

Optical Biometry and Influence of Media Opacity Due to Cataract on Development of Axial Length in Pediatric Eyes

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Abstract

Aim: To study the influence of media opacity due to cataract on the development of axial length in paediatric eyes with the help of optical biometry.

Method: In this prospective, observational study, all patients attending the paediatric outpatient department (OPD) of the institute underwent a comprehensive ocular and systemic evaluation. Patients suffering from any other ocular disease and systemic disease were excluded. Optical biometry was performed to measure the axial length in all the eyes. In each eye, five biometric measurements were acquired and average of these five readings were considered for the study. Patients were divided into three groups after proper age matching – 1. Group A (Bilateral cataract) 2. Group B (Unilateral cataract) 3. Group C (Bilateral normal). The axial length of the various groups were then compared.

Results: A total of 540 eyes of 270 patients were involved in the study. 120 cases (n = 240 eyes) in Group A (bilateral cataract), 30 cases (n = 60 eyes) in Group B (unilateral cataract) and 120 (n = 240 eyes) in Group C (no cataracts). The mean age of the patients in all the groups was 9.38 ± 3.67 years (range: 1-17 years). In Group B, the difference in the AL between the cataractous eyes (22.44 ± 1.48 mm; n = 30) and the fellow eyes (22.09 ± 0.93 mm; n = 30) was not statistically significant (P = 0.277). The difference in the AL between the cataractous right eyes of Group A (22.9 ± 3.51 mm, n = 120) and the non-cataractous right eye of Group C fellow eyes (22.57 ± 0.71 mm, n = 120) was not statistically significant (P = 0.316). The difference in the AL between the cataractous left eyes of Group A (23.06 ± 2.33 mm, n = 120) and the non-cataractous left eyes of Group C fellow eyes (22.56 ± 0.78 , n = 120) was statistically significant (P = 0.028).

Conclusion: The results of our study and reported literature to date, seem to indicate a more significant role of genetic factors in comparison to media opacity, in the proportionate development of the AL.

Introduction

Paediatric cataract accounts for 7.4%–15.3 % of cases of childhood blindness.^{1,2} Khanna et al found amblyopia in 50.9% cases of congenital and developmental cataract and amblyopia was more common in congenital than developmental cataract (93% vs 14.9%, $p < 0.001$).³ Uncertainty, regarding selection of appropriate intra-ocular lens (IOL) power is a very important limitation^{4,5} that seriously compromises the visual outcome. The unpredictable development of post-surgical axial growth in children probably triggered by the media opacity at the time of development may contribute to poor visual outcome.

Various hypothesis have been postulated on the probable factors regulating the growth of the axial length (AL) of the eye though the exact nature is yet to be explained. The current understanding is based on the observations from avian⁶ and primate models.⁷ Two school of thoughts exist on what plays a major role in determination of AL. One group believe it to be majorly guided by the media opacity and another believe it to be due to genetic factors.⁸

The effect of the media opacity on the AL of the growing human eye have been studied by the various authors.⁹⁻¹² A majority of these studies have used ultrasound biometry for calculation of AL. In the present study, we have studied the influence of media opacity due to cataract on the development of axial length in paediatric eyes in a north-east Indian population, with the help of optical biometry,(Carl Zeiss Meditech IOL Master) for a more accurate measurement of AL. The effects of media opacity on the AL of the eye, has been studied and the findings compared with current literature, so as to determine the predominant factor regulating eye growth. This knowledge can assist in more reliable prediction of AL and IOL power calculation for a more satisfactory visual outcome in paediatric cataract patients.

Materials And Methods

This was a prospective, observational study that was conducted after obtaining approval from Sri Sankaradeva Nethralaya Institutional Ethics Committee and it adhered to the Declaration of Helsinki. All patients attending the paediatric outpatient department (OPD) of the institute underwent a comprehensive ocular and systemic evaluation. All cases having cortical, zonular or central lenticular opacity and in which the disc and retina were hazily visible on direct ophthalmoscopic examination, with the other eye normal, were labelled as unilateral cataract. An emmetropic eye without any media opacity was considered as a normal eye. Bilateral cataract was labelled when both eyes had a zonular, cortical or central lenticular opacity providing a hazy view of the disc and retina. Subjects who were not willing to participate, those with any other ocular disease or a history of any other ocular surgery or any systemic diseases and the cases where optical biometry was not possible such as cases with dense cataract, nystagmus or patients uncooperative or unable to fixate for optical biometry measurements were excluded from the study. Informed consent was taken in all cases from the parents and guardians of the patients. Patients upto the age of 17 were included in the study. 270 patients (540 eyes) that who fulfilled the inclusion criteria were further divided into the following three groups: Group A – Bilateral cataract, Group B – Unilateral cataract with normal fellow eye and Group C – Bilateral normal eyes.

In all patients, non-contact biometry working in the principle of partial coherence interferometry (Carl Zeiss Meditech IOL Master) was used to measure the distance between corneal vertex to the retinal pigment epithelium and was considered as the AL of the given eye. Optical measurements were taken before any ocular examination that required eye contact or application of drops, was done. The machine was regularly calibrated against the ultra-high resolution 40Mhz Grieshaber system which is an internal algorithm to maintain the accuracy of measurement within $\pm 0.02\text{mm}$ or better. The instrument table, the head rest, and the IOL Master were adjusted before each measurement, so as the child was seated in a relaxed and stable position. The measurement procedure was explained and the requirement for the patient's head to remain in a fixed position with no unnecessary eye movements was also pointed out. Before taking the measurements, the patients were asked to blink and then to focus on the fixation light. It was also reaffirmed whether the fixation light was visible to the patient. The AL, keratometric readings and predicted IOL power calculation was measured for both the eyes in each subject. In each eye, five biometric measurements were acquired and average of these five readings were considered for the study.

The biometric data were collected and entered into Microsoft Excel 2013 (Redmond, WA, USA). Descriptive statistical methods were used to assess the characteristics such as AL, age and keratometry readings. Pearson correlation between attributes with scatter plot displaying regression line was depicted. IBM SPSS 20 and JMP 10 of SAS 9.3 was used in data processing.

Results

A total of 540 eyes of 270 patients were involved in the study. 120 cases (n = 240 eyes) in Group A (bilateral cataract), 30 cases (n = 60 eyes) in Group B (unilateral cataract) and 120 (n = 240 eyes) in Group C (no cataracts) (Table 2 and Table 3). The mean age in Group A was 7.99 ± 3.4 years (range: 1–16 years). The mean age in Group B was 7.93 ± 3.69 years (range: 2–17 years). The mean age in Group C was 7.86 ± 3.2 years (range: 3–16 years). The mean age of the patients in all the groups was 9.38 ± 3.67 years (range: 1–17 years). (Table 1)

Table 1
Age Distribution

| No. of Patients | Age (Years) | | |
|-----------------|-------------|------|------|
| | Range | Mean | SD |
| 270 | 1–17 | 9.38 | 3.67 |

Table 2
Group-wise distribution of Patients

| Group | No. of Patients | Percent |
|------------------------------------|-----------------|---------|
| A Bilateral Cataract | 120 | 45.0% |
| B Normal + Cataract | 30 | 11.1% |
| C Bilateral Normal (Control Group) | 120 | 43.9% |
| Total | 270 | 100.0 |

Table 3
Group-wise distribution of Eyes

| Group | | Eye | | Total |
|--|----------------------------------|-----|-----|-------|
| | | OD | OS | |
| A | Bilateral Normal (Control Group) | 120 | 120 | 240 |
| B | Normal + Cataract | 30 | 30 | 60 |
| C | Bilateral Cataract | 120 | 120 | 240 |
| | Total | 270 | 270 | 540 |
| A = Both Eyes Normal; B = One Eye Cataract, Other Eye Normal; C = Both Eyes Cataract | | | | |

Axial Length Changes

Mean axial length was 22.75 ± 1.67 mm in OD and 22.73 ± 2.09 mm in OS

Comparison between age and axial length (Table 4)

