Characteristics of axial length and interocular axial length difference in Chinese children and teenagers

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Article

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Abstract

Purpose

To investigate axial length and interocular axial length difference distributions and correlating factors in Chinese children and teenagers.

Methods

This study retrospectively reviewed the axial lengths (AL) and interocular axial length differences (ALD) of 4422 children. Sex, ocular alignment, outdoor activities, total media exposure (TV watching and electronic devices), sleep duration, parental myopic state, and parental age and their relationships with mean AL and the ratio of axial length to corneal radius curvature (AL/CR) were assessed. Factors associated with the mean AL, AL/CR, ALD, and the interocular difference in AL/CR (△AL/CR) in all participants and four age groups.

Results

The mean AL and ALD varied mainly by age. Children with esotropia (in preschoolers, $P = 0.014$, 0.029), 15–21 h of outdoor durations per week(all, $P = 0.017$), and > 14h total media exposure per week (all, $P = 0.033$) were more likely to have shorter AL or AL/CR. Esotropia(in primary school, $P = 0.001$), shorter weekdays sleep duration (all, $P = 0.009$), or long weekend sleep duration (all, $P = 0.033$) were positively associated with ALD or △AL/CR.

Conclusion

AL and ALD were mainly associated with age and esotropia. Sleep duration on weekdays or weekends might associate with the mean or interocular difference in axial length distribution.

Introduction

Anisometropia, a phenomenon that could cause anomalous refractive development or visual stimuli, varies throughout childhood and puberty. The degree of anisometropia could be reduced during emmetropization or remain unchanged or even increase in strabismic amblyopia[1]. Anisometropia could also be detrimental to stereopsis, leading to aniseikonia[2] or amblyopia[3,4] if it is not identified and treated promptly. According to previous studies, myopia[5], hyperopia[6], strabismus[1], and accommodative responsibility[7] are factors that possibly contribute to anisometropia. It was generally described as refractive anisometropia, an interocular difference in cycloplegic refraction > 1.0D[8], or > 2.5D[9], and aniso-astigmatism and axial anisometropia were sometimes mentioned[6,10,11].

Children in different study periods or of different sexes spend time differently regarding study and leisure. It is necessary to investigate whether these factors affect the axial length or interocular differences in axial length. Our study aimed to present the mean AL and ALD in children with a large age range and tried to find the correlating factors of these two parameters.

Methods

Participants and measurements

This was a cross-sectional school-based study, and 4422 children and teenagers aged 3 to 17 years were enrolled in four kindergartens, two primary schools, two junior high schools, and two senior high schools in Pujiang Downtown, Shanghai, China. All were of the Han race. Uncorrected visual acuity (UCVA), noncycloplegic autorefraction, keratometry, and axial length

(AL, from at least three consecutive examinations by IOL Master (Carl Zeiss, Jena, Germany)) were obtained. Exclusion criteria included cataracts, glaucoma, and previous ocular history in either eye. Parents or their legal guardians were required to fill in a questionnaire that recorded children's daily duration of TV-watching, electronic device usage, outdoor activities, and sleep duration as well as parental myopic state and education degree.

The study was approved by the Review Board of Fudan Eye and ENT Hospital and adhered to the tenets of the Declaration of Helsinki. The study's purpose and methods were fully explained to parents or legal guardians, and informed consent was obtained from a parent and legal guardian as subjects were under the age of 18 years.

Statistical analysis

Statistical analyses were performed with the Statistical Package for Social Sciences (SPSS, Version 22) (IBM, Armonk, NY, USA). Continuous data were presented as mean ± standardized deviation (if normally distributed) or meridian (interquartile range) (if not normally distributed). Differences between gender were performed with Pearson's chi-square tests, independent-t tests, Mann-Whitney tests, and differences between four age groups were analyzed with Pearson's chi-square tests, one-way ANOVA, or Kruskal-Wallis tests. Univariate linear regression analysis and multivariable linear regression analysis were conducted to investigate the correlations between independent ocular and nonocular parameters and AL, AL/CR, the interocular difference in AL(ALD), and AL/CR(△AL/CR). All *P* values were two-sided, and $P < 0.05$ indicated statistical significance.

Results

General characteristics

A total of 4422 children and teenagers were enrolled in this study, and their general characteristics are listed in Table 1. Interocular axial length difference is referred to as ALD. Boys had an average AL of 0.49 mm longer than girls (Mann–Whitney test: $P < 0.001$), but ALD did not vary by sex (Mann–Whitney test: $P = 0.159$). There was no significant sex difference in ocular alignment ($\chi^2 = 1.688$, $P = 0.640$), parental educational degree (paternal educational degree: $\chi^2 = 2.804$, $P = 0.730$; maternal educational degree: $\chi^2 = 4.247$, $P = 0.514$), parental myopic state ($\chi^2 = 4.144$, $P = 0.126$). There were significantly fewer girls with over 14 hours of total media exposure per week (including TV watching and electronic device usage) and 22–28 hours of outdoor activities per week than boys ($\chi^2 = 6.319$, $P = 0.042$, $\chi^2 = 16.162$, $P = 0.001$, respectively).

Table 1
General characteristics of participants (mean ± SD or meridian (IQR)).

Characteristics	Boys	Girls	*P* value
Age (years)	8.22 ± 4.05	8.36 ± 4.14	0.232
UCVA (OD, logMAR)	0.137 ± 0.269	0.159 ± 0.280	0.324
UCVA (OS, logMAR)	0.133 ± 0.260	0.154 ± 0.278	0.295
AL (OD, mm)	23.44 ± 1.36	22.95 ± 1.37	< 0.001
AL (OS, mm)	23.43 ± 1.34	22.92 ± 1.33	< 0.001
AL (OU, mm)	23.43 ± 1.34	22.94 ± 1.34	< 0.001
ALD (mm)	0.16 ± 0.23	0.17 ± 0.24	0.005
Flat K (OD, D)	42.36 ± 1.37	43.07 ± 1.37	< 0.001
Flat K (OS, D)	43.45 ± 1.50	44.22 ± 1.50	< 0.001
Steep K (OD, D)	42.31 ± 1.37	43.04 ± 1.38	< 0.001
Steep K (OS, D)	43.47 ± 1.51	44.21 ± 1.52	< 0.001
Corneal curvature (OD, D)	1.097 ± 0.60	1.147 ± 0.58	0.004
Corneal curvature (OS, D)	1.167 ± 0.65	1.187 ± 0.59	0.240
Corneal radius (OD, mm)	7.88 ± 0.26	7.74 ± 0.25	< 0.001
Corneal radius (OS, mm)	7.88 ± 0.26	7.74 ± 0.25	< 0.001
Corneal radius (OU, mm)	7.88 ± 0.25	7.74 ± 0.25	< 0.001
AL/CR(OD)	2.97 ± 0.19	2.97 ± 0.18	0.088
AL/CR(OS)	2.98 ± 0.17	2.96 ± 0.16	0.005
Paternal age (years)	28.5 ± 4.2	28.5 ± 4.3	0.633
Maternal age (years)	26.3 ± 3.6	26.4 ± 3.7	0.705
Daily sleep duration (h)			
Weekdays	9.00(7.75–9.50)	9.00(7.50–9.50)	0.018
Weekends	10.00(9.00-10.50)	10.00(9.50–10.50)	0.004

Relationship between AL, ALD, and age

A marked increasing trend in average AL was found with age (Fig. 1a). The average AL was 22.28 ± 0.70 mm in preschoolers, 23.21 ± 0.98 mm in primary school students, 24.35 ± 1.17 mm in junior high school students and 25.02 ± 1.18 mm in senior high school students ($P < 0.001$, Fig. 1b). The distribution of ALD also varied by age (Fig. 1c). ALD distribution was significantly different among the four groups (Fig. 1d). OD AL was 0.022 mm longer than OS ($P < 0.001$).

Univariate analysis of AL and AL/CR

The independent variables and their associations with AL and AL/CR in the right eyes of the children are presented in Table 2. Positive correlations were found between age, AL, and AL/CR, while female sex, esotropia, longer outdoor duration, longer media exposure, longer sleep duration during weekdays and weekends, parental myopia, and parental age were negatively correlated with AL or AL/CR.

