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Distribution, Progression, and Associated Factors of Refractive Status of Children in Lhasa, Tibet, after COVID-19 Quarantine

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Keywords
Myopia · Refractive error · Tibetan · Children · Coronavirus disease-19

Abstract

Introduction: Uncorrected refractive error is one of the major causes of visual impairment in children and adolescents worldwide. During the COVID-19 epidemic, home isolation is considered a boost to the progression of children's myopia. Under geographical conditions of high altitude and strong sunshine, the Tibetan plateau is the main residence of the Tibetan population, where little information is available about the refractive status and developmental trajectory. Therefore, this article aimed to evaluate the distribution, progression, and associated factors of the refractive status in second-grade children in Lhasa after COVID-19 quarantine. ***Materials and Methods:*** Students from 7 elementary schools completed comprehensive ocular examinations in the Lhasa Childhood Eye Study. Data regarding cycloplegic refraction and corneal biometry parameters, including axial length (AL), corneal power, anterior chamber depth (ACD), and other demographic factors, were analyzed. ***Results:*** A total of 1,819 students were included, with a mean age of 7.9 ± 0.5 years, of which 961 were boys (52.8%), and 95.1% were Tibetan. The prevalence of myopia, emmetropia, mild hyperopia, and hyperopia was 10.94%, 24.02%, 60.80%, and 4.24%, respectively. Besides, the average cycloplegic spherical equivalent refraction (SER) was +1.07 ± 0.92 diopter (D) before the COVID-19 quarantine and +0.59 ± 1.08D after the quarantine ($p < 0.05$), with a growth rate of 7%. Moreover, the prevalence of hyperopia in girls was significantly higher than that of boys ($p < 0.001$). Nonetheless, the proportion of myopia and emmetropia was similar ($p = 0.75$). Meanwhile, children in suburban schools had a significantly lower proportion of myopia ($p < 0.001$). The average AL, ACD, lens power (LP), and AL-to-corneal radius (AL/CR) ratio were 22.79 ± 0.78 mm, 3.54 ± 0.21 mm, 25.12 ± 1.48D, and 2.93 ± 0.08, respectively. The results of AL, ACD, and AL/CR for girls were significantly lower than for boys, while the result of LP is the opposite ($p < 0.001$). Finally, multivariate regression analysis revealed that SER was negatively correlated with AL, LP, and AL/CR ratio, while positively correlated with CR and ACD ($p < 0.001$). ***Conclusion:*** This study found that after the COVID-19 confinement, myopia progressed faster in Lhasa children but was still significantly lower than that of plain cit-

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ies in China. Compared to short-term confinement, this acceleration was more likely related to the growth and general trend of myopia in children. Collectively, these findings help to explore the differences in ocular growth and development among children of different ethnic groups.

Introduction

Uncorrected refractive errors are one of the major causes of visual impairment in children and adolescents worldwide. In recent years, under the influence of external environmental alterations such as the decrease in outdoor activities, overuse of electronic products, and intensive education, myopia has the trend of a younger onset and faster progression. In the latest large-scale screening of refractive status, myopia prevalence of school-age children in China is about 50% and that of high school students is equal to or greater than 90% [1]. Furthermore, myopia is more likely to develop into high myopia or even pathological myopia in young children, whose complications, such as macular holes and retinal detachment, could induce permanent and irreversible visual impairment [2]. Therefore, early childhood periodic ocular assessment is fundamental for not only screening latent and early symptomatic ocular disorders but also for the early prevention and management of myopia.

As an infectious disease sweeping the globe, the emergence of COVID-19 has pushed forward lockdowns for the purpose of slowing the spread of the pandemic. As a result of the outbreak, it is estimated that more than 220 million school-age children and adolescents are restricted at home to take online courses for academic learning [3, 4]. Ametropia, especially myopia, is closely related to long-term eye use in short distances. It is widely accepted that the progression of myopia accelerated during the epidemic, especially in young children [5, 6]. By accurately measuring the real refractive status before and after the epidemic, the association between home quarantine and the progression of children's myopia can be investigated.

To date, few studies have focused on ocular refractive status and biometric information of Tibetan children and only focused on noncycloplegic optometry. It is known that young children possess a comparatively stronger accommodative ability. Therefore, this study aimed to evaluate the refractive status of Tibetan children by automatic optometry after cycloplegia, compare the refractive changes before and after the COVID-19 epidemic, and explore the influencing factors associated with the myopia onset. As a high-altitude region, Tibet is the province with the least number of infections during the epidemic period in China. Nevertheless, local Tibetan children were still studying at home in April. The findings of this study complement the effect of home isolation on the refractive status in children of different races and improve our understanding of the ocular development of children in high latitude and strong sunlight environments.

Materials and Methods

Study Population and Design

The Lhasa Childhood Eye Study (LCES) was a school-based, observational cohort epidemiological study on childhood ocular diseases among grade-one students with a 5-year follow-up time in Lhasa, Tibet. The study protocol adhered to the Declaration of Helsinki and was approved by the Ethics Committee of the Beijing Tongren Hospital, Capital Medical University (No. TRECKY2019-058). A comprehensive ocular examination was performed according to a standard operating procedure and supervised by an ophthalmologist and an epidemiologist. All participants' parents or legal guardians gave written informed consent prior to the study. The methodology and examination of the LCES have been published elsewhere [7].

Eye Examinations and Definitions

All students underwent a comprehensive ocular examination in November 2020, including uncorrected and best-corrected visual acuity (250300; Goodlite, Elgin, IL, USA), stereopsis acuity (S0001; STEREO, Covina, CA, USA), ocular dominance, slit-lamp biomicroscopy (SL-3G, Topcon, Tokyo, Japan), noncontact tonometry (CT-800, Topcon, Tokyo, Japan), ocular alignment, autorefraction before and after cycloplegia, axial length (AL), anterior chamber depth (ACD), and corneal curvature (IOLMaster, ZEISS, Germany) and macular-centered 45° fundus photography. The process for cycloplegic optometry is reflected in other articles [8]. In 2019, 2020, and 2021, we have conducted the above examinations on the same group of students including autorefraction after cycloplegia, but only in 2020, we measured the biometry parameters like AL, ACD, etc.

Myopia, emmetropia, mild hyperopia, and hyperopia were defined as spherical equivalent refraction (SER) ≤ -0.50 diopters (D), $-0.50\text{D} < \text{SER} < 0.50\text{D}$, $0.50\text{D} \leq \text{SER} < 2.0\text{D}$, and $\text{SER} \geq 2.0\text{D}$, respectively, in one or both eyes. The corneal power was calculated as the mean of k1 and k2. Corneal radius (CR) was converted from the corneal power data using the following formula: corneal power (D) = 0.3375/CR (mm) × 1,000; the AL-to-CR (AL/CR) ratio was computed as AL in millimeters divided by CR in millimeters. Lens power (LP) was calculated using the Bennett-Rabbetts method with unknown lens thickness, using measured values for SER, CR, AL, and ACD [9].

Statistical Analysis

Values for the continuous variables were presented as mean ± standard deviation and as percentages for categorical variables. The statistical analysis system software (version 9.4, SAS Inc., Cary, NC, USA) was used to analyze the data. The *t*-test was used

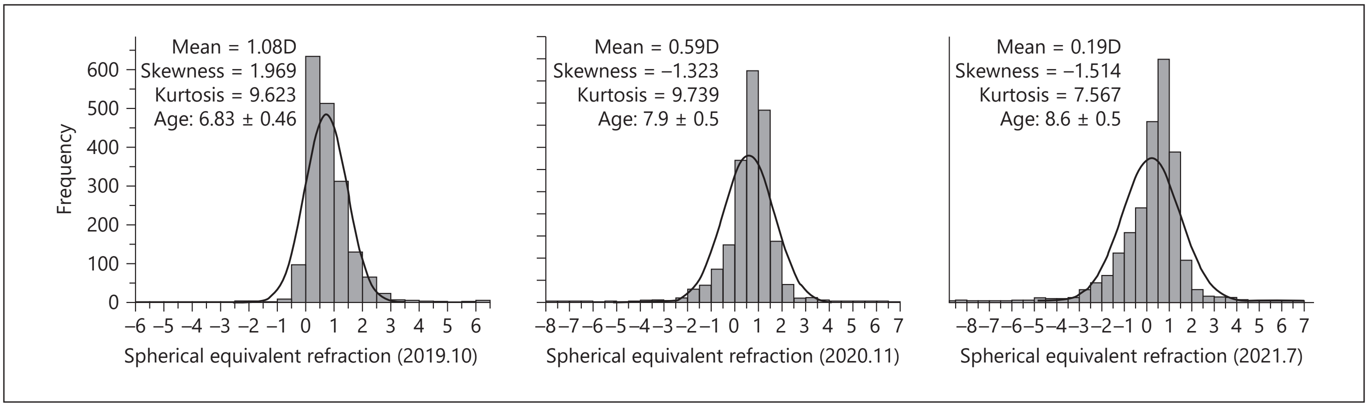

Fig. 1. Distribution of SER before and after COVID-19.

Table 1. Refractive and biometric characteristics of the population

Characteristics	Total	Girls	Boys	*p* value
SER before COVID-19 (October 2019)	1.07±0.92	1.12±0.94	1.03±0.89	0.02*
SER after COVID-19 (November 2020)	0.59±1.08	0.62±1.07	0.56±1.08	0.25
SER after COVID-19 (July 2021)	0.19±1.28	0.21±1.28	0.17±1.28	0.52
November 2020				
AL, mm	22.79±0.78	22.53±0.73	23.02±0.75	<0.001*
ACD, mm	3.54±0.21	3.50±0.19	3.58±0.21	<0.001*
CR, mm	7.78±0.27	7.71±0.25	7.85±0.27	<0.001*
AL/CR ratio	2.93±0.08	2.92±0.08	2.94±0.08	<0.001*
LP, D	25.12±1.48	25.67±1.42	24.62±1.35	<0.001*

SER, spherical equivalent refraction; D, diopters. * $p < 0.05$ girls versus boys.

to compare changes in refractive error before and after confinement in the past 3 years; the χ^2 test was employed to compare the proportion of myopia, hyperopia, and astigmatism between genders, schools, and age-groups; multiple regression analysis was used to assess the effects of gender, age, ethnicity, body mass index, intraocular pressure, and blood oxygen saturation on the refractive error; correlation analysis was used to calculate the correlation coefficients between refractive error and AL, corneal parameters, and other indicators.

Results

Study Population, General Characteristics, and Refractive Error

In the second year of the cohort study, about half a year after the quarantine, a total of 1,819 students with complete available data were included in the analysis. Their average age was 7.9 ± 0.5 years, of which 961 were boys (52.8%) and 95.1% were Tibetan ethnic minority children. The binocular SER of all the children was highly correlated ($R = 0.91$); thus, the right eye was selected for statistical analyses. The average cycloplegic SER of the participants was +1.07 ± 0.92D before the COVID-19 quarantine (October 2019) and +0.59 ± 1.08D after the quarantine (November 2020). Compared with the pre-epidemic period, the proportion of myopia increased by about 7% in one year, and the SER decreased by 0.49 ± 0.57D on average ($p < 0.05$). Besides, the SER acquired in the last year of follow-up was 0.19 ± 1.28D (July 2021), and the proportion of myopia increased by more than 10% compared with the previous year. The distribution of SER before and after the epidemic is illustrated in Figure 1, with no Gaussian distribution observed. The SER, as a function of gender, is presented in Table 1. There was no significant difference between the SER of boys and girls ($p = 0.25$).

Prevalence of Refractive Error

The prevalence of refractive error in contrasting age-groups, genders, and school locations are summarized in Table 2, and the distributions of the different refractive categories are displayed in Figure 2. Overall, mild hyper-

Table 2. Prevalence of myopia, emmetropia, mild hyperopia, and hyperopia in Lhasa grade-2 students

	N	Myopia			Emmetropia			Mild hyperopia			Hyperopia		
		n	%	95% CI	*n*	%	95% CI	*n*	%	95% CI	*n*	%	95% CI
Before COVID-19 in October 2019	1,853	73	3.94	3.1–4.8	186	10.04	8.7–11.4	1,436	77.50	75.6–79.4	158	8.52	7.3–9.8
After COVID-19 in November 2020	1,819	199	10.94	9.5–12.4	437	24.02	22.1–26.0	1,106	60.80	58.6–63.0	77	4.24	3.3–5.2
Age, years													
7	1,131	124	6.82	5.7–8.0	277	15.23	13.6–16.9	675	37.11	34.9–39.3	55	3.02	2.2–3.8
8 and above	688	75	4.12	3.2–5.0	160	8.80	7.5–10.0	431	23.69	21.7–25.6	22	1.21	0.7–1.7
p value		0.9669			0.5497			0.2093			0.0871		
Sex													
Boys	961	103	5.66	4.6–6.7	246	13.52	12.0–15.1	586	32.22	30.0–34.3	26	1.43	0.9–2.0
Girls	858	96	5.28	4.3–6.3	191	10.50	9.1–11.9	520	28.59	26.5–30.7	51	2.80	2.0–3.6
p value		0.7481			0.0963			0.8711			<0.001*		
School location													
Urban	1,434	173	9.51	8.2–10.9	344	18.91	17.1–20.7	854	46.95	44.7–49.2	63	3.46	2.6–4.3
Suburban	385	26	1.43	0.9–2.0	93	5.11	4.1–6.1	252	13.85	12.3–15.4	14	0.77	0.4–1.2
p value		<0.001*			0.9457			0.03*			0.5125		

* $p < 0.05$, statistical differences between groups.

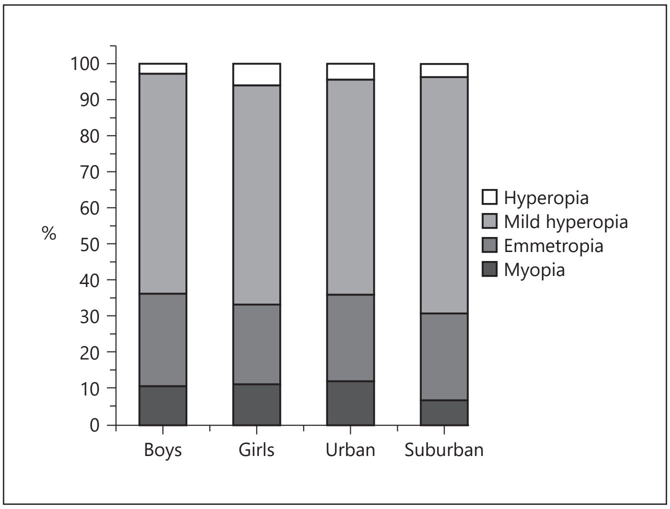

Fig. 2. Distributions of refractive error in sexes and school locations.

opia was the predominant refractive status (60.80%), followed by emmetropia (24.02%), myopia (10.94%), and hyperopia (4.24%). No significant difference was found in the distribution of refractive error between children aged 7 years and over 8 years. In terms of gender, the proportion of hyperopia in girls was significantly higher than that in boys ($p < 0.001$), but the proportion of myopia and emmetropia was similar ($p = 0.75, 0.10$). Moreover, compared with children in urban schools, children in suburban schools had a significantly lower proportion of myopia ($p < 0.001$), while the proportion of hyperopia and emmetropia was similar ($p = 0.51, 0.95$).

Factors Influencing Refractive Errors

Detailed distributions of ocular biometry by gender are outlined in Table 1. Biological parameters such as AL, ACD, and CR were lower in girls than boys ($p < 0.001$ for all). Likewise, the calculated AL/CR ratio was significantly lower in girls. In contrast, LP was higher in girls ($p < 0.001$).

Multivariate regression analysis was used to explore the associations between SER and other factors (Table 3). Among them, blood oxygen saturation was correlated with SER ($p = 0.01$), whereas other demographic factors such as gender, age, ethnicity, body mass index, and intraocular pressure were not significantly correlated. For the biometric characters, SER was negatively correlated with AL, LP, and the AL/CR ratio but positively correlated with CR and ACD (after adjusting for age and gender).

Discussion

This is the first article to comprehensively describe the distribution of the true refractive status after cycloplegia in Tibetan minority children inhabiting the plateau region and the changes in refractive error before and after the epidemic. LCES has established a representative ophthalmology database for children's refractive error in Lhasa. According to the study, the overall refractive error in children before and after the epidemic has significant-

Table 3. Demographic and ocular independent variables associated with SER

Factors	*B*	Standard error	*t* value	Standardized coefficient	*p* value
Ethnic	−0.05	0.12	−0.43	−0.01	0.67
Sex	0.06	0.05	1.11	0.03	0.27
Age	−0.05	0.05	−1.07	−0.03	0.28
BMI	−0.01	0.01	−0.77	−0.02	0.44
Blood oxygen saturation	−0.01	0.01	−2.60	−0.06	0.01*
IOP	−0.01	0.01	−1.61	−0.04	0.11
AL	−1.27	0.07	−19.08	−0.94	<0.001*
ACD	1.56	0.01	126.17	0.31	<0.001*
CR	0.41	0.20	2.13	0.10	0.03*
AL/CR ratio	−13.32	0.52	−25.77	−0.95	<0.001*
LP	−0.62	0.00	−288.12	−0.86	<0.001*

BMI, body mass index; IOP, intraocular pressure. * Independent factors significantly associated with SER.

ly progressed toward myopia. Considering the refractive status of second-grade children after the epidemic, girls had a higher proportion of hyperopia than boys, while children in suburban schools had lower myopia rates than urban schools. Furthermore, the values of various ocular biological parameters of girls were significantly lower than those of boys.

The mean SER for 8-year-old Tibetan children was +0.59 ± 1.08D, which is significantly higher compared to the children in Hong Kong [10] of the same age (0.10 ± 1.38D and 0.04 ± 1.36D, pre- and post-epidemic). This comparison is also similar to that of other provinces in China like Shandong [4] (−0.59~−0.31D), Zhejiang [1] (−0.7 ± 1.6D), He Bei [11] (−0.50 ± 1.25D), and Shanghai [12](−1.86 ± 0.76D). Most children are still in a state of mild hyperopia even after the COVID-19 epidemic in Lhasa. The observation is consistent with the conclusion obtained a year before the pandemic situation, that is, the proportion of myopia among Tibetan children in the plateau was lower than that of Han children in other plains in China [13, 14]. This may be related to the long daylight hours in high-altitude areas and the living habits of Tibetans. Previous evidence [15–18] has established that sunlight can improve children's visual development, and long-term outdoor activities can slow down the progression of myopia.

Comparing the refractive status between pre- and post-COVID-19 quarantine, the average SER decreased by −0.49 ± 0.55D for one year, with the proportion of myopia increasing by 7% accordingly. Ma et al. [12] reported that the SER of children around 10 years old decreased by −0.39D in the first half year without quarantine and then −0.98D in the half year after the epidemic occurred. Chang et al. [1], Wang et al. [4], etc., reported that the SER changes in children during COVID-19 were around −0.5D, greater than the annual SER changes before the epidemic. Compared with other provinces in China, the rate of myopia in eight-year-old children in Shandong province [4] and Zhejiang province [19] exceeded 10%, whereas the growth rate of myopia in Lhasa was significantly lower. Lhasa is one of the regions least affected by the epidemic in China. Its blockade policy lasted for only 1 month in 2020, with 2-h online classes daily for primary school. Still, the SER of grade-1 students significantly dropped in the second year. With the lifting of the lockdown, in the follow-up examinations in 2021, nearly 8 months after the last study, the myopia rate of children in Lhasa significantly increased by over 10%. The average SER decline was also similar to the change in the past year. This seems to indicate that the short-term epidemic isolation policy had minimal impact on the refractive status of grade-two Lhasa children. Under the trend of global myopia, the development of myopia in Lhasa children is also accelerating, but its overall distribution is still biased toward farsightedness. Therefore, most children are still in the process of normal ocular development without prematurely developing myopia.

This study determined that students in urban schools had a higher rate of myopia while girls had a higher rate of hyperopia. Multiple regression analysis established that the blood oxygen saturation was negatively correlated with SER. Previous articles [20–22] have confirmed that children in cities have a higher rate of myopia than children in rural or remote areas. This observation is mainly related to the greater learning pressure on urban children, more time for using electronic applications, and less time for outdoor activities [23]. Several documents [14, 20, 24] have also proposed the difference in refractive power between male and female students, but the conclusions are contrasting. This difference in refractive power between genders may be related to retinal thickness [25, 26], but this hypothesis must be further validated in future follow-ups. Past studies [27, 28] have shown significant differences in the refractive distribution between races. However, in this study, the number of non-Tibetan children was small, and hence, the differences between races were not apparent.

The AL/CR ratio has been proposed as a better calculated biometric and predictive parameter correlated with SER than AL, and a high AL/CR ratio of not less than 3.0 is considered a risk factor for developing myopia [29, 30]. In this study, the AL/CR ratio (2.93 ± 0.08) was lower than children of the same age in other cities [31–33]. This finding demonstrates that the potential risk of myopia developing in Lhasa children is indeed lower. Similarly, the AL value of children in Lhasa was also lower than that of children in other cities in China [33, 34]. Consistent with previously reported studies [35–39], it was observed that boys have longer AL, ACD, and lower LP than girls. Linear correlation analysis found that SER was negatively correlated with AL and LP, while positively with ACD, consistent with other studies. In He et al.'s [34] research on Shenzhen kindergarten children aged 3–6 years, girls had shorter AL and ACD and higher LP, and the differences were statistically significant. Other local and foreign studies [40–42] have also reported this association numerous times, but the rationale remains to be elucidated. Considering that LP decreases with age, maybe among the same age, boys grow faster and earlier than girls. Therefore, boys are more likely to have advanced AL and ACD increases with lower LP.

The main strengths of this study are the large, unbiased samples; special ethnic groups; standardized comprehensive inspections; and detailed analyses. However, some limitations include the lack of comparisons with other ethnic samples and the lack of detailed investigations regarding life habits and environmental effects. These questions can be further supplemented and answered in the future.

Conclusion

This study described and analyzed the distribution, related factors, and comparison of the refractive status in Lhasa children after COVID-19. These findings help strengthen the understanding of ocular conditions in Lhasa children, explore the differences as well as changes in ocular growth of ethnic minorities, and contribute to the establishment of a normal ophthalmological database for children in Lhasa. At the same time, it is also the foundation for long-term eye health monitoring and protection in plateau areas.

Acknowledgments

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Statement of Ethics

The study protocols adhered to the declaration of Helsinki and were approved by the Ethics Committee of the Beijing Tongren Hospital, Capital Medical University (No. TRECKY2019-058). All participants' parents or legal guardians gave written informed consent prior to the study.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Jing Fu initiated the study design. Weiwei Chen and Yao Yao prepared the consent form. All the authors are involved in the research process and data collation. Yao Yao and Jing Fu drafted and finalized the study protocol. Lei Li assisted in collation and analysis of the data. Jiawen Liu assisted in article writing and proofreading. All the authors reviewed the study protocol and approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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