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Analysis of factors related to the development of ocular biometric parameters in Chinese children aged 6–10 years: a cross-sectional study

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ABSTRACT

Objectives Emmetropia depends on the precise coordination of ocular biometry, including axial length (AL), corneal curvature, lens thickness and anterior chamber depth (ACD). Disruption of this coordination leads to refractive errors such as myopia. This article aimed to determine the factors affecting ocular biometry and myopia development in young children.

Design A cross-sectional study.

Setting This study was conducted in a primary school in the Yanqing district of Beijing, China.

Participants 792 students in grades 1–3 without hyperopia (>+2.00 D), strabismus, or amblyopia were selected. Exclusions: students had conditions affecting best corrected visual acuity and whose guardians refused to provide informed consent. Ocular biometric measurements and non-cycloplegia autorefraction were performed. The questionnaire addressed factors such as perinatal factors and environmental factors.

Interventions None.

Primary and secondary outcomes Ocular biometry and myopia.

Results According to the multivariate logistic regression analysis, electronic screen use >2 hours/day (OR=2.175, p=0.013), paternal myopia (OR=1.761, p=0.002), maternal myopia (OR=1.718, p=0.005), taller height (OR=1.071, p<0.001), maternal education (OR=0.631, p=0.012) and maternal gestational hypertension (OR=0.330, p=0.042) were associated with myopia. AL was affected by female sex (OR=0.295, p<0.001), older age (OR=1.272, p=0.002) and taller height (OR=1.045, p<0.001). Female sex (OR=0.509, p<0.001), taller height (OR=1.046, p<0.001), use of electronic screens >2 hours each day (OR=3.596, p<0.001) and time spent outdoors >2 hours each day (OR=0.431, p=0.001) influenced ACD incidence. Central corneal thickness (CCT) was associated with older age (OR=1.113, p=0.008), paternal education (OR=1.474, p=0.007), premature birth (OR=0.494, p=0.031), history of blue light therapy in infancy (OR=0.636, p=0.041) and history of incubator therapy in infancy (OR=0.263, p=0.009). Only sex influenced corneal curvature.

Conclusions The factors associated with myopia were partly related to ACD and AL, and perinatal factors were associated with myopia and CCT.

Trial registration number ChiCTR2200065398.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ A retrospective study was conducted using 792 completed surveys from participants in a suburb of Beijing, China.
⇒ The population in this study included suburban students and may not be representative of students in urban areas.
⇒ The definition of myopia was based on non-cycloplegia refraction rather than cycloplegia refraction, but this definition was crucial in a pragmatic setting.
⇒ The factors were self-reported using a questionnaire, and recall bias may be present.

INTRODUCTION

Myopia is a global public health problem. By 2050, the number of myopic patients is expected to reach nearly 5 billion, of whom 20% are predicted to have high myopia.[1] Patients with high myopia are at risk of vision-threatening complications, such as myopic macular degeneration.[2] The aetiology of myopia remains unclear, although in recent years, studies have suggested that both genetic and environmental factors are related to myopia.[3]

Emmetropisation is an active mechanism in which the eye modulates its growth to minimise the mismatch between its size and the focal length of its optics. That is, the biological parameters of the eye should be precisely coordinated.[4] Disruption of this coordination leads to refractive errors such as myopia and hyperopia.[5–7] Ocular biometry is partly controlled by genetic background. Previous studies have shown that many of the loci associated with refraction are also associated with axial length (AL), whereas genes associated with AL are not necessarily associated with refractive error.[8 9] However, it remains unclear whether environmental factors, such as time spent outdoors, have differential effects on myopia and ocular biometric parameters.

Research has indicated that environmental or internal factors may influence both variables. Indeed, previous studies have reported differences in the age-stratified and sex-stratified distributions of refraction and ocular biometry among different countries and races.[7 10 11] The relationships of these variables with height and residential location were also reported.[12] Rauscher FG *et al*[4] found that eye growth in girls lagged by approximately 4 years compared with that in boys. The increase in aqueous water depth matches the decrease in lens thickness from ages 4 to 10 years in girls and boys. The minimum lens thickness is reached at 11 years in girls and at 12 years in boys. All dimensions of the ocular components are closely correlated with the AL. Different combinations of biological parameters are associated with myopia.[13] It is worth considering what breaks the balance between these parameters and causes myopia during the process of emmetropisation and whether perinatal conditions are one of the influencing factors, especially whether the trend of younger myopia in recent years was related to these perinatal factors. Therefore, in the present study, we aimed to determine the factors affecting the onset of myopia and the development of ocular biometric parameters in young children.