Table 2
Univariate linear regression analysis for associations of AL and AL/CR with ocular and nonocular parameters (coefficient of regression β).

	AL	**AL/CR**
Age (yrs)	0.752**	0.713**
Sex	-0.177**	-0.010
Astigmatism(D)	-0.112**	-0.164**
Keratometry(D)	0.001	0.116**
Ocular alignment		
Orthophoria	Ref	Ref
Esotropia	-0.038*	-0.114*
Exotropia	0.143**	0.137**
Vertical tropia	-0.002	-0.139
Outdoors		
< 7 h/w	Ref	Ref
7 h-14 h/w	-0.338**	-0.116**
15 h-21 h/w	-0.525**	-0.206**
22 h-28 h/w	-0.245**	-0.172**
Media exposure		
< 10 h/w	Ref	Ref
10 h-14 h/w	-0.164**	-0.089**
> 14 h/w	-0.253**	-0.160**
Sleep duration		
Weekday(hrs)	-0.330**	-0.314**
Weekend (hrs)	-0.045**	-0.020
Parental myopia		
No	Ref	Ref
Either	-0.055**	-0.055**
Both	-0.087**	-0.058**
Parental age(yrs)		
Paternal age	-0.094**	-0.101**

** $P < 0.01$, * $P < 0.05$

	AL	AL/CR
Maternal age	-0.188**	-0.184**
**P< 0.01, *P< 0.05		

Multivariable analysis of AL and AL/CR

The results revealed that AL and AL/CR were significantly associated with ocular alignment, after adjustment for age, sex, astigmatism, keratometry, parental age, and parental myopia in the total study population and the four age groups (Table 3). Those with shorter AL were more likely to have esotropia (especially in preschools), and spent more time outdoors (15–21 h per week vs. <7 h per week). Those with lower AL/CR were more likely to have esotropia (especially in preschools), total media exposure (> 14 h per week vs. <10 h per week), and shorter sleep duration on weekends.

Table 3
Multivariable linear regression analysis for associations of AL (right eye) and AL/CR (right eye) with independent variables(regression coefficient β).

	All		Preschool		Primary		Junior		Senior	
	AL	AL/CR	AL	AL/CR	AL	AL/CR	AL	AL/CR	AL	AL/CR
Ocular alignment										
Esotropia	-0.029**	-0.031**	-0.053*	-0.053*	0.016	0.016	-0.058	-0.045	-0.076	-0.046
Exotropia	0.016	0.019	0	-0.011	0.032	0.053	0.050	0.049	0.026	0.048
Vertical tropia	0.011	-0.006	0.018	0	0	-0.033	0	0	0	0
Outdoors										
7 h-14 h/w	-0.018	-0.004	-0.043	0.007	-0.093	-0.096	-0.029	0.014	0.001	-0.029
15 h-21 h/w	-0.045*	-0.038	-0.082	-0.046	-0.087	-0.053	-0.042	-0.011	-0.003	-0.061
22 h-28 h/w	-0.019	-0.020	-0.017	-0.010	-0.012	-0.016	-0.071	-0.051	0.012	-0.020
Total media										
10 h-14 h/w	-0.011	-0.025	-0.140	-0.122	-0.018	-0.048	-0.010	-0.026	0.103	0.082
> 14 h/w	-0.031	-0.037*	-0.124	-0.111	-0.031	-0.075	-0.106*	-0.080	-0.100	-0.060
Sleep duration										
Weekday (h)	-0.022	-0.009	0.016	0.030	-0.015	0.020	-0.035	-0.075*	-0.059	0.003
Weekend (h)	0.017	0.038**	-0.019	0.028	0.072*	0.082*	-0.008	-0.017	-0.005	0.075
**P< 0.01, *P< 0.05										

Multivariable analysis of ALD and △AL/CR

The correlating factors of ALD and interocular difference in AL/CR (△AL/CR) are listed in Table 4 and are adjusted for age, sex, cylindrical power, corneal astigmatism, parental myopia, and parental age. Ocular alignment and sleep duration were significantly correlated with ALD. Those with esotropia, especially those in preschools and junior high schools, were more likely to have a larger ALD. Children who had longer sleep duration on weekdays (in preschools and senior high schools) had a greater △AL/CR. Those who had shorter sleep duration on weekends (especially in senior high schools) had a lower ALD and △AL/CR.

