Co-first authors: Ke-Ke Zhao and Yuan Yang

Correspondence to: Fan Jiang and Ji-Fang Qu. Shanghai Children's Medical Center, Shanghai Jiao Tong University School of Medicine, Shanghai 200127, China. fanjiang@shsmu.edu.cn; rachelqu@163.com

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Abstract

● AIM: To measure and analysis axial length (AL)/corneal radius of curvature (CRC) ratio and other refractive parameters, provide a medical reference range for refractive development evaluation and earlier visual impairment screening of 3 to 4y kindergarten students.

● METHODS: Between April and June 2017, a total of 4350 participants aged 3- to 4-year-old (8700 eyes) from 10 cluster random sampling kindergartens in Shanghai, Pudong District were involved. According to the measurement and analysis of the unaided visual acuity (VA), AL, CRC, AL/CRC ratio, astigmatism and other refractive parameters, the data distribution and reference range were obtained.

● RESULTS: Uncorrected VA of examined children was 0.23±0.08 (logMAR, mean±SD) [95% confidence interval (CI) range ≤0.36]; AL was 22.10±0.79 mm (95%CI 20.55-23.65); CRC was 7.86±0.26 mm (95%CI, 7.35-8.37); AL/CRC ratio was 2.81±0.12 (95%CI, 2.57-3.05). The median of astigmatism was -0.5 D, a total of 56.3% had astigmatism <-0.50 D, 85.3%<-1.00 D, 6.7%>-1.50 D; 71% were astigmatism with the rule. Eye-specific analyses were conducted. Statistical difference of VA was in right and left eyes. There were no significant differences between two eyes of AL, CRC, AL/CRC ratio and astigmatism (*P*>0.05).

● CONCLUSION: VA and AL/CRC ratio reference could be used to assess refractive development in children and screening uncorrected refractive errors or amblyopia. Astigmatism needs to be considered in the diagnosis.

● **KEYWORDS:** children; axial length/corneal radius of curvature ratio; refractive development; visual impairment; reference

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INTRODUCTION

Recent population-based studies have revealed that the most frequent cause of irreversible visual impairment and blindness in China was degenerative myopia[1-6]. Because of the detection failure, children with refractive errors are easily to be ignored and stayed unnoticed for years, which will lead to severe decrease in visual acuity (VA). Since 3 years of age is a sensitive period for visual development, any alternation in the developing brain can leads to permanent visual loss in the affected eye[7]. The United States Preventive Services Task Force (USPSTF) recommends vision screening for all children at least once between the ages of 3 and 5 years[7]. Identification, diagnosis and treatment of visual impairment before school entry could help improve VA outcomes for children with vision disorders, and reduce the prevalence of refractive errors in the population[8-10].

Cycloplegic refraction is considered to be the golden standard for pediatric refractive errors diagnosis[11]. However, accurate technical requirement for environment and examiners, lack of cooperation with children and long inspection time limiting its application in vision impairment screening[12]. Effective strategies are needed to assess refractive development in children and diagnosis uncorrected refractive errors. Axial length (AL) grows while corneal radius of curvature (CRC) flattens in the process of emmetropization. A previous study revealed that the correlation between spherical equivalent (SE) and AL/CRC is stronger than that between AL or CRC alone, which suggests that AL/CRC may be a potential reference for refractive error, especially when cycloplegic refraction is unavailable in children[13].

This Pudong school-based, cross-sectional study involved 4350 kindergarten students aged 3 to 4y. All the participants were examined by ophthalmologists with comprehensive ocular examinations, including distance VA (without spectacles, if worn), noncycloplegic autorefraction, ocular biometric measurement and ocular movement examination. According to the measurement and analysis of the unaided VA, AL, CRC, AL/CRC ratio and other refractive parameters, obtained the mean value and 95% confidence interval (CI), which will provide a medical reference range of 3 to 4y kindergarten students and make visual impairments screening more effective and practical.

SUBJECTS AND METHODS

Ethical Approval The study adhered to the tenets of the Declaration of Helsinki. Ethics Committee approval was obtained from the Shanghai Children's Medical Center review board, and written informed consent was obtained from all subjects' parents.

Populations Shanghai, one of four municipalities under the direct jurisdiction of China's central government, is the financial capital of China, with a population of 24.15 million[14]. The Pudong new district, one of 17 administrative districts in Shanghai with both the maximum land area (1210.41 km^2) and resident population (5.47 million), was identified for the study because of its relatively stable population, representative demographic and socioeconomic characteristics. The majority residents are the Han ethnicity, which is the main ethnicity (91.60%) of China on 2010 census data[15], distributed all over the country. Per capita gross domestic product of Pudong residents is 103 795 RMB ($ 16 665 USD)[14]. These advantages ensured that the sample in this study is representative of the local population.

Sample Selection Cluster random sampling was used to select the study sample. According to the geographical position, the education bureau has set up four education departments in charge of all schools in Pudong new district. All 188 kindergartens were fairly subdivided and managed by four government education departments[16]. Ten kindergartens of each education department were selected for the study, a total of 40, by random sampling of statistical software (SPSS for Windows, version 22.0; IBM-SPSS, Chicago, IL, USA). The eligible students were 3 to 4 years of age, which have been living in Pudong district for at least half a year and will continue to live there for at least 5y. Children with ocular position abnormality, nystagmus and other diseases of the anterior and posterior segment were excluded.

Quality Control Procedures With the support of the local government, principals and teachers of each kindergarten, quality control procedures were implemented throughout the entire study. All examinations were performed based on the standard operating procedure by one clinical team between April and June, 2017. Five well-trained optometrists and ophthalmologists were in charge of ocular examinations respectively during the whole screening. Examinations were implemented in kindergartens, during the week while classes were in session. All data was verified after double data entry and analyzed by blinded statistician.

Ocular Examinations

Distance visual acuity VA was measured both with and without spectacles, using a retroilluminated logarithm of the minimum angle of resolution (logMAR) chart with tumbling-E optotypes (Precision Vision, La Salle, IL, USA) at a distance of 4 m. The children were examined monocularly (right eye followed by the left eye).

Noncycloplegic autorefraction An autorefractor (KR 8800, Topcon Corp, Tokyo, Japan) was used to measure for their refractive status and CRC without cycloplegic. After alignment, three repeated measurements for each children and machine-calculated an average value.

Ocular biometric measurement AL was measured by IOL Master (Carl Zeiss Meditec AG, Jena, Germany). Three repeated measurements were taken and averaged. AL/CRC was calculated by statistical software.

Ocular movements Students were asked to follow a moving penlight without moving their heads. Nine directions of gaze were examined and recorded, including primary (straight ahead), secondary (right, up, left, and down), and tertiary (upper right, lower right, upper left and lower left).

Statistical Analysis All data were independently entered into the database with Epidata software (version 3.1, The Epidata Association, Odense, Denmark) by two individuals. Statistical analysis was performed by SPSS software (SPSS for Windows, version 22.0; IBM-SPSS, Chicago, IL, USA)[17]. Qualitative data were expressed by frequency (percentage). Quantitative data were validated by normality. For continuous traits, *t*-tests model will be used, both person-specific and eye-specific analyses will be conducted. 95%CIs were calculated[2]. The P value <0.05 was statistically significant.

RESULTS

During the period from April to June 2017, 4350 participants (8700 eyes) were examined and completed at least one test at ocular examination station. Distance VA was measured in 4313 (99.15%) students. Noncycloplegic autorefraction examinations were available in 4342 (99.82%) students. Ocular biometric measurement was completed in 4340 (99.77%) students. All participants did ocular movements test. The age range of students was 3-4y. The 47.69% of the students were female and 52.31% were male.

Table 1 Refractive parameters comparison of two eyes by paired sample *t*-test in the Shanghai Pudong Eye Study

Factors	Right eye		Left eye		*P*
	n	Mean±SD	*n*	Mean±SD	
VA, logMAR	4278	0.225±0.081	4276	0.228±0.086	0.005[a]
AL, mm	4339	22.102±0.662	4338	22.099±0.900	0.760
CRC, mm	4341	7.859±0.260	4339	7.862±0.262	0.076
AL/CRC	4337	2.812±0.102	4340	2.810±0.128	0.268

VA: Visual acuity; AL: Axial length; CRC: Corneal radius of curvature. [a]$P<0.05$.