METHODS

Study design and population

This cross-sectional study was conducted in a primary school in the Yanqing district of Beijing, China, from September 2022 to October 2022. Students in grades 1–3 of the school were included in the study. All the subjects were invited to participate voluntarily. The guardians of the students signed informed consent forms. The inclusion criteria for students were as follows: grade 1–3; without strabismus, hyperopia (>+2.00 D) or amblyopia. The exclusion criteria for students were as follows: had metabolic or congenital systemic diseases; had ocular conditions, such as congenital cataract, glaucoma, uveitis, or corneal pathologies; had strabismus or amblyopia; had a history of ocular surgeries; had a history of contact lens use or low-concentration atropine use; and whose guardians refused to provide informed consent.

Refractive error and ocular biometry measurements

Non-cycloplegia refractive errors were measured with an autorefractor (KR-1, Topcon, Tokyo, Japan), and ocular biometrics were determined using a Lenstar LS900 (Haag-Streit Koeniz, Switzerland) as the average of three recordings. The spherical equivalents (SEs) were calculated as the sphere error plus half of the cylindrical error. Myopia was defined as an SE≤−0.75 dioptres (D).

Questionnaire

The questionnaires were completed by parents and schoolchildren. The questionnaire items addressed potential risk factors such as demographic characteristics, parental myopia status, family history of myopia (genetics), maternal health during pregnancy (gestational diabetes mellitus, gestational hypertension, anaemia or infection), fetal and infant health conditions (umbilical cord wrapped around the neck during the fetal period, mode of delivery, history of blue light therapy and pattern of infant feeding), and multiple environmental factors such as the time spent outdoors each day and dietary habits. Additionally, parental smoking status, height and weight were assessed. Age was calculated on a monthly basis.

Sample size calculation

The sample size was calculated according to the 10EVP principle. Including 20 indicators, the incidence of myopia among primary school students was 35%,[14] and the calculated sample size was 571.

Patient and public involvement statement

None.

Statistical analysis

Analysis was performed using IBM SPSS Statistics V.25.0 with data from right eyes only, as there were no significant differences in refractive error or ocular biometrics between right and left eyes. The normality of the distributions of continuous variables was assessed with the Shapiro-Wilk test. Continuous variables with a normal distribution are presented as the mean±SD, while nonnormal variables are presented as the median±IQR. Categorical variables are presented as percentages of the total. Student's t-test, one-way analysis of variance and the Mann-Whitney U test were used to detect differences in continuous variables, and the χ^2 test was used to detect differences in categorical variables associated with myopia incidence. Biological parameters, such as the AL, were converted into binary variables through the median. To determine the risk factors associated with ocular biometry parameters and myopia, univariate logistic regression analysis was used to calculate ORs and 95% CIs. Multivariate logistic regression analysis (with the stepwise backward method) was used to determine the independent factors. A difference of $p<0.05$ was considered to indicate statistical significance.

RESULTS

Subject characteristics

A total of 1028 children were eligible to participate in the eye physical examinations. All the people included were of Han nationality. Of those, 911 completed the questionnaire, and 117 were excluded from the study because their guardians refused to provide informed consent. Of the 911 participants, 119 (15%) were not included in the data analysis due to inadequate questionnaire completion. The incomplete questionnaires included incomplete and ambiguous information.

Finally, 792 children were included in the analyses, 47% of whom were male. The mean age was 98.53±19.51 months. A total of 189 (23.90%) participants had myopia,

Table 1 Demographic characteristics and ocular biometry parameters of the study population

Variable	All (n=792)	Myopia	Emmetropia	P value
Age, median (IQR), months	98 (80, 109)	109 (96, 126)	94 (79, 105)	<0.001
Sex				0.970
Male, n (%)	420 (53)	100 (23.8)	320 (76.2)	
Female, n (%)	372 (47)	89 (23.9)	283 (76.1)	
AL, median (IQR), mm	23.15 (22.58, 3.68)	23.84 (23.17, 24.41)	23.01 (22.47, 23.40)	<0.001
ACD, median (IQR), mm	3.14 (2.91, 3.36)	3.32 (3.13, 3.58)	3.09 (2.87, 3.30)	<0.001
CR, mean (SD), mm	7.74 (0.26)	7.74 (0.27)	7.75 (0.25)	0.563
Height, median (IQR), cm	134 (125, 143)	140 (132.5, 150)	130 (124, 140)	<0.001
Weight, median (IQR), kg	30 (24, 40)	35 (28, 45)	27.5 (24, 37)	<0.001
CCT, mean (SD), μm	543.10 (30.81)	544.73 (32.38)	542.49 (30.20)	0.361

ACD, anterior chamber depth; AL, axial length; CCT, central corneal thickness; CR, corneal radius of curvature.

100 (52.9%) of whom were male. Table 1 summarises the demographic characteristics and ocular biometry parameters of the study population. Individuals with myopia were older, taller, and heavier than individuals without myopia (p<0.05). The AL and anterior chamber depth (ACD) differed between the two groups (p<0.05).

The clinical characteristics of the study participants stratified by age and sex are summarised in figure 1. Clear trends were found in central corneal thickness (CCT), AL, ACD and the prevalence of myopia in both boys and girls.

Risk factors for myopia

According to the univariate analyses, eight indicators, namely, age, maternal gestational hypertension, maternal education, daily electronic screen use, maternal myopia, paternal myopia, height and weight, were significantly different between individuals with and without myopia (p<0.05; table 2).

Multivariate logistic regression analysis (figure 2) revealed that four factors, namely, an electronic screen use >2 hours per day (OR=2.175, 95% CI 1.182, 4.004, p=0.013), paternal myopia (OR=1.761, 95% CI 1.235,

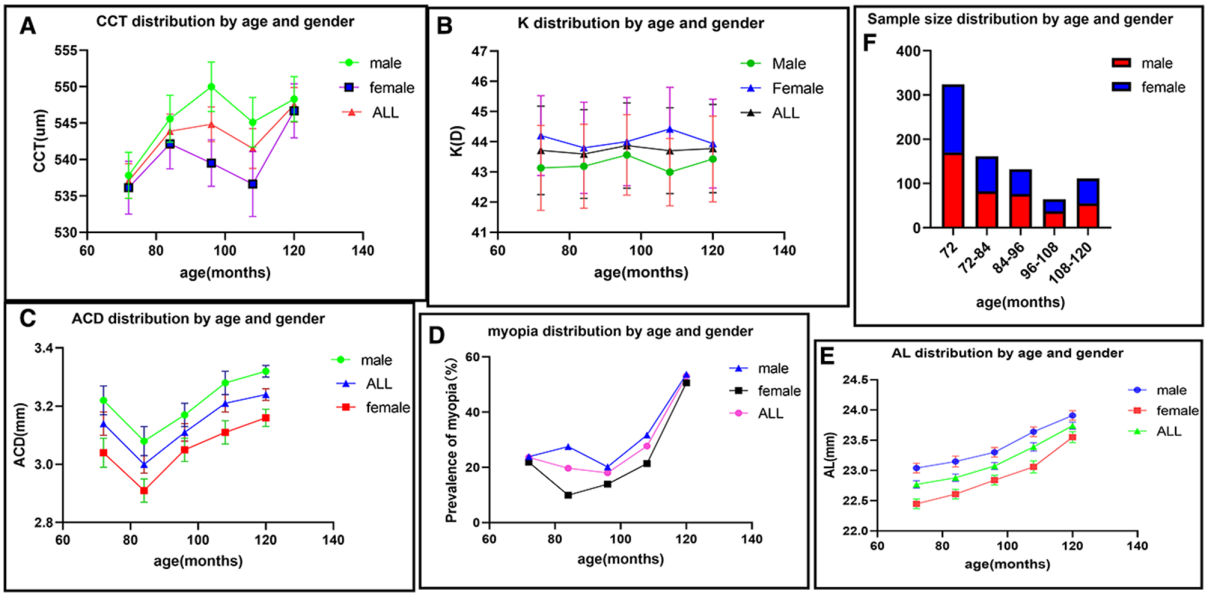

Figure 1 Age and sex distributions of myopia incidence and biological parameters. K is the average K of corneal curvature. ACD, anterior chamber depth; AL, axial length; CCT, central corneal thickness.