Table 4
Multivariable linear regression analysis for associations of ALD, △AL/CR with independent variables (regression coefficient β)

	All		**Preschool**		**Primary**		**Junior**		**Senior**	
	ALD	△AL/CR	ALD	△AL/CR	ALD	△AL/CR	ALD	△AL/CR	ALD	△AL/CR
Ocular alignment										
Esotropia	0.035*	0.018	0.055*	0.029	-0.025	-0.021	0.152*	0.060	-0.037	-0.029
Exotropia	0.010	0.027	-0.013	0.036	0.043	0.060	-0.013	0.008	0.035	0.014
Vertical tropia	-0.007	-0.005	-0.004	-0.007	-0.032	-0.013	0	0	0	0
Outdoors										
7 h-14 h/w	-0.016	-0.035	-0.043	0.058	0.082	0.112	-0.016	-0.089	-0.012	-0.028
15 h-21 h/w	-0.039	-0.039	-0.052	0.047	0.007	0.064	0.020	-0.016	-0.043	-0.006
22 h-28 h/w	-0.036	-0.030	-0.041	0.032	0.042	0.038	-0.037	-0.063	-0.077	-0.020
Total media										
10 h-14 h/w	-0.050	0.009	0.001	-0.011	0.057	0.080	-0.123*	-0016	-0.094	-0.034
> 14 h/w	-0.012	0.029	-0.005	0.001	0.113*	0.106*	0.079	0.038	-0.068	-0.031
Sleep duration										
Weekday (h)	0.028	0.061**	0.019	0.060*	0.048	0.068	0.026	0.047	0.124*	0.143**
Weekend (h)	-0.048**	-0.017	-0.013	0.016	0.017	0.041	0.006	0.019	-0.142**	-0.123*
** $P < 0.01$, * $P < 0.05$										

Discussion

Our results showed that age was significantly associated with axial length (AL), axial length-to-corneal radius ratio (AL/CR), and interocular difference in axial length (ALD) during childhood and puberty. Sex and parental myopic state were also significantly associated with AL and AL/CR.

Previous studies showed that the annual ocular axial elongation of children in lower grades (age 6 to 9 years) was between 0.21 mm[12] and 0.70 mm[13]. In children aged 6 to 12 years, the annual axial elongation was 0.36 mm[14]. In our study, the difference in AL between either two consecutive ages is 0.12 mm to 0.38 mm (from age 3 to 15 years), which is consistent with previous studies. Although data on cycloplegic refraction was not available in the current study, we analyzed the ratio of axial length to the corneal radius (AL/CR) as a substitute for refraction, which is also a reliable parameter in presenting refractive errors[15]. The sex difference in AL distribution was similar to that described in the previous studies[16–18], while a larger corneal radius (CR) was also observed in boys. A higher mean AL/CR in the left eyes of boys was found, implying that there might be some biological differences that influence refractive development between sexes. We found that parental myopic state was significantly correlated with AL and Likewise, the myopic state of parents[19–22], parental age[10,23], and education level[18] are correlated with the refractive status of the children. Parental socioeconomic background[18] and living environment[24] also affect myopic patterns.

Physical growth synchronizes with ocular growth, in which children with taller body height[23] or greater height spurts[25] are more likely to experience increasingly faster myopic progression. Even though the children's height or bodyweight data were not acquired in the current study, we discovered that the AL of teenagers was not significantly longer than that of younger children after the age of 15 years. Our findings suggested that ocular growth adapts to physical development, and the average AL progression reaches a steady-state as physical growth stabilizes.

