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ORIGINAL RESEARCH

Relationship Between Early-Life Factors and Self-Reported Age at Myopia Onset: A Study Based on a Sample of Chinese Adults

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Aim: To investigate the influence of early-life factors (Season of birth, premature birth and breastfeeding) on the age at myopia onset.

Methods: A total of 331 myopic students aged 18 years or above were recruited from one medical university in Wenzhou, China. Questionnaires were administered to collect data on age at myopia onset, early-life factors, and vision hygiene habits. Participants underwent noncycloplegic autorefraction. Generalized Linear Model was used to analyse the influencing factors of the age at myopia onset, early life factors as independent variables, spherical equivalent, parental myopia and eye hygiene habits as confounding factors into the generalized linear model.

Results: In this study, the mean spherical equivalent (SE) of myopic university students was −4.55±2.19 D, and the mean age at myopia onset was 13.31±2.64 years old. Subjects born in the summer had a younger age at myopia onset (β=−1.79, P=0.001); subjects born prematurely tended to have a younger age at myopia onset (β=−1.50, P=0.011); and breastfeeding was not statistically associated with the age at myopia onset.

Conclusion: Season of birth and premature birth were associated with age at myopia onset, and children born in the summer and born prematurely had a younger age at myopia onset.

Keywords: myopia, age at myopia onset, season of birth, premature birth

Introduction

Myopia constitutes a formidable global public health challenge. Projections indicate that 49.8% of the world's population will be affected by myopia, with 9.8% experiencing high myopia.[1] High myopia is frequently associated with an array of complications, including retinal detachment, macular degeneration, and glaucoma,[2–5] imparting substantial physical and psychological burdens on affected individuals. Prior research has underscored the age at myopia onset is the paramount predictor of high myopia among children. The Singapore Cohort Study of Risk Factors for Myopia (SCORM) revealed a significant correlation between an earlier age of myopia onset and the incidence of high myopia (odds ratio [OR] = 2.86; 95% confidence interval [CI]: 2.39–3.43). Notably, in the Receiver Operating Characteristic (ROC) curve analysis, the age at myopia onset alone accounted for the prediction of 85% of high myopia cases.[6] However, most previous studies have focused on the influencing factors of myopia onset and progression, while the age of myopia onset is relatively scarce. Consequently, it is essential to reduce the risk of high myopia by delaying in myopia onset.

It is well-known that myopia is the result of a combination of genetic and environmental factors.[7,8] Numerous prior investigations have correlated myopia with environmental factors, typically concentrating on the corresponding environmental factors at the onset of myopia while neglecting those in earlier life stages before myopia develops, such as the intrauterine environment and environmental influences during infancy. The Developmental Origins of Health and Disease (DOHaD) hypothesis elucidates that adverse developmental circumstances in early life,[9–12] spanning pregnancy, fetal,

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and infant stages, may elicit enduring metabolic alterations, influencing postnatal growth trajectories and augmenting the vulnerability to certain chronic non-communicable diseases in adulthood. Recently, a multitude of studies have indicated that the gestational and perinatal milieu may modulate the secretion and metabolism of monoamine neurotransmitters, such as dopamine and serotonin, with their prolonged impacts extending well into adulthood.[13,14] Notably, dopamine stands as a pivotal neurotransmitter within retinal signal transduction pathways, facilitating the growth and development of refractive components, thereby modulating the occurrence of myopia,[15,16] hinting at a potential influence of the season of birth on myopia. A large-scale population-based study conducted in Israel reported an association between the season of birth and the incidence and progression of myopia, revealing a propensity for higher myopia among individuals born in summer or autumn compared to those born in winter.[17]

In addition to the season of birth, studies have further identified that factors such as pregnancy complications, preterm delivery, and breastfeeding during early life stages may impact the onset of myopia in children.[18–21] However, these findings exhibit variability across different countries and populations. Therefore, the present study endeavors to elucidate the influence of early life factors on the incidence of myopia in the Chinese population.

Subjects and Methods

Ethical Approval

The research was conducted in accordance with the tenets of the Declaration of Helsinki, and the study protocol was approved by the ethics committee of Eye Hospital of Wenzhou Medical University.