Table 2 Results of Univariate analysis of factors related to myopia and ocular biometric parameters

Variable	β	OR	95% CI (lower)	95% CI (upper)	P value
Risk factors for myopia					
Age	0.346	1.413	1.284	1.556	<0.001
Maternal gestational hypertension	−1.516	0.220	0.052	0.931	0.040
Child characteristics	0.324	1.383	0.992	1.927	0.056
Maternal education	−0.411	0.663	0.475	0.924	0.015
Height	0.064	1.066	1.051	1.082	<0.001
Weight	0.040	1.040	1.027	1.054	<0.001
Screen time 1	0.268	1.308	0.754	2.269	0.340
Screen time 2	−0.469	0.625	0.436	0.896	0.011
Paternal myopia	0.424	1.527	1.124	2.076	0.007
Maternal myopia	0.329	1.389	1.003	1.924	0.048
Factors related to AL					
Age	0.441	1.555	1.420	1.703	<0.001
Sex	−1.115	0.328	0.245	0.438	<0.001
Height	0.073	1.076	1.061	1.091	<0.001
Weight	0.049	1.051	1.036	1.065	<0.001
Meat-based diet	0.349	1.417	1.030	1.950	0.032
Child characteristics	0.315	1.370	1.027	1.827	0.032
Maternal education	−0.407	0.666	0.498	0.891	0.006
Screen time 1	−0.484	0.616	0.451	0.843	0.002
Screen time 2	−0.086	0.918	0.547	1.541	0.746
Paternal myopia	0.013	1.013	0.766	1.340	0.926
Maternal myopia	0.034	1.034	0.774	1.383	0.819
Factors related to ACD					
Sex	−0.646	0.524	0.395	0.695	<0.001
Age	0.170	1.186	1.096	1.283	<0.001
Height	0.045	1.046	1.033	1.059	<0.001
Weight	0.040	1.040	1.027	1.054	<0.001
Meat-based diet	0.375	1.455	1.058	2.003	0.021
Paternal education	−0.293	0.746	0.564	0.987	0.041
Maternal education	−0.319	0.727	0.544	0.972	0.031
Screen time 1	−0.358	0.699	0.512	0.955	0.025
Screen time 2	1.061	2.890	1.607	5.196	<0.001
Outdoor time 1	−0.925	0.396	0.250	0.629	<0.001
Outdoor time 2	−0.568	0.567	0.411	0.782	0.001
Factors related to central corneal thickness (CCT)					
Age	0.103	1.108	1.026	1.198	0.009
Premature birth	−0.771	0.463	0.246	0.868	0.016
History of blue light therapy in infancy	−0.467	0.627	0.410	0.958	0.031
History of incubator treatment in infancy	−1.340	0.262	0.097	0.708	0.008
Paternal education	0.372	1.451	1.096	1.921	0.009
Factors related to the corneal curvature					
K1					
Sex	−0.860	0.423	0.318	0.563	<0.001

Continued

Table 2 Continued

Variable	β	OR	95% CI (lower)	95% CI (upper)	P value
K2					
Sex	−0.934	0.393	0.295	0.524	<0.001

Screen time 1=electronic screen use between 1 and 2 hours per day compared with more than 2 hours per day. Screen time 2=electronic screen use less than 1 hour versus more than 2 hours. Outdoor time 1=outdoor activity for more than 2 hours versus less than 1 hour. Outdoor time 2=1–2 hours of outdoor activity versus more than 2 hours. K1=the flat K of corneal curvature. K2=the steepness K of the corneal curvature.
ACD, anterior chamber depth; AL, axial length; CCT, central corneal thickness.

2.511, p=002), maternal myopia (OR=1.718, 95% CI 1.176, 2.510, p=0.005) and taller height (OR=1.071, 95% CI 1.055, 1.087, p<0.001), were associated with a greater risk of myopia. Maternal education (OR=0.631, 95% CI 0.440, 0.904, p=0.012) and maternal gestational hypertension (OR=0.330, 95% CI 0.113, 0.960, p=0.042) were associated with a lower risk of myopia.