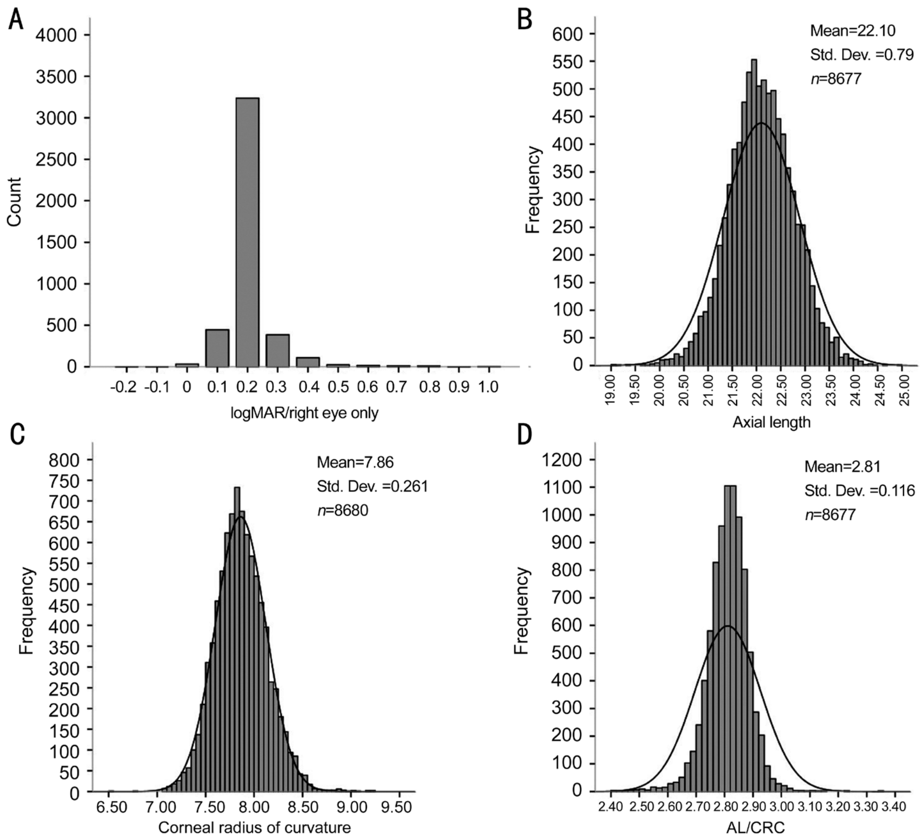

Figure 1 Refractive parameters distribution of the participants in the Shanghai Pudong Eye Study A: Distribution of uncorrected VA (logMAR) in 4278 measured right eyes. Statistical difference of VA was in right and left eyes. Therefore, only data for right eyes were used for analysis of VA. B: Distribution of AL in 8677 measured eyes; C: Distribution of CRC in 8680 measured eyes; D: Distribution of AL/CRC in 8677 measured eyes. VA, AL, CRC and AL/CRC were obeyed normal distribution.

VA, AL, CRC and AL/CRC were obeyed normal distribution, paired sample *t*-test was used to compare refractive parameters between two eyes. In this sample, statistical difference of VA was in right and left eyes (Table 1). Therefore only data for right eyes were used for analysis of VA. There were no significant differences between two eyes of AL, CRC, AL/CRC.

VA findings are presented in Figure 1A, which was double ensured by distance VA and noncycloplegic autorefraction and obeyed normal distribution. Among 4278 measured right eyes, the mean uncorrected VA of 3 to 4y children was 0.23±0.08 range -0.2 to 1.0. The distribution was 75.64% of logMAR 0.2, 9.02% of logMAR 0.3 and 10.43% of logMAR 0.1. A cumulative percent under logMAR 0.3 was 95.9%. Visual impairment was defined as any (VA≥logMAR 0.3) or severe (VA≥logMAR 1.0) for both better and worse eyes[2]. A total of 175 (4.09%) eyes were examined exceeded logMAR 0.3. Single upper 95%CI bound of logMAR was 0.36 (mean+1.64 SD). Figure 1 illustrated the AL, CRC and AL/CRC of 3 to 4y kindergarten students. All data were listed in Table 2.