Subjects

This study was a cross-sectional investigation conducted from December 2021 to April 2022 at one medical university in Wenzhou, China with convenience sampling. We computed the sample size using the formula: $N=(u_\alpha/\delta)^2/p(1\text{-}p)$ with a significance level of $\alpha=0.05$ and a power of 95%.[22] The study required at least 259 subjects. We added a 10% dropout rate for possible loss to follow-up or refusals, which increased the final sample size to 285 subjects. A total of 331 freshmen with myopia were included in this study. These 331 students come from all over the country, and 59.7% were from rural, 40.3% from urban. Participants with the SE ≤ -0.50 D in either eye who could successfully undergo ophthalmic examinations and complete questionnaires were included. Participants with serious systemic or ophthalmic diseases that affect visual acuity, such as eye injury, glaucoma, and diabetic retinopathy, or those undergoing treatment with atropine eye drops or orthokeratology were excluded.

Eye Examinations

All students included in the study underwent noncycloplegic refraction, and all instruments were checked and adjusted before measurement. An autorefractor (TOPCON-RM8900) was used to measure the noncycloplegic refraction of both eyes at least thrice. The average of the three measurements was taken and recorded. If the difference between two measurements was greater than 0.5 D, another measurement was taken for averaging. Each value was measured at least thrice, and the average value was taken and recorded.

Questionnaires

Students completed the self-administered questionnaire at the beginning of the study. The questionnaire included basic questions about sex, date of birth, age at myopia onset, parents' education level and refractive status, prematurity and breastfeeding, sleep duration, near work related behaviors (such as reading/writing distance, continuous near work time and so on), near work time and outdoor activities time. Near work time included time spent doing reading and writing, watching TV, mobile phone use and computer use. Questions about time spent in outdoor activities concerned both leisure and sports. Students need to answer the following questions: "Were you premature when you were born?" (Yes/ No), "Breastfeeding or not?" (Yes/ No), "Spent time on mobile phone use every time?" (less than 30 mins/30 mins ~1 hour/1 hour ~2 hours/more than 2 hours). After on-site collection, investigators checked the questionnaires one by one to identify logical errors, omissions and unclear handwriting and modifications by the subjects themselves.

Definition and Statistical Analysis

Statistical analysis was performed using SPSS 26.0. SE was calculated as follows: SE = sphere + 1/2 cylinder. Myopia was defined as a condition in which the spherical equivalent objective refractive error is ≤ −0.50 D in either eye. The season of birth was determined based on the date of birth: spring (March–May), summer (June–August), autumn (September–November), and winter (December–February). Age at myopia onset was defined as the self-reported age at the first use of glasses.

Measurements that conformed to a normal distribution are described by the mean ± standard deviation, and enumeration data are described by the frequency (percentage). *T*-test and ANOVA test was used to analyse the differences in the age at myopia onset among subjects with different characteristics. Spearman's test was used to analyse the relationship between the age at myopia onset and SE. Generalized Linear Model was used to analyse the influencing factors of the age at myopia onset. The model fits the data well (model 1, R-squared value was 38.922, P<0.001; model 2, R-squared value was 42.652, P<0.001). The level of significance for the 2-sided test was set at p<0.05. The SE of the right and left eyes were highly correlated (r=0.823; p<0.001); thus, the analysis used the SE of the right eye only.

Results

A total of 331 students with myopia were enrolled in this study, and 303 subjects (91.5%) were completed self-administered questionnaires and eye examination. Socio-demographic characteristics were provided in Table 1. Mean age of all subjects was 19.03 ± 0.90 years (18–22 years). 67.3% of subjects were female. Mean SE was −4.55 ± 2.19 D,

Table 1 Population Characteristics of the Sample

Characteristic	Subjects	Mean±SD or %
Age (years)	303	19.03±0.90
Age at myopia onset (years)	303	13.31±2.64
Body mass index (kg/m^2)	302	21.30±3.19
SE (D)	303	−4.55±2.19
Sex	303	
Male	99	32.70%
Female	204	67.30%
With or without premature birth	250	
Yes	30	12%
No	220	88%
With or without breastfeeding	264	
Yes	246	93.20%
No	18	7.80%
Season of birth	303	
Spring	74	24.40%
Summer	74	24.40%
Autumn	99	32.50%
Winter	56	18.70%
Number of myopic parents	271	
0	147	54.20%
1	99	36.50%
2	25	9.20%
Duration of mobile phone use	303	
≤30 min	26	8.60%
>30 min	277	91.40%
Duration of reading/writing	303	
≤30 min	21	7.10%
>30 min	282	92.90%
Sleep duration (Hours)	302	8.38±1.17

Abbreviations: SE, Spherical equivalent; D, diopters; SD, standard deviation.

and the mean age at myopia onset was 13.31±2.64 years. Spearman's test revealed no significant difference between age at myopia onset and the SE (p=0.55) in adulthood. The distribution of birth season was as follows: spring (24.4%), summer (24.4%), autumn (32.5%), and winter (18.7%).

We found there was a trend in the age of onset of myopia. The number of people with myopia onset increased with age before 12 years old and subsequently presented a declining pattern. And another peak of myopic onset was observed at the ages of 15–16 years (Figure 1).

As shown in Table 2, there was a significant difference in the age at myopia onset in subjects of different characteristics (p<0.05). Age at myopia onset was 12.37±2.85 years in students with premature birth and 13.45±2.66 years in students without premature birth (p=0.038). The age at myopia onset was youngest in students with born in summer (13.69±2.31 years(spring), 12.31±3.13 years(summer), 13.61±2.31 years(autumn), 13.63±2.63 years(winter), p=0.002). However, there was no significant difference in the age at myopia onset in subjects with breastfeeding and without breastfeeding (13.28±2.68 years, 13.11±2.72 years, p=0.801).

The relationship among the age at myopia onset with birth season, prematurity and breastfeeding were shown in Figure 2. Individuals born in the summer and born prematurely had an earlier onset of myopia, which were statistically significant. However, breastfeeding or not had no effect on the age at myopia onset.

We also analysed risk factor of age at myopia onset using the Generalized Linear model after adjusting for sex, the number of myopic parents, spherical equivalent (SE), the Body Mass Index (BMI), the duration of reading/writing and the duration of mobile phone use. Subjects born in the summer and born prematurely had a younger age at myopia onset (β=−1.79, P=0.001; β=−1.50, P=0.011, Table 3). There was no significant difference between breastfeeding and the age at myopia onset.

Discussion

Birth Season and Myopia

Our study showed that the subjects born in the summer self-reported a younger age at myopia onset, and this correlation persisted after adjusting for age, sex, SE, the number of myopic parents, BMI, the duration of reading/writing and the duration of mobile phone use in a generalized linear model (P<0.01, 95% CI: −2.82~-0.80). Most of the subjects in this study were born around 2000. According to the fifth census by the National Bureau of Statistics (stats.gov.cn), during the period from November 1, 1999,