Risk factors for myopia associated with ocular biometric parameters

The results of the univariate logistic regression analysis are shown in table 2. The variables affecting AL included age, sex, maternal education, electronic screen use each day, height, weight, meat-based diet, paternal myopia, maternal myopia and child characteristics (p<0.05). Nine factors were associated with ACD (p<0.05): age, sex, daily use of electronic screens, maternal education, paternal education, height, weight, diet based on meat and time spent outdoors each day. Factors associated with CCT included age, paternal education, preterm birth, history of blue light exposure and history of incubator treatment in infancy (p<0.05). However, only sex influenced corneal curvature (p<0.05).

Multivariate logistic regression was used to evaluate the effects of the above factors on each ocular biometric parameter (figure 2). The independent factors influencing AL included female sex (OR=0.295, 95% CI 0.213, 0.410, p<0.001), older age (OR=1.272, 95% CI 1.092, 1.482, p=0.002) and taller height (OR=1.045, 95% CI 1.022, 1.069, p<0.001). The factors associated with ACD included female sex (OR=0.509, 95% CI 0.3750,

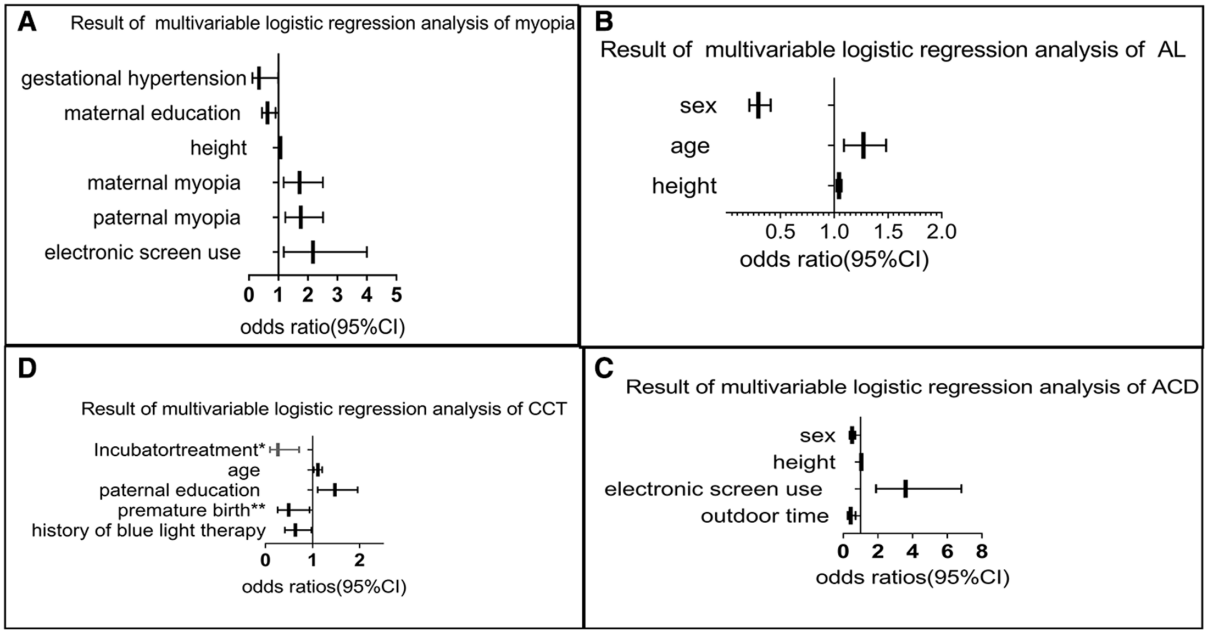

Figure 2 Results of multivariate logistic regression analysis. (A) Independent factors related to myopia. (B) Independent factors affect axial length. (C) Independent factors influencing anterior chamber depth. (D) Independent factors associated with central corneal thickness: **Age, paternal education, preterm birth and history of blue light therapy in infancy were incorporated into the model, and all four factors were correlated with central corneal thickness. *Age, paternal education, history of incubator therapy in infancy and history of blue light therapy in infancy were incorporated into the model, excluding the history of blue light treatment. The remaining three factors were associated with CCT. Electronic screen use=electronic screen use >2 hours each day; outdoor time=outdoor time >2 hours each day. ACD, anterior chamber depth; AL, axial length; CCT, central corneal thickness.

0.692, p<0.001), taller height (OR=1.046, 95% CI 1.033, 1.060, p<0.001), electronic screen use >2 hours each day (OR=3.596, 95% CI 1.897, 6.817, p<0.001) and outdoor time >2 hours each day (OR=0.431, 95% CI 0.263, 0.707, p=0.001).

According to the multivariate analysis of CCT, although there was no collinearity between preterm birth and incubator treatment in the statistical analysis, considering that preterm infants were more inclined to receive incubator therapy clinically, we constructed two models. In the first model, we incorporated age, paternal education, preterm birth and history of blue light therapy in infancy. The results showed that these four factors were all independent predictors (p<0.05). In the second model, preterm birth was replaced with a history of incubator treatment. The results showed that age (OR=1.113, 95% CI 1.029, 1.205, p=0.008), paternal education (OR=1.474, 95% CI 1.110, 1.959, p=0.007) and history of incubator treatment in infancy (OR=0.263, 95% CI 0.096, 0.716, p=0.009) were correlated with CCT. Both the flat K of corneal curvature (K1) (OR=0.423, 95% CI 0.318, 0.563, p<0.001) and the steep K (K2) (OR=0.393, 95% CI 0.295, 0.524, p<0.001) were associated with sex.

Factors associated with both myopia and biological parameters were more than 2 hours of electronic device use per day and height. Among the perinatal factors, pregnancy-induced hypertension was related to myopia. A history of incubator therapy in infancy and prematurity and a history of blue light therapy in infancy affected CCT. The outdoor time was only associated with the ACD.

DISCUSSION

Emmetropisation is a process of coordinated development of ocular biological parameters. Violation of this coordination can cause refractive errors. Knowledge of changes in refraction and biometric parameters during childhood is essential for identifying the failure of the immortalisation process. Studying the factors influencing this process allows for the possibility of intervening in the process of emmetropisation earlier to reduce the occurrence of refractive errors. In addition to factors commonly associated with myopia in the literature, such as outdoor activities,[15 16] we also included less frequently reported factors, such as preterm birth, maternal gestational hypertension, maternal gestational diabetes mellitus, history of incubator treatment in infancy and history of blue light therapy in infancy.[17 18] In contrast to the findings of previous studies,[19] we found that maternal gestational hypertension (OR=0.148) was a protective factor against myopia. Li *et al*[19] found that hypertensive disorders during pregnancy, especially early-onset and severe pre-eclampsia, were associated with an increased risk of high refractive errors in children during childhood and adolescence. This may be related to the changes in circulating antiangiogenic factors caused by gestational hypertension[20 21] and the effects of excessive oxidative stress and inflammation on refractive development.[22] They also found that maternal hypertension was associated with hyperopia, myopia and astigmatism. However, the risk of myopia was slightly greater among offspring aged 7–12 years, which may be due to the accompanying academic burden at that age and worse eye habits.[23] Therefore, whether these findings can be understood as the children of mothers with pregnancy-induced hypertension have a greater probability of refractive error is unclear. However, the incidences of hyperopia, myopia and astigmatism may be similar unless the eyes are under heavy load. The offspring of people with pregnancy-induced hypertension may have a slower orthotopic process, but after myopia occurs, the risk of developing high myopia is greater. In this way, pregnancy-induced hypertension was a protective factor against myopia.

Moreover, in their study, Li *et al* analysed the influence of maternal health status on children's high refractive errors (not only myopia) but also did not include environmental factors such as eye habits. In contrast, our study involved a multivariate analysis of the prevalence of myopia. The results showed that pregnancy-induced hypertension was a protective factor against myopia. This may be because children with maternal gestational hypertension, due to a poor intrauterine environment, exhibit slower emmetropisation after birth, between the ages of 6 and 10 years.[18 24] In addition, their study population was Danish, and our study included a Chinese Han population. Different ethnic groups may cause this difference. Nevertheless, the relationship between pregnancy-induced hypertension and high myopia in children merits further attention.[19] However, pregnancy-induced hypertension did not influence ocular biometric parameters. These findings indicate that hypoxia caused by hypertension leads to the abnormal development of other fetal ocular structures, such as the retina,[17 25] and thus indirectly affects the risk of myopia rather than directly affecting the AL, ACD or CCT.[26] However, further studies are needed to evaluate this possibility.