Table 4
Showing Mean Axial Length (AL) and Standard Deviation(SD) values given Eye-wise for each group.

| Group | | AL OD (mm) | AL OS (mm) | |
|-------|----------------------------------|------------|------------|-------|
| A | Bilateral Normal (Control Group) | Mean | 22.56 | 22.57 |
| | | SD | 0.78 | 0.71 |
| | | n | 120 | 120 |
| B | Normal + Cataract | Mean | 22.09 | 22.44 |
| | | SD | 0.93 | 1.48 |
| | | n | 30 | 30 |
| C | Bilateral Cataract | Mean | 23.06 | 22.94 |
| | | SD | 2.35 | 3.55 |
| | | n | 120 | 120 |

Linear regression analysis of age versus axial shows a statistically significant positive correlation ($P < 0.05$), suggestive of increase in axial length with age. (Fig. 1)

Unilateral Versus Normal Fellow Eyes in Unilateral cataract group (Table 5)

Table 5
Comparing difference in AL between Cataractous and Normal Eyes of each patient in Group B.

| Eye | Mean | SD | Mean Difference | SE Difference | p-value |
|--|-------|------|-----------------|---------------|---------------------|
| Control (n = 30) | 22.09 | 0.93 | -0.35 | 0.32 | 0.277 ^{NS} |
| Cataract (n = 30) | 22.44 | 1.48 | | | |
| ^{NS} Not Significant $p > 0.05$; SE: Spherical Equivalent. | | | | | |

The difference in the AL between the cataractous eyes (22.44 ± 1.48 mm; n = 30) and the fellow eyes (22.09 ± 0.93 mm; n = 30) was not statistically significant (P = 0.277).

Comparison between the Right Eyes of Group A (Bilateral Cataract) and Right Eyes of Group C (Bilateral Normal) (Table 6)

Table 6
Comparing AL differences between the Right eyes of Group A (Control Group) and Right eyes of Group C (Bilateral Cataract)

| Eye | n | Mean | SD | SE | Mean Difference | SE Difference | p-value |
|---|-----|-------|------|------|-----------------|---------------|---------------------|
| Control OS | 120 | 22.57 | 0.71 | 0.07 | -0.33 | 0.33 | 0.316 ^{NS} |
| Cataract OS | 120 | 22.90 | 3.51 | 0.32 | | | |
| ^{NS} Not Significant $p > .05$; SE: Spherical Equivalent. | | | | | | | |

The difference in the AL between the cataractous right eyes of Group A (22.9 ± 3.51 mm, n = 120) and the non-cataractous right eye of Group C fellow eyes (22.57 ± 0.71 mm, n = 120) was not statistically significant (P = 0.316).

Comparison between the Left Eyes of Group A (Bilateral Cataract) and Left Eyes of Group C (Bilateral Normal) (Table 7)

Table 7
Comparing AL difference between left Eye of Group A and Left Eye of Group C

| Eye | n | Mean | SD | SE | Mean Diff | SE Diff | p-value |
|---|-----|-------|------|------|-----------|---------|---------|
| Control OD | 120 | 22.56 | 0.78 | 0.07 | -0.50 | 0.23 | 0.028* |
| Cataract OD | 120 | 23.06 | 2.33 | 0.21 | | | |
| * Significant at $p < 0.05$; SE: Spherical Equivalent. | | | | | | | |

The difference in the AL between the cataractous left eyes of Group A (23.06 ± 2.33 mm, n = 120) and the non-cataractous left eyes of Group C fellow eyes (22.56 ± 0.78 , n = 120) was statistically significant (P =

0.028).

Comparison between the Right Eyes of Group A (Bilateral Cataract) and Left Eyes of Group C (Bilateral Normal) (Table 8)

Table 8
Comparing AL difference between Right Eye of Group A and Left Eye of Group C

| Eye | n | Mean | SD | SE | Mean Difference | SE Difference | p-value |
|-------------|-----|-------|------|------|-----------------|---------------|---------|
| Control OS | 120 | 22.57 | 0.71 | 0.07 | -0.49 | 0.22 | 0.028* |
| Cataract OD | 120 | 23.06 | 2.33 | 0.21 | | | |

* Significant at $p < .05$; SE: Spherical Equivalent.

The difference in the AL between the cataractous right eyes of Group A (22.90 ± 3.51 mm, $n = 120$) and the non-cataractous left eyes of Group C fellow eyes (22.56 ± 0.78 mm, $n = 120$) was not statistically significant ($P = 0.310$).

Comparison between the Left Eyes of Group A (Bilateral Cataract) and Right Eyes of Group C (Bilateral Normal) (Table 9)

Table 9
Comparing AL difference between Left Eye of Group A Vs Right Eye of Group C

| Eye | n | Mean | SD | SE | Mean Difference | SE Difference | p-value |
|-------------|-----|-------|------|------|-----------------|---------------|---------------------|
| Control OD | 120 | 22.56 | 0.78 | 0.07 | -0.34 | 0.33 | 0.310 ^{NS} |
| Cataract OS | 120 | 22.90 | 3.51 | 0.32 | | | |

^{NS} Not Significant $p > .05$; SE: Spherical Equivalent.

The difference in the AL between the cataractous left eyes of Group A (23.06 ± 2.33 mm, $n = 120$) and the non-cataractous right eyes of Group C fellow eyes (22.57 ± 0.71 mm, $n = 120$) was statistically significant ($P = 0.028$).

Discussion

Numerous factors determine how the axial growth of the eye behaves in paediatric eyes. Some of the factors which have been known to be associated are age, general health and growth, clarity of ocular media. Even more factors seem to come into play in cases of paediatric cataracts, such as child's age at surgery, aphakia, pseudophakia, cataract laterality, and visual deprivation.¹³⁻¹⁵

The theories explaining the regulation of ocular growth are diverse. The key premise amongst them is that ocular growth has mainly two components-the active component, governed by the retinal image

formation and the passive component, controlled by genetic factors.⁸ How exactly they control the axial growth, and which component plays a major role is yet unanswered.

The role of retinal image formation has been widely studied in animal as well as human subjects. The concept is that the degradation in quality of retinal image (form deprivation) or the alteration in focal point of image (lens defocus) provides a feedback for adjustment of AL and mechanical modelling of the eye.¹⁶ Media opacity compromises the image quality on the retina and results in form deprivation.¹⁷ Large alteration of retinal image quality due to congenital cataract,^{17,18} corneal opacity,^{9,19} vitreous haemorrhage,²⁰ ptosis,²¹ and other ocular diseases²² might influence the growth pattern of the paediatric eye. Regarding lens defocus, a number of studies have been conducted in animals as well as humans. In avian experiments, increased AL has been noted after myopic defocus.⁶ In animal models, Smith III et al found a decrease in AL in 5 out of 8 monkeys with hyperopic defocus.⁷ In humans, Nickla et al found variable change in the AL with hyperopic defocus depending on the time of the day.²³ Read et al demonstrated that a short hyperopic defocus resulted in an increase in the AL and in a study conducted by Chakraborty et al, the eye undergoing myopic defocus, developed increase in AL.^{16,24}

The other school of thought regarding the growth of the eyeball is in the vast universe of genetics. Physiologically, the eye at birth is hypermetropic, the AL grows as the child ages so as to reach an emmetropic state. Emmetropization is a physiological process that harmonizes the globe elongation, with the optical power of the cornea and lens to reduce refractive error.²⁵ The genetic regulation of refraction may be via the control of the process of emmetropisation, to result in proportionate growth of the various components of refraction.²⁶

AL loci using gene-based tests have been identified and suggest that the growth of different parts of the eyeball are regulated by different gene expression. Some genes such as ZC3H11A, GJD2, and LAMA2 show constant changes in expression in different eye sections in the same direction while other genes like RSP01, C3orf26, and ZNRF3 show variable directions of differential expression. Compensatory changes in corneal curvature or optical power with axial growth in order to balance their effect on spherical equivalent, maybe regulated by genes such as PSP01.²⁷⁻³⁰

Media opacities such as cataracts, deprive the retina of form. Our study demonstrates that in almost all cases, the AL in the cataractous eyes, was longer when compared to the normal eyes, although the difference was not statistically significant in every case. The cataractous right eyes of Group A (22.9 ± 3.51 mm, $n = 120$) had a longer axial length in comparison to the non-cataractous right eye of Group C fellow eyes (22.57 ± 0.71 mm, $n = 120$) (difference not statistically significant). Similarly, cataractous left eyes of Group A (23.06 ± 2.33 mm, $n = 120$) was significantly longer ($P = 0.028$) than the non-cataractous left eyes of Group C fellow eyes (22.56 ± 0.78 , $n = 120$). Other studies that have also compared the AL of the cataractous eye against the AL of the fellow normal eye have found variable results. Capozzi et al (USG biometry) found a shorter AL in cases of bilateral congenital cataract and no change in cases of unilateral congenital cataracts.³¹ A study by Trivedi et al (Biometry method not mentioned) reported

longer AL in case of bilateral congenital cataract than those with unilateral cataract in paediatric patients younger than 60 months of age and a shorter AL when compared to unilateral cataract paediatric patients older than 60 months of age.³² In a study by Lambert et al, cases of unilateral congenital cataract had a shorter AL in comparison to the fellow eye.³³

In the previously mentioned studies, Capozzi et al utilised an ultrasonographic biometer whereas the biometry method was not mentioned in Trivedi et al and Lambert et al. Other studies comparing the biometry characteristics in paediatric cataract cases have also employed the ultrasonic biometer for axial length measurement.^{1,7,8,31,34} This technique being a contact procedure, can give falsely shorter axial length readings, especially in pediatric patients because of lower corneal and scleral rigidity.^{16,35} The procurement of inaccurate measurements is also higher due to lack of cooperation in paediatric patients.³⁵ Optical biometry technique, employed in our study, has been shown to provide contact-free measurements, observer independence and high reproducibility and accuracy over conventional ultrasound.³⁶

The results of our study, along with the review of the various studies which have been done previously, show conflicting results regarding the influence of media opacity on AL, suggesting that genetics may be playing a crucial role in AL development. Apart from the studies on specific genes related to the axial growth of the eyeball, strong evidence of genetic influence on the axial length has also been demonstrated by studies in twins.^{37,38} Dirani et al also showed high heritability for AL in which 90% of the variance was accounted to be due to additive and dominant genetic effects.³⁹ Other additional factors such as the aqueous humour (AH) level of vascular endothelial growth factor (VEGF) protein levels show a negative correlation with preoperative AL.⁴⁰

The patients included in this study were mainly from a specific geographical region (North-East India) and whether the results extend to a global population, can only be determined with larger studies with a varied cohort. Also, only patients with visually significant media opacity in whom optical biometry readings were possible, were included in the study. Future studies incorporating both, refractive and genetic testing of children with cataract would be more beneficial in understanding the growth of the eye.

In conclusion, the results of our study and reported literature to date, seem to indicate a significant role of genetic factors in the proportionate development of the AL and the various refractory components, which definitely needs to be explored with the help of genetic testing. Although important, a subsidiary and somewhat transient role, role may be played by the environmental factors such as media opacity.

Declarations

Ethics approval for the study taken from Sri Sankaradeva Nethralaya Institutional Ethics Committee.

Consent to participate: Obtained from the parents/ guardian (whichever applicable)

Consent for publication : Obtained from the parents/ guardian (whichever applicable)

Availability of data and materials: Data pertaining to the results and conclusions of this study are included within the manuscript file. Any additional data can be obtained by writing to the corresponding author for the same. Details of the corresponding author are as below:

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Figures

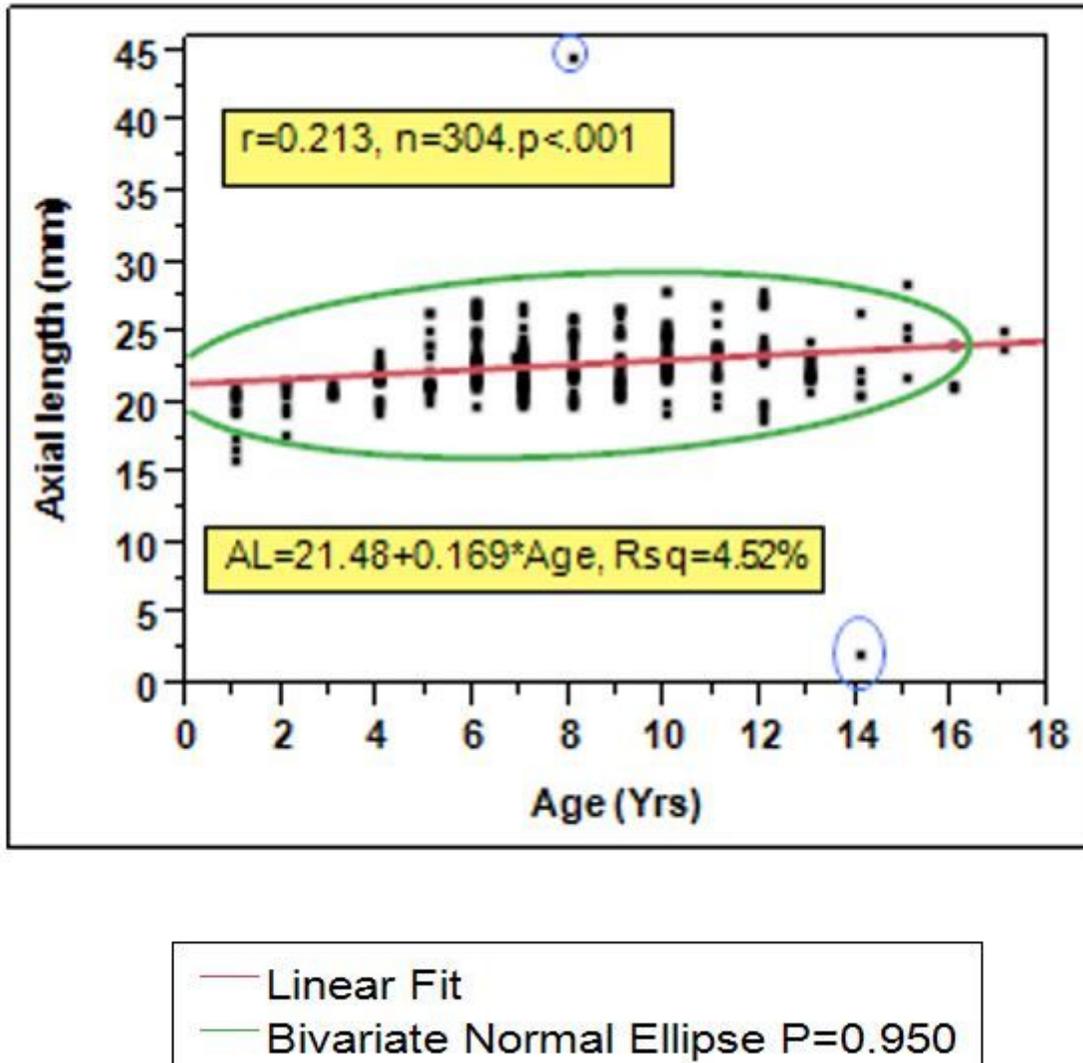


Figure 1

Bivariate Scatter Plot of Axial length (mm) and Age (Yrs) Pearson Correlations found that age was significantly and positively associated with Axial Length ($r=0.213, p<.001, n=204$). The simple linear regression of Axial Length on Age found a significant effect of age on AL, $AL = 21.477 + 0.169 * Age$; $R Sq = 5.42\%, n = 304$. It indicated that increase in one year of age increased Axial length by 0.18 mm. It explained about 5.42% of total variability in Axial length.