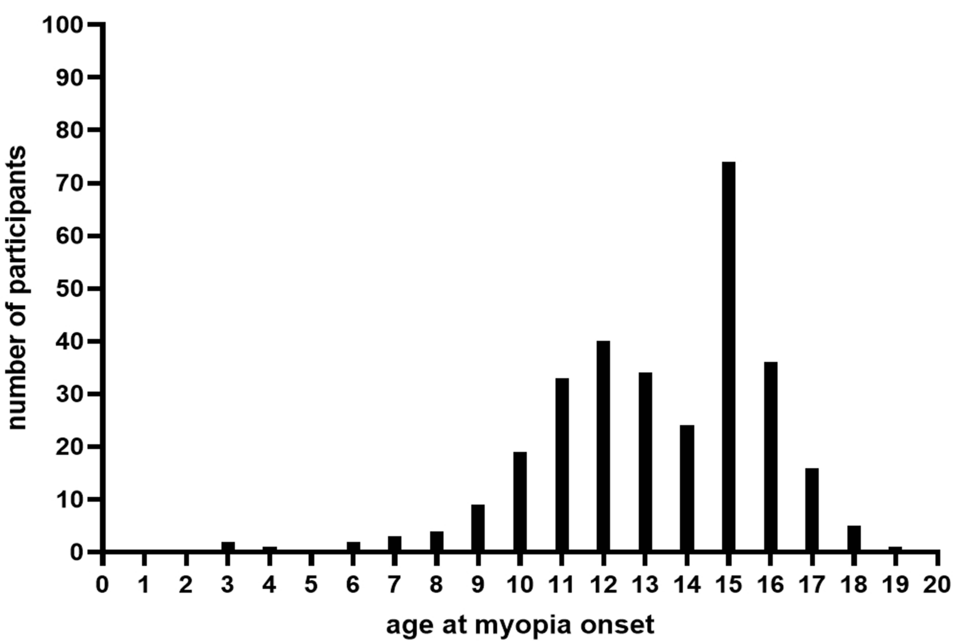

Figure 1 Frequency distribution plot of age at myopia onset.

Table 2 Early-Life Factors and Covariates (N=303)

Variable	No.	Age at Myopia Onset	P value
Sex			0.710
Male	99	13.23±2.46	
Female	204	13.35±2.73	
With or without premature birth			0.038
Yes	30	12.37±2.85	
No	220	13.45±2.66	
With or without breastfeeding			0.801
Yes	246	13.28±2.68	
No	18	13.11±2.72	
Season of birth			0.002
Spring	74	13.69±2.31	
Summer	74	12.31±3.13	
Autumn	99	13.61±2.31	
Winter	56	13.63±2.63	
Number of myopic parents			<0.001
0	147	13.88±2.32	
1	99	12.77±2.93	
2	25	11.80±2.38	
Duration of mobile phone use			0.090
≤30 min	26	14.75±1.71	
>30 min	277	13.23±2.70	
Duration of reading/writing			0.055
≤30 min	21	14.38±1.91	
>30 min	282	13.23±2.67	

to October 31, 2005, the number of spring births was 3,080,365 (21.82%), summer births 2,887,298 (20.46%), autumn births 4,203,452 (29.78%), and winter births 3,943,421 (27.94%). The number of births was similar in the four seasons.

The mechanism by which the season of birth influences myopia may be associated with dopamine's regulation of ocular growth and development. Previous studies have indicated that the season of birth may modulate the secretion and metabolism of monoamine neurotransmitters, such as dopamine and serotonin, with long-term effects extending even into adulthood.[13,14] A study conducted in Sweden has provided compelling evidence for the impact of the season of birth on adult dopamine transmission, revealing that individuals born between November and December exhibit the fastest dopamine transmission speeds in adulthood, whereas those born between May and June display the slowest.[23] Recent research has demonstrated that dopamine plays a role in the growth and development of the ocular refractive system. Fluctuations in dopamine levels, whether increases or decreases, can inhibit or promote the progression of myopia.[15,16] Consequently, individuals born in summer may exhibit reduced dopamine transmission efficiency in adulthood, accelerating the onset and progression of myopia.

Furthermore, some researchers have suggested a correlation between the deepening of myopia and the age of school entry.[24–26] In China, children born before September 1st must start school at age 6, whereas those born on or after that date must start at age 7. Therefore, students who begin school earlier than their peers tend to engage in continuous and close-up eye use for longer periods and have heavier academic burdens, which may accelerate the onset and progression of myopia. Additionally, nutrition is closely related to early ocular development in infants and young children. According to WHO standards, infants can be introduced to complementary foods at 6 months. Therefore, children born in summer often enter the period requiring complementary foods during autumn and winter, when food diversity is relatively limited compared to spring and summer.

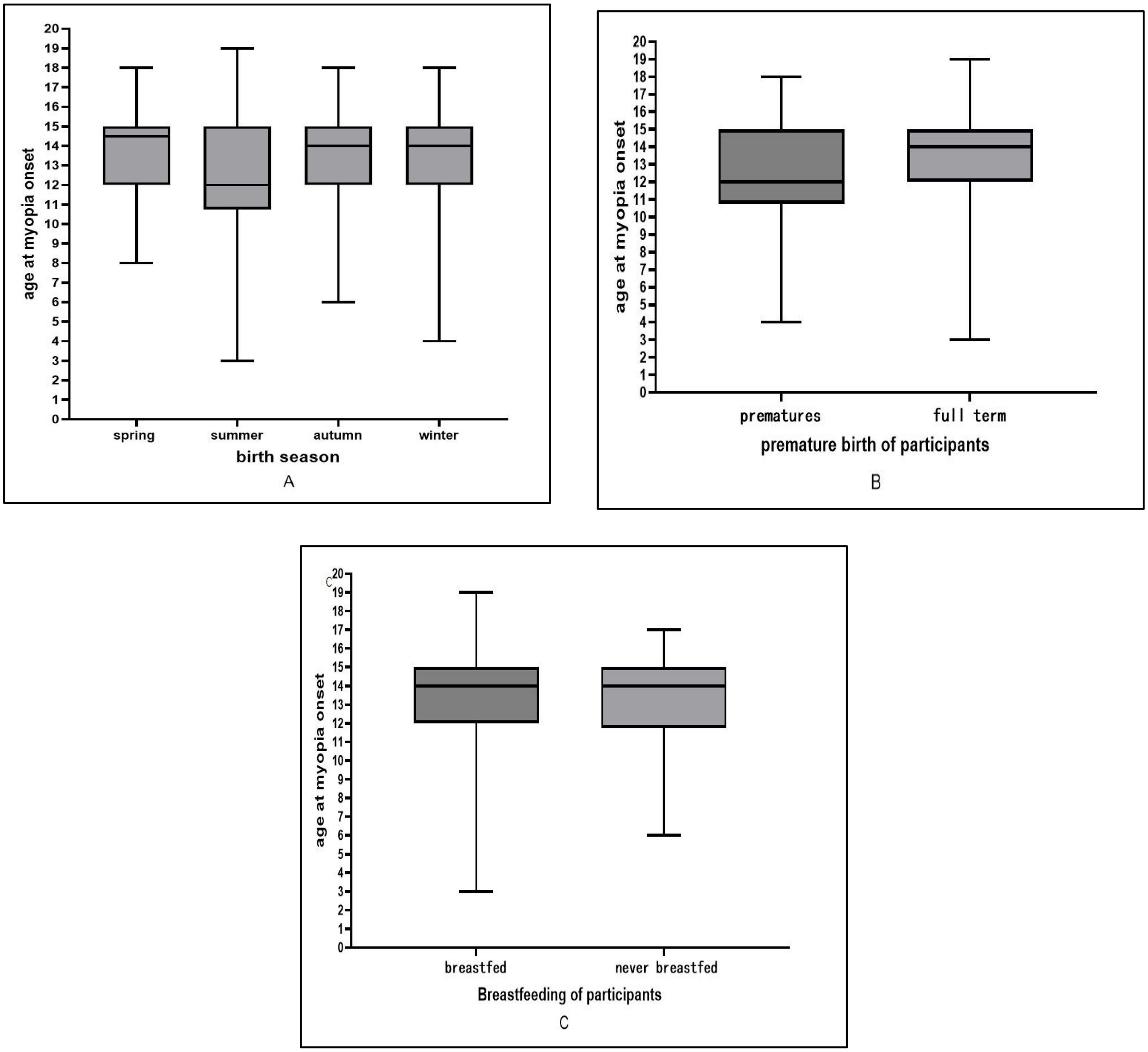

Figure 2 Box plots of age at myopia onset of the different study groups: (**A**) the relationship between season of birth and age at myopia onset; (**B**) the relationship between premature birth and age at myopia onset; (**C**) the relationship between breastfeeding and age at myopia onset.

Preterm and Myopia

We also found a trend towards a younger age of self-reported myopia onset in subjects born preterm (P=0.04, 95%:-2.35~-0.05). Recently, a study discovered that, compared to full-term infants, preterm infants have greater corneal refractive power, thicker lenses, and a shorter AL ($p<0.05$). Moreover, there is less variation in lens thickness in preterm infants at 3–8 years of age, and thicker lenses are the main cause for the high prevalence of myopia in premature infants.[27] Preterm infants' susceptibility to developing myopia may be attributed to lower levels of growth factors, such as IGF-1, that promote foetal retinal development during early pregnancy. These factors are often secreted in greater quantities during late pregnancy, leading to the delayed maturation of retinal vasculature in full-term foetuses.[28] Preterm infants experience inadequate endogenous production of IGF-1 after birth and lack a maternal supply of IGF-1, thereby affecting retinal vascularization and resulting in low degrees of ocular development. During the process of emmetropization, poor ocular development in preterm infants leads to a mismatch between ocular biometric parameters. The growth