Age and sex independently predicted AL but not myopia, consistent with previous research.[5 27] This difference may be related to compensatory changes in other refractive parameters. Significant differences in ACD and corneal curvature were also observed between boys and girls in the present study,[28 29] but corneal curvature was not associated with age,[30] which is consistent with the literature, as corneal curvature reaches adult levels by the age of 3 years.[31 32]

Age influenced the ACD, but it was not an independent predictor of the ACD. Rauscher *et al*[4] found that, compared with that of boys, the eye growth (ie, AL) of girls lagged by approximately 4 years. In his study, ACD increased mainly between the ages of 4 and 10 years, and there were sex differences in ACD increase during this period; however, this increase was no longer evident at the ages of 10–17 years. These findings support our findings. We found that taller height was associated with an increasing tendency for myopia, longer AL and deeper ACD. These findings were consistent with those of Jonas

et al.[33] Other factors influencing the ACD included an outdoor time <2 hours per day and an electronic screen use >2 hours per day. According to Rauscher *et al*,[4] an increase in ACD was driven by two factors: a decrease in lens thickness and an increase in AL. Because of these two effects, ACD increased up to 10 years of age, matching the decrease in lens thickness. After age 10, ACD follows the combined effect of the plateau and an increase in lens thickness combined with the continuous growth of the AL. Increased outdoor activity may promote dopamine release, which reduces the growth of the eye axis.[34] Excessive close-range work can cause spasm of the ciliary muscle, while a larger and stiffer ciliary muscle might distort the growing eye.[35]

Our study included children aged 6–10 years, and we found that the CCT varied with age. This finding is consistent with the findings of Ma *et al*'s report of age differences in corneal thickness in Asian individuals.[36] However, another study suggested that the CCT decreases with age and becomes stable at 3 years of age in black children.[37] The discrepancy between these findings indicates the presence of ethnic and regional differences in corneal thickness.[38]

Another factor contributing to CCT was a history of blue light therapy and incubator therapy in infancy and prematurity. In paediatric medicine, prematurity and low birth weight are the main indicators for incubation therapy. It has been reported that preterm infants have greater corneal thickness, with corneal thickness gradually decreasing with increasing age until term, while the corneal diameter increases. The growth of the eye, possibly through the remodelling and stretching of collagen fibres, plays an important role in reducing CCT.[39] Fieß *et al*[40] suggested that a lower birth weight percentile in preterm subjects (used as a proxy for restricted fetal growth) was associated with reduced corneal thickness in adults aged 18–52 years, indicating that corneal thickness, particularly in the corneal centre, may be determined during the fetal stage. Therefore, the effect of incubator therapy in infancy on CCT may be related to preterm birth and low birth weight. In our study, children born preterm and with a history of incubator therapy in infancy were found to have thinner CCTs, consistent with the findings of previous literature.[41] The effect of blue light on CCT may be related to collagen fibres and needs further confirmation.

Peng Zhou *et al*[28] found that the CCT was negatively correlated with the rate of myopia progression and AL increase but was positively correlated with the age of myopia onset. Therefore, further attention should be devoted to the influence of fetal and infantile factors on myopia and eyeball development.

These results may be affected by the fact that the children were observed only in suburban areas. Future studies could incorporate assessments made in various regions. Although non-cycloplegia was used, it had little effect on the overall analysis. Biological parameter measurements were not influenced by cycloplegia, which was the main focus of the article. In addition, the investigation of risk factors using self-report questionnaires may be subject to recall bias, and the results need to be further confirmed by prospective studies.

In conclusion, the factors associated with myopia partly affect the biological parameters of the eye. Perinatal factors influenced both myopia and biological parameters. It is worth considering whether the younger age and higher incidence of myopia in recent years are related to these factors, especially the effect of pregnancy-induced hypertension and gestational diabetes mellitus on the incidence of myopia. These findings need to be confirmed by large, prospective studies.

Contributors XP conceived and designed the study. TH wrote the draft. XP revised the draft. TH and RW performed the statistical analysis. HL and WW oversaw data acquisition and implementation on site. All authors reviewed and approved the final manuscript. XP is the guarantor of this paper and is primarily responsible for the study

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by Ethics Committee of Peking University Third Hospital Yanqing Hospital (number: 20223200101). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

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