It has been recognized that outdoor durations, indoor studying, near work[26], and sleep also have roles in ocular development, and these light-oriented activities are indispensable for normal ocular growth. There have been many studies

One of the vital chemicals in the light-related pathway, or circadian rhythm, is melatonin, also known as the most potent *Zeitgeber*[27]. Lieberman et al[28] first hypothesized that sufficient natural outdoor illumination and artificial indoor lighting might suppress melatonin secretion. The high intensity of light exposure stimulates the intrinsically photosensitive retinal ganglion cells (ipRGCs), and triggers dopaminergic pathways[29]. Furthermore, $Opn4^{-/-}$ mice with impaired melanopsin-expressing retinal ganglion cells (mRGCs) were susceptible to myopic shift and reduced retinal dopamine and 3,4-dihydroxyphenylacetic acid (DOPAC) in form-deprivation[30]. Higher morning melatonin was observed in myopes than in emmetropes and in those who spent more time outdoors or were exposed to light[31]. Likewise, in myopic young adults[32], the concentration of melatonin was higher than that in nonmyopic patients, but myopic ones were discovered to have poorer subjective sleep than nonmyopic patients[31]. Children with high myopia were also estimated to have severer sleep problems[33]. Short-wavelength light like blue light, which can be perceived by melanopsin, was shown to increase ipRGC- induced melatonin suppression in mice's pineal gland[34]. Moreover, it was the middle-wavelength light instead of the short-wavelength light that induced a more myopic shift. It could be implicated that the effect of melanopsin on sleep is not dose-dependent. In our study, weekends sleep duration is positively associated with AL/CR in primary school students. In contrast, weekdays sleep duration is negatively associated with AL/CR in junior high school students. The difference between the two age periods might be contributed to other factors, including the difference in the workload.

Excessive "screen time" was significantly correlated with sleep deprivation in preschoolers, school-aged children[35], adolescents[36], and young adults[37]. Liu et al[24] further suggested that it was the late bedtime that had a better predictive value in myopia progression. Some studies have ascribed myopia to electronic device usage or TV watching [18,38]. Using electronic devices or watching TV is associated with a potential risk of eye overuse at a near or moderate distance, accommodative spasm, or acute acquired comitant esotropia[39] in some cases. Inadequate sleep, much exposure to electronic devices or TV, or a heavy workload were raising concerns of myopic progression in children and teenagers worldwide, especially in eastern Asia. Our study found that neither outdoor durations nor total media exposure was significantly associated with AL or AL/CR in all ages except in individual age groups, which could not be conclusive due to the cross-sectional design. Since online courses have gained popularity in recent years, we should be aware that more "visual display terminal related syndrome" is taking place, and the progressively overwhelming study pressure may deprive children and teenagers of their sleep, aggravating myopic development.

The occurrence of anisometropia, or asymmetrical ocular development, is mainly attributed to monocular light suppression or abnormal visual stimuli. Therefore, activities that affect both eyes are less likely to be noticed. Our study found that age was significantly correlated with ALD and interocular difference in AL/CR (△AL/CR), while outdoor duration and total media exposure were not. The ALD of teenagers was not significantly larger than that of younger children after the age of 12 years. These findings highlight the variability in anisometropia during physical growth.

Previous studies have shown that in children aged 3 to 5 years, a higher level of hyperopia was the leading risk factor for amblyopia and strabismus[40,41]; in children aged 7 to 8 years who had anisometropic amblyopia (interocular difference of spherical equivalent refraction > 3D), there was an average ALD of 1.57 mm (average 0.32 to 3.16 mm)[4]; and in those age 11–12 years with unilateral amblyopia (BCVA < 80 ETDRS letters (0.8 Snellen) and a ≥ 2-line difference between the eyes), the average AL was 0.6 mm shorter than that of the other eyes[42]. Anisometropic amblyopia often features a significantly shorter axial length, and the eyeball would undergo extension during emmetropization. However, the hyperopic anisometropia produced by strabismus is often not compensable. Smith et al[1] found that relative myopic defocuses in the deviating eye suppressed axial elongation, while the improved accommodative function in the fixating eye reduced opticalDATA error and initiated the emmetropization process increasing the interocular difference in AL or AL/CR. We also found that preschoolers' esotropic eyes had shorter AL, less AL/CR, and ALD. To avoid strabismus-related axial anisometropia in the future, early detection, and intervention of strabismic amblyopia with anisometropia are crucial for normal ocular development.

Studies that have focused on axial anisometropia are listed in Table 5.

Table 5
Reports on refractive/axial anisometropia during childhood and adolescence

No.	Author, year	Age	Number	ALD (mm)	Highlights
1	Abrahamsson et al[43]	1 year until 4 years	310	N/A	Anisometropia was variable during emmetropization or decreased from infancy.
2	Tong et al[44]	7–9 years	1979	0.70(0.65)	Anisometropia was correlated with ALD and was more prominent in myopic anisometropia
3	Chia et al[45]	9 years	543	0.05	1. Right eyes were longer(0.05 mm) 2.Dominant eyes were less astigmatic (0.20D).
4	Deng et al[46]	6-month 5 years, 12-15years	1827	N/A	1. The prevalence of anisometropia increases in children aged 12–15 years 2.Anisometropia was more prominent in nonemmetropes.
5	Donoghue et al[6]	6–7 years 12–13 years	1050	0.40(anisometropia ≥ 1D) and 0.10(anisometropia < 1D)	1. Anisometropia was more common in children aged 12 to 13 years with hyperopia ≥ + 2DS 2. Anisometropic eyes had greater ALD.
6	Deng et al[47]	9.29 ± 1.30 (at baseline)	358(at baseline)	< 0.025 mm/y (93.3%)	1. Children who had more axial elongation would have greater ALD. 2. The amount of anisometropia at commencement did not affect myopia progression.
7	Hu[10]	10.0 ± 3.3 years (4–18years)	6025	N/A	1. Refractive anisometropia was associated with longer AL and larger ALD. 2. Myopic anisometropia was correlated with paternal education and more time indoors, while hyperopic anisometropia did not connect with eye care habits.
8	Palamar et al[48]	11.09 ± 5.27 (4 to 33 months)	42	-0.95 ± 0.50	AL and mean keratometry were the leading causes of hyperopic anisometropia.
9	Bach et al[49]	30.62 ± 18.04 months (3 months to 7 years)	165	N/A	1. The steepest increase in AL was present at ten months of age 2. ALD was not significantly different.
N/A: not available					

Our study has several limitations. First is the lack of cycloplegic refraction data. It prohibited us from comparing our findings with other myopic or anisometropic epidemiological studies. However, we provided a complete analysis of ocular development in students aged 3 to 17 years. This could be a reference for other studies in the absence of cycloplegia. Second is the cross-sectional nature of this study; we could not conclude whether children with longer ALs were more likely to have axial anisometropia, and a long-term prospective study is warranted. Despite a large population being involved, some statistical fluctuations might make the results less representative. The third is the extensive age range of the study population, rendering the comparisons of age-related daily activities difficult. To reasonably eliminate the age effect, we divided the study populations into four based on their study stage, and age still played a vital role in AL or ALD in the four age groups.

In conclusion, age was the main factor associated with axial length, and the interocular difference in axial length and sex difference between AL and ALD was also recognized in our study. Outdoor duration and total media exposure did not strongly correlate with AL or ALD in our study. Instead, sleep duration on weekends or weekdays might associate with the AL or ALD. Young age esotropia was correlated with shorter AL, AL/CR, or ALD. The measurement of axial length is a direct way to estimate the prevalence of anisometropia at young ages, and the mechanism between sleep durations and ocular development needs more biological investigations.

Abbreviations

AL: Axial length; ALD: Interocular difference in axial length; AL/CR: Axial length to corneal radius ratio; UCVA: Uncorrected visual acuity

Declarations

Consent for publication

Not applicable.

Data availability statement

The data and the analysis of the current study could be acquired from the corresponding authors if needed.

Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

XYM and MJC wrote the main manuscript text and prepared figures and tables for the research; XYM and MJC performed the statistical analysis; MXY, MJC, and JHD interpreted the data; JHD and XHS supervised and critically revised the manuscript. All authors reviewed and approved the manuscript.