Table 3 Generalized Linear Model of Age at Myopia Onset

Variable	Model 1			Model 2		
	β	P value	95% CI	β	P value	95% CI
Season of birth						
Spring	Reference	–	–		–	–
Summer	−1.90	<0.001	−2.92 ~ −0.89	−1.79	0.001	−2.79 ~ −0.76
Autumn	0.03	0.951	−0.95 ~ 1.01	0.18	0.727	−0.81 ~ 1.16
Winter	−0.31	0.587	−1.45 ~ 0.82	−0.12	0.836	−1.26 ~ 1.02
With or without breastfeeding						
No	Reference	–	–		–	–
Yes	−0.75	0.332	−2.253 ~ 0.760	−0.82	0.285	−2.31 ~ 0.68
With or without premature birth						
No	Reference	–	–		–	–
Yes	−1.48	0.012	−2.63 ~ −0.32	−1.50	0.011	−2.64 ~ −0.35

Notes: Model 1 was adjusted for sex, SE, BMI and the number of myopic parents. Model 2 was adjusted for duration of reading/writing and duration of mobile phone used based on Model 1.

in AL and thickening of the lens do not contribute to the eye's progression towards emmetropia, thereby leading to the formation of early myopia.

Breastfeeding and Myopia

The relationship between breastfeeding and myopia remains a subject of controversy. Our study reported that breastfeeding was not significantly related to age at myopia onset. Some researchers believe that breast milk, which is rich in ω-3 unsaturated fatty acids and antioxidants, can positively affect early retinal development and eye growth in children.[19,20] However, other studies do not support the protective effect of breastfeeding against myopia.[29] In this study, data on breastfeeding status were collected through children's recollections, which may introduce bias. Furthermore, any protective effect of breastfeeding on children's vision might be limited to early childhood and may not have a long-lasting impact on their visual health.

Other Factors About Myopia

In this study, the relationship between the number of myopic parents and offspring myopia was also observed, with a greater number of myopic parents leading to an earlier onset of myopia in offspring, which is similar to previous research findings.[30–32] However, this study did not find an association between near work activities such as reading and using electronic devices and the age at myopia onset. This may suggest that the occurrence of myopia can be influenced by genetic factors and early life factors, while environmental factors such as near work may play a more significant role in the later stages of myopia progression.

Innovatively, this study provides additional evidence for the influence of early-life factors on the development of myopia. However, there were some potential limitations. First, this study employed a cross-sectional design and cannot establish causal relationships. Follow-up studies with longitudinal data are necessary to investigate whether the season of birth affects the early growth and development of infants and young children. Second, the accommodation of the ciliary muscle for adults is weaker and noncycloplegic refraction is allowed to conduct refraction in adult, but it is more accurate to use cycloplegic refraction. Third, data on the age at myopia onset and eye hygiene habits were self-reported by the subjects, potentially introducing recall bias. However, some studies maintain that self-reported age at onset is accurate when compared to computerized refraction as the gold standard (area under the curve 0.928, 95% CI: 0.926–0.930).[33]

Conclusion

Early-life factors have a long-lasting effect on the development of myopia. Children born in the summer and born prematurely had a younger age at myopia onset. Therefore, attention needs to be paid to the visual acuity of these children, and eye health education needs to be strengthened to prevent myopia onset. It's important for these children to spent more time on outdoor activities and less time on near work.

Data Sharing Statement

The datasets analysed in this study are available from the corresponding author (Dan dan Jiang, jiangdandan@eye.ac.cn) upon reasonable request.

Ethics Approval and Consent to Participate

The Ethics Committee of the Eye Hospital of Wenzhou Medical University approved this study. Informed consent was gathered from all individual participants. The research stuck to the tenets of the Declaration of Helsinki.

Consent for Publication

Participants in the study were informed and provided informed consent for publication.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; Sun B, Jiang DD and Chen YY took part in drafting, revising or critically reviewing the article; Jiang DD gave final approval of the version to be published; Chen YY have agreed on the journal to which the article has been submitted; Jiang DD and Chen YY agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

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