According to autorefraction results, astigmatism was characterized by skewed distribution, ranged -8.00 D to 0 D with median -0.50 D. As illustrated in Figure 2A, the most common distribution of children was astigmatism below -0.50 D, accounting for 56.3%, and 85.3% below -1.00 D. Only 6.7% children with astigmatism exceed -1.50 D. As for 395 eyes with VA exceed logMAR 0.3, only 22.4% under -0.50 D, while 52.3% over -1.50 D (Figure 2B). The distribution of astigmatic

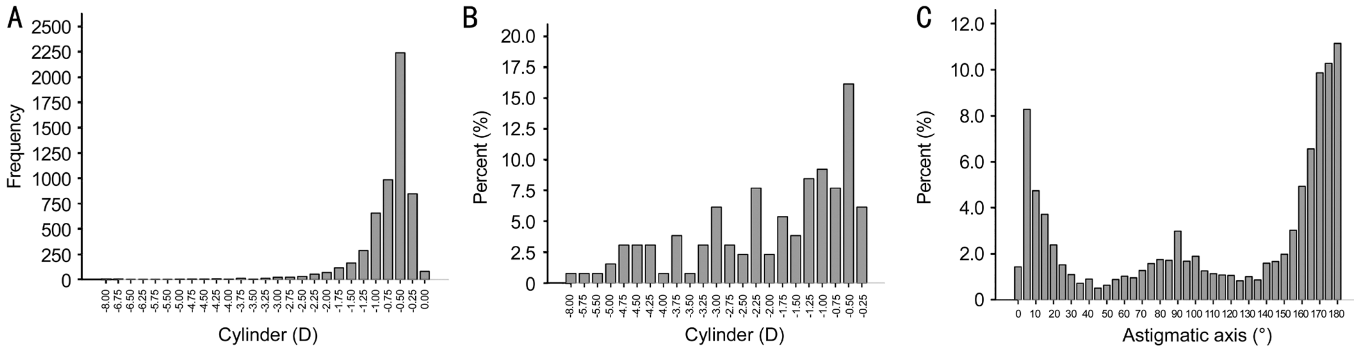

Figure 2 Astigmatic parameters distribution of the participants in the Shanghai Pudong Eye Study A: Distribution of astigmatism in 5661 measured eyes. Astigmatism was characterized by skewed distribution. B: Percentage of astigmatism in children (395 eyes) with VA exceed logMAR 0.3; C: Distribution of astigmatic axis in 5656 measured eyes, mainly astigmatism with the rule (71%).

Table 2 Refractive parameters distribution of 3 to 4y students in the Shanghai Pudong Eye Study

Factors	Measured eyes (*n*)	Range	Median	Mean±SD	95%CI	
					Lower bound	Upper bound
VA (R)	4278[a]	-0.2-1.0	0.22	0.23±0.08	-	0.36
VA (L)	4276[a]	-0.1-1.0	0.22	0.23±0.09	-	0.38
AL	8677	18.83-24.90	22.09	22.10±0.79	20.55	23.65
CRC	8680	6.55-9.24	7.85	7.86±0.26	7.35	8.37
AL/CRC	8677	2.27-3.35	2.82	2.81±0.12	2.57	3.05

VA: Visual acuity; AL: Axial length; CRC: Corneal radius of curvature; CI: Confidence interval. [a]Statistical difference of VA was in right and left eyes.

axis was shown in Figure 2C, mainly astigmatism with the rule (71%), 20.3% of astigmatism against the rule.

DISCUSSION

The specific aims of this study were to measure and analysis a number of refractive parameters, mainly AL/CRC, to investigate refractive development characteristics of children in 3 to 4 years age group based on a large-scale survey, and to provide meaningful data for earlier diagnosis of vision disorders. According to previous research findings, the increasingly prevalence and more severe degree of visual disorders in children, mainly correctable, such as myopia, hyperopia, astigmatism, amblyopia and strabismus, has become a crucial public health issue worldwide during the past two decades[2,17-18]. Considering the current status and development of vision disorder of Chinese children, it is predicable that visual impairment caused by refractive error and amblyopia in China might be a heavier load, not only for family but also for society, in the coming future. Effective strategies are needed to eliminate this situation. The USPSTF recommends at least one vision screening in all 3 to 5y group children to detect amblyopia or its risk factors[19].

This study suggested that the mean AL was 22.10±0.79 mm, the mean CRC was 7.86±0.26 mm, the mean AL/CRC was 2.81±0.12. Previous studies have shown that the correlation between SE and AL/CRC is stronger than that between AL or CRC alone[13]. R^2 coefficients for SE and AL/CRC, AL, CRC, lens thickness and anterior chamber depth (ACD) were 0.607, 0.351, 0.012, 0.038 and 0.091 respectively, which indicated that AL/CRC was a highly correlated refractive parameters to diopter[20]. There is a linear relationship between AL/CRC and diopter, a 0.1 unit increase in AL/CRC leads to a 1.2 D increase in SE[20-21]. Other studies also have shown that AL/CRC was one of the most important indicators of myopia[22]. An AL/CRC over 3 was highly accurate in the diagnosis of myopia both in adolescents and children[23], which could be a screening reference for myopia.

The 95%CI of AL/CRC was 2.57 to 3.05 in 3 to 4 years of age group students. A screening AL/CRC exceed this range may indicates high risks of refractive error like hyperopia or myopia, which may lead to refractive amblyopia. Cycloplegic refraction will be needed for further definite diagnosis, then refractive correction treatment. AL/CRC also could be used in monitoring refractive development and tendency of myopia. Since autorefractor for CRC and IOL Master test for AL were objective ocular examination, less inspection time and easy cooperation with children, accurate ocular development parameters could be collected in kindergarten visual impairment screening or pediatric ophthalmology diagnosis. The application of AL/CRC reference as an indicator of refractive errors has the effect of simplifying examination procedure and reducing unnecessary cycloplegia, especially when cycloplegic refraction is difficult to perform on 3 to 4 years old children. The number of uncooperative eyes in distance VA examination was 146 (1.68%), while only 23 (0.26%) in autorefraction and ocular biometric measurement.

The most common refractive error finding in this study was astigmatism, mainly lower diopter and astigmatism with the rule. The median of astigmatism was -0.5 D. The most common distribution of astigmatism in 3 to 4y children was below -0.50 D, accounting for 56.3%, and 85.3% below -1.00 D. A total of 6.7% for children with astigmatism exceed -1.50 D. However, only 22.4% under -0.50 D in 395 astigmatic eyes with VA exceed logMAR 0.3, the majority were over -1.50 D, accounting for 52.3%. Previous studies have shown that the correlation between AL/CRC and SE is much stronger than that between cylinder[20]. R^2 coefficients for AL/CRC and SE, cylinder were 0.560 and 0.071, respectively. Meanwhile, most astigmatism in children has lower diopter. Both of them indicate that astigmatism has little effect on AL/CRC reference for visual impairment evaluation. However, this study also found that either degree or proportion of astigmatism was increased in visual impaired children. Whether or how much impact it would have to assess visual impairment with AL/CRC reference will be further researched in subsequent studies. Therefore, using AL/CRC to evaluate refractive error and VA in children, especially uncooperative children, astigmatism screening by autorefraction are needed.

There are limitations to our study. First, this study is a large-scale epidemiological survey with numerous participants therefore cycloplegic refraction was not carried out. As a result, the correlation between AL/CRC and diopter cannot be analyzed in this study. However, the main purpose is to understanding the AL, CRC, AL/CRC, and other refractive parameters of 3 to 4y kindergarten students, then provide a medical reference range for refractive development evaluation and earlier visual impairment screening. Cycloplegic refraction in the hospital is required to confirm the diagnosis of refractive errors. Second, this study is a school-based study and restricted to urban areas, nonparticipant might have led to bias.

In conclusion, using AL/CRC reference to assess refractive development in children and screening uncorrected refractive errors is practicable and effective. Astigmatism need to be considered in the diagnosis.

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