PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

Title (Provisional)

Associations between refraction and ocular biometry in Chinese preschoolers aged 3-6 years: a cross-sectional study in Shunyi, Beijing

Authors

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VERSION 1 - REVIEW

Reviewer	**1**
Name	**Chiu, Cheng-Jen**
Affiliation	**Tzu Chi University**
Date	**14-Feb-2025**
COI	**None**

The authors conducted a cross-sectional study to evaluate the associations between refraction and ocular biometry of preschool children (3-6 years old) in Shunyi District, Beijing. Due to the scarcity of refractive data on children aged 3–6 years, this topic holds significant clinical importance. To provide more objective results, some modification is needed

Major:

1. Due to the nature of a cross-sectional study, differences between age groups may not be solely attributed to aging but could also be influenced by environmental factors, lifestyle variations, and other unmeasured confounders. The authors should address this limitation in the Discussion section.
2. In Table 2, the alternative hypothesis for the one-way ANOVA is that the means across the groups are not equal. However, based on the description on Page 4, Lines 28–43, the authors appear to be testing an alternative hypothesis that the responses systematically increase or decrease with age. A p-value for trend should be provided, and the corresponding statistical method should be specified in the Methods section.
3. In Table 3, the p-value for lens power was not provided. Additionally, Figure 2 suggests that two or more independent variables in the regression model are highly correlated. Did the authors verify whether multicollinearity exists in the regression models presented in Table 3?
4. R^2 measures the proportion of variance in the dependent variable explained by the

independent variables in a regression model. It indicates the overall fit of the model to the data and is not specific to any single independent variable. Please revise the wording on Page 6, Lines 12–18 accordingly. Additionally, please specify the purpose of fitting each of the different regression models.

5. The number of subjects varies across different regression models in Table 3, indicating the presence of missing data in certain covariates. The issue is most pronounced for lens power, with approximately 10% of subjects missing
6. The study employs a cross-sectional design, capturing data at a single time point rather than tracking changes over time. This inherently limits the ability to establish causality. While associations between ocular biometry and refraction are observed, it remains unclear whether specific ocular parameters actively contribute to myopia development or merely correlate with refractive status. A longitudinal approach would be necessary to clarify these relationships.
7. The estimation of lens power using the Bennett-Rabbetts formula introduces potential inaccuracies due to inherent assumptions regarding ocular geometry. Given the absence of direct lens thickness measurements, the reliability of estimated lens power is uncertain. This limitation complicates the interpretation of the lens's role in refractive error, particularly considering inter-individual variability in lens characteristics.
8. The inclusion of participants exclusively from kindergartens raises concerns about selection bias. Children not enrolled in these educational settings may differ in socioeconomic background, visual habits, and parental engagement, potentially affecting the findings. The extent to which this bias impacts the study's conclusions warrants further consideration.
9. While the study acknowledges certain environmental influences on myopia development, such as outdoor activity and screen exposure, it is unclear whether all relevant confounding factors have been adequately controlled. Genetic predisposition, familial history of myopia, and other lifestyle variables may also play significant roles. A more comprehensive adjustment for these potential confounders would strengthen the validity of the findings.
10. The study predominantly examines pre-myopia and hyperopia, potentially overlooking other refractive errors, such as myopia and astigmatism, and their associations with ocular biometry. This selective focus may limit broader insights into refractive development in early childhood and how different refractive errors interact with ocular growth.
11. If parental reports were utilized for data collection, the potential for recall bias and reporting inaccuracies should be considered. Information regarding family ocular history and environmental exposures may be subject to misreporting, which could introduce additional variability into the findings.

Minor:

1. What does the error bar in Figure 1 represent—standard deviation (SD) or standard error of the mean (SEM)? Please specify this in the figure legend. In addition, there were no remarks for significant findings.
2. A typo was identified in Reference 13. Please revise it.

VERSION 1 - AUTHOR RESPONSE

Reviewer 1:

The authors conducted a cross-sectional study to evaluate the associations between

refraction and ocular biometry of preschool children (3-6 years old) in Shunyi District, Beijing. Due to the scarcity of refractive data on children aged 3–6 years, this topic holds significant clinical importance. To provide more objective results, some modification is needed:

Major：

Comment 1. Due to the nature of a cross-sectional study, differences between age groups may not be solely attributed to aging but could also be influenced by environmental factors, lifestyle variations, and other unmeasured confounders. The authors should address this limitation in the Discussion section.

Response 1: First of all, thank you very much for your valuable suggestions and comments. In our study, children were divided into groups according to age and refraction separately. The differences in ocular biometric parameters across age groups should not be solely attributed to aging, which was not adequately considered in the previous manuscript , and we have added this limitation to the discussion section.

Comment 2. In Table 2, the alternative hypothesis for the one-way ANOVA is that the means across the groups are not equal. However, based on the description on Page 4, Lines 28–43, the authors appear to be testing an alternative hypothesis that the responses systematically increase or decrease with age. A p-value for trend should be provided, and the corresponding statistical method should be specified in the Methods section.

Response 2： Thank you for pointing out the incorrectness of statistical methods.Through one-way ANOVA, we observed statistically significant differences in AL,ACD,AL/CR and LP across different age groups. However, we did not apply trend analysis, so the p-value was obtained from one-way ANOVA in the previous manuscript. We performed a trend analysis and recorded the p-value for trend accordingly. In the methods section, the corresponding statistical methods were added.

Comment 3. In Table 3, the p-value for lens power was not provided. Additionally, Figure 2 suggests that two or more independent variables in the regression model are highly correlated. Did the authors verify whether multicollinearity exists in the regression models presented in Table 3?

Response 3: Thank you for pointing out the shortcomings in the regression model. In Table 3, we forgot to provide p-value for lens power. In the previous model, we failed to take multicollinearity fully into account between the independent variables. Therefore, based on the results of the correlation(SE was negatively correlated with AL, ACD, AL/CR and LP), we developed four regression models(AL, ACD, AL/CR and LP as independent variables respectively) after being adjusted for age and gender. The regression model 2 and model 4 were not well explained and therefore removed.

	Model 1 (n=1141)		Model2 (n=1026)		Model3 (n=1130)		Model4 (n=1019)	
Variables	β	P value	β	P value	β	P value	β	P value
Age(yrs)	0.043	0.079	0.024	0.379	0.114	<0.001	-0.077	0.007
Gender	-0.169	<0.001	-0.050	0.298	-0.085	0.025	0.162	0.001
AL(mm)	-0.455	<0.001						
ACD(mm)			-0.886	<0.001				
AL/CR ratio					-7.203	<0.001		
LP(D)							-0.093	<0.001
R^2	0.133		0.077		0.313		0.027	

Comment 4. R^2 measures the proportion of variance in the dependent variable explained by the independent variables in a regression model. It indicates the overall fit of the model to the data and is not specific to any single independent variable. Please revise the wording on Page 6, Lines 12–18 accordingly. Additionally, please specify the purpose of fitting each of the different regression models.

Response 4: Our previous interpretation of the statistics was incorrect, and we have revised it accordingly in response to your comments.

Comment 5. The number of subjects varies across different regression models in Table 3, indicating the presence of missing data in certain covariates. The issue is most pronounced for lens power, with approximately 10% of subjects missing.

Response 5: Since ACD data is required for the calculation of LP, the missing ACD data in biometric measurements resulted in approximately 10% fewer subjects in model 4 than model 1.Model 1 and model 2 have similar subjects(n=1141 vs n=1130) .

Comment 6. The study employs a cross-sectional design, capturing data at a single time point rather than tracking changes over time. This inherently limits the ability to establish causality. While associations between ocular biometry and refraction are observed, it remains unclear

whether specific ocular parameters actively contribute to myopia development or merely correlate with refractive status. A longitudinal approach would be necessary to clarify these relationships.

Response 6: At the time of data collection, we observed associations between ocular biometric parameters and refraction.The cross-sectional design restricts the ability to establish the causal relationships between ocular biometry and myopia. We pointed out this limitation in the Discussion section as well. We performed 3 follow-up visits every six months after completing the first year's examination,data from the 2-year longitudinal study have been statistically analyzed.

Comment 7. The estimation of lens power using the Bennett-Rabbetts formula introduces potential inaccuracies due to inherent assumptions regarding ocular geometry. Given the absence of direct lens thickness measurements, the reliability of estimated lens power is uncertain. This limitation complicates the interpretation of the lens's role in refractive error, particularly considering inter-individual variability in lens characteristics.

Response 7: Biometric examination was performed with the Lenstar LS 900, measurements of lens thickness were not available due to the equipment. Lens power was calculated based on results of SE, ACD, AL and K,which could affect the accuracy of lens power measurements. Depending on your comments, we added this limitation to the Discussion section. There was scarce research focus on lens power in preschoolers, which is an important part of ocular biometric components. In this study, we observed the baseline results in the first year, and we observed the dynamic trends over 1 year based on the available data, which might help us to better understand the refractive development of preschool children.

Comment 8. The inclusion of participants exclusively from kindergartens raises concerns about selection bias. Children not enrolled in these educational settings may differ in socioeconomic background, visual habits, and parental engagement, potentially affecting the findings. The extent to which this bias impacts the study's conclusions warrants further consideration.

Response 8: Our failure to consider children not enrolled in kindergartens in the initial study design led to selection bias. Due to the relative large sample size and the difficulty of follow-up, we chose public kindergartens and completed the study with the assistance of

teachers.That's why our study could only provide findings based on kindergartens, and we also mention this limitation in the Discussion section.

Comment 9. While the study acknowledges certain environmental influences on myopia development, such as outdoor activity and screen exposure, it is unclear whether all relevant confounding factors have been adequately controlled. Genetic predisposition, familial history of myopia, and other lifestyle variables may also play significant roles. A more comprehensive adjustment for these potential confounders would strengthen the validity of the findings.

Response 9: In our study, refractive development profiles were created for enrolled children, and questionnaires were completed by parents or caregivers at the same time when the examination was being conducted. The questionnaire included basic information about the parents (age, education, income, and history of myopia),children's medical history, lifestyle, time spent on screen-based devices and outdoor activities. We hope to combine the results of the questionnaire with existing findings to strengthen the validity of conclusions. The results of the questionnaire have not yet been fully analyzed.

Comment 10. The study predominantly examines pre-myopia and hyperopia, potentially overlooking other refractive errors, such as myopia and astigmatism, and their associations with ocular biometry. This selective focus may limit broader insights into refractive development in early childhood and how different refractive errors interact with ocular growth.

Response 10: We divided preschoolers into 3groups based on the calculated results of SE. A total of 31 preschoolers had myopia.We only considered results of SE and did not categorize them by different refractive status. We investigate the changes of refraction before and after cycloplegia (Published in the Chinese Journal of Optometry Ophthalmology and Visual Science) , astigmatism before and after cycloplegia was mainly with-the-rule, followed by oblique astigmatism, no astigmatism and against-the-rule. We will adjust the categorization

in longitudinal comparison.

表3. 不同年龄儿童的散光度数分类在睫状肌麻痹前后的分布差异

Table 3. The distribution of astigmatism in children of different age groups before and after cycloplegia based on the degree of astigmatism

Groups	Mild astigmatism (*n*)	Moderate astigmatism (*n*)	High astigmatism (*n*)	χ^2	*P*
3 year-old					
Before	102	13	4	0.47	0.789
After	100	16	3		
4 year-old					
Before	392	91	4	0.79	0.674
After	381	101	5		
5 year-old					
Before	303	56	3	2.93	0.231
After	291	63	8		
6 year-old					
Before	149	23	2	0.21	0.898
After	146	26	2		
Total					
Before	946	183	13	2.59	0.274
After	918	206	18		

n, number of eyes.

Comment 11. If parental reports were utilized for data collection, the potential for recall bias and reporting inaccuracies should be considered. Information regarding family ocular history and environmental exposures may be subject to misreporting, which could introduce additional variability into the findings.

Response 11: In our study, questionnaires were distributed to be filled out by parents with basic information, history of myopia, screen exposure etc., and there was recall bias. Parents also filled out the questionnaires at the subsequent follow-up visit. Due to the lack of objective evaluation indexes suitable for the questions in the questionnaire, there was misreporting. Thank you very much for your comments, and we will conduct as comprehensively as possible the design of future studies, and minimize the occurrence of recall bias by instructing the investigators .

Minor:

Comment 1.What does the error bar in Figure 1 represent—standard deviation (SD) or standard error of the mean (SEM)? Please specify this in the figure legend. In addition, there were no remarks for significant findings.

Response 1: We had difficulty adding statistical significance remarks to the line graphs, so we replotted graphs with remarks for significant findings. The error bar in the replotted figure 1 represent standard error of the mean(SEM).

Comment 2.A typo was identified in Reference 13. Please revise it.

Response 2： Thank you for reading our manuscript carefully and pointing out our spelling mistakes. We have revised Reference 13.