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Figures

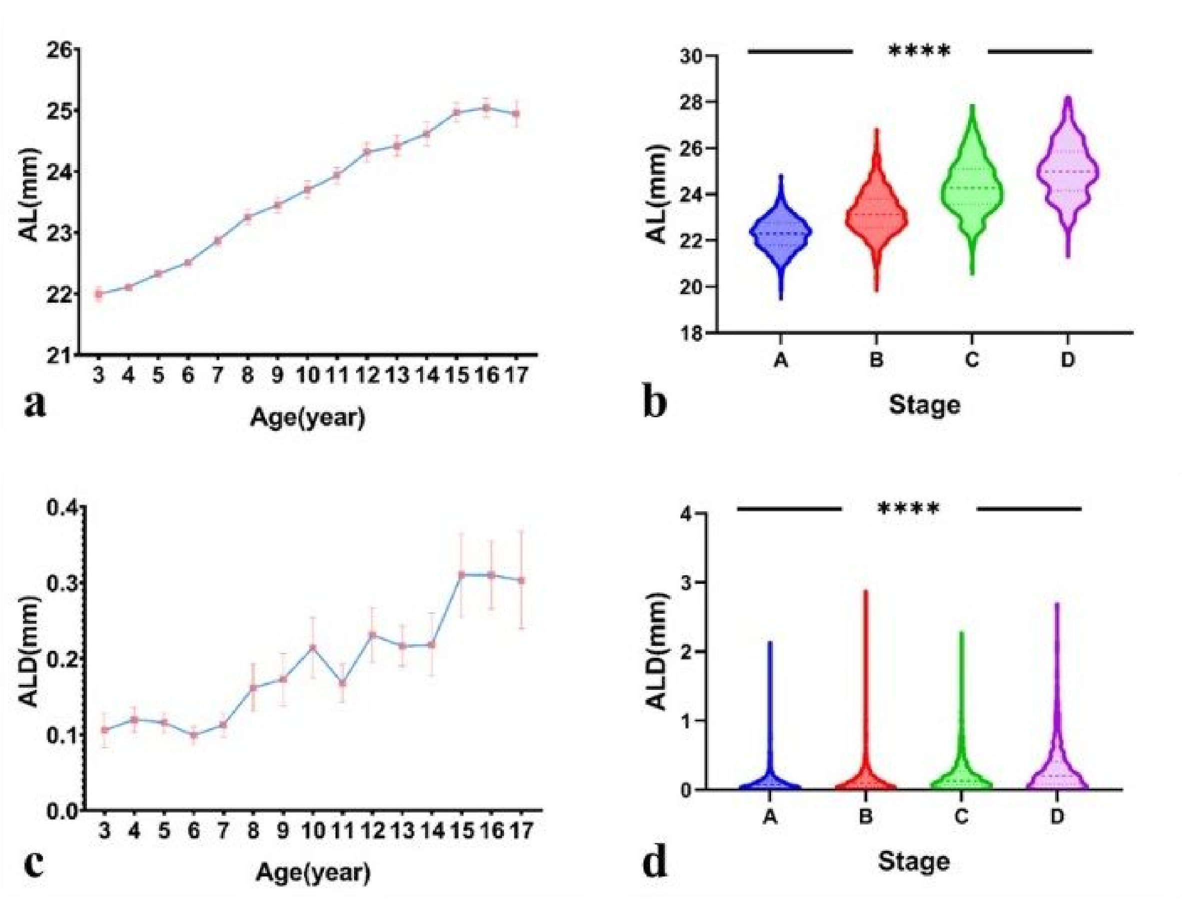

Figure 1

a. AL distribution by age. **b**. AL distribution among four stages. (Stage A: preschoolers; Stage B: primary school; Stage C: junior high school; Stage D: senior high school) **c**. ALD distribution by age. **d**. ALD distribution among four stages (the mean value is presented as dots and lines while the standardized deviation is presented as error bars in **a** and **c**, and a P value <0.001 of intergroup difference is presented as "****" in **b** and **d**)