• Investigation •

Axial length development in children

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Abstract

• AIM: To study ocular axial lengths in pediatric subjects without intraocular pathology.

• METHODS: An Institutional Review Board-approved consecutive retrospective chart review of axial lengths measured in pediatric subjects who underwent examination under anesthesia due to positive family history of retinoblastoma or other inherited ocular disease. Only subjects without any intraocular pathology in either eye were included. Subjects were stratified into age groups. An axial length model using a logarithmic regression algorithm was calculated.

• RESULTS: Data from 330 eyes of 165 subjects were included in the study. The mean age at the time of examination was 30.62 (SD 18.04)mo. The steepest increase in axial length was present during the first 10mo of life. After 36mo, there was no statistically significant axial length growth.

• CONCLUSION: This study presents the biggest series of pediatric axial lengths in healthy eyes. The axial length model developed with these data may assist in the diagnosis and management of a wide variety of pediatric ophthalmic diseases.

• KEYWORDS: pediatric; axial length; model; biometry; eye development

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INTRODUCTION

Studying the development of the human eye is essential to better understand complex visual pathophysiologic processes. There are many factors that affect the differentiation and maturation of the eye. Most important of all are genetic factors. Neural input, refractive error, and other generalized pathologic disorders can cause differentiation and maturation of ocular tissues in a non-physiologic manner[1-4]. One of the earliest signs of pathology in the eye is an alteration of normal axial length. Examples of such disorders include nanophthalmos, microphthalmos, and retinoblastoma, which classically have a decrease in axial length. In contrast, congenital glaucoma is usually associated to an increase in axial length.

Multiple studies have reported ocular axial length in pediatric subjects with intraocular pathology, mostly with congenital cataracts and glaucoma[1-11]. However, only a few small studies have been performed to evaluate the axial length in healthy pediatric patients without ocular disease in either eye[4,9,11-14]. The purpose of our study is to develop a growth curve for pediatric ocular axial lengths in healthy eyes.

SUBJECTS AND METHODS

Ethical Approval An Institutional Review Board-approved retrospective consecutive chart review was undertaken at the Bascom Palmer Eye Institute in 165 subjects that underwent examination under anesthesia due to a positive family history of retinoblastoma or other inherited disease, none of whom developed any disease by the end of the study.

Data regarding age of subjects at examination and ocular axial length was recorded. Axial length was determined using an immersion A-scan (Eye Cubed, Ellex, Adelaide, Australia) sonogram and a standardized A-scan probe directly over the cornea. Subjects with intraocular pathology in either eye were excluded from the study. Subjects were stratified to different age groups by 3, 6 or 12mo intervals, depending on the age of the patient.

Statistical Analysis Axial lengths were compiled and divided into those subjects 3 years of age and younger and those above the age of 3. Linear, logarithmic, quadratic, cubic, growth, exponential, and logistic regression models were then applied to each group of data to determine the best fit for the data of each group.

RESULTS

A total of 165 subjects (330 eyes) were evaluated under anesthesia. The mean age at the time of examination was 30.62 (SD 18.04)mo with a mean axial length of 21.37 (SD 1.03) mm. The subjects were stratified based on age (Table 1; Figure 1). A one-way ANOVA was performed to calculate the mean difference of axial length among the age groups. One-way

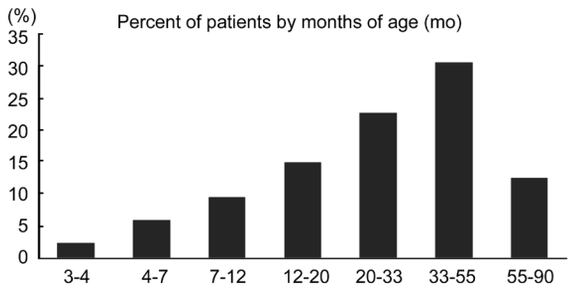

Figure 1 Stratification of patients by age.

Table 1 Axial lengths based on age group

Age group	Mean axial length (mm)	SD (mm)	*n*	95%CI	
				Lower bound	Upper bound
3-6mo	19.7643	0.62340	14	19.370	20.159
6-8mo	20.0956	1.06732	18	19.748	20.443
9-12mo	20.5692	0.90544	26	20.280	20.859
13-15mo	20.7317	0.88479	24	20.430	21.033
16-18mo	21.3114	0.87441	14	20.917	21.706
19-21mo	21.0700	0.70120	20	20.740	21.400
22-24mo	20.8144	0.56548	16	20.445	21.183
25-3y	21.4499	0.69585	72	21.276	21.624
4-5y	22.0354	0.67873	108	21.893	22.177
6-7y	22.4156	0.75723	18	22.068	22.763
Total	21.3675	1.02690	330	-	-

One way ANOVA was performed to evaluate the mean difference in eye length among the age groups. A statistically significant difference was present between each of the age groups (P<0.001).

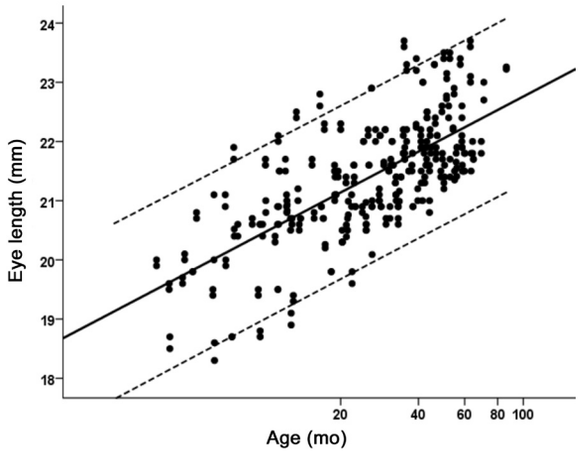

Figure 2 Logarithmic regression model of axial lengths Mean (solid line) and 95% standard deviation (dotted lines) are plotted.

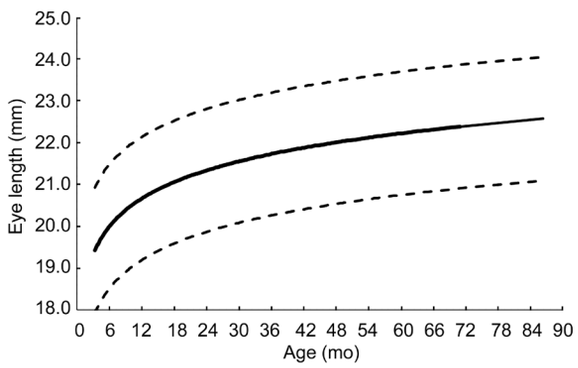

Figure 3 Template for plotting axial lengths based on age with mean (solid line) and 95%CI (dotted lines) curve.

ANOVA showed a statistically significant difference in the mean axial lengths between each of the age groups (P<0.001). The t-test analysis failed to show a statistical difference between the right and left eye of subjects (P=0.25, 95%CI: -0.01 to 0.04). Multiple regression models were then applied across all ages (Table 2; Figure 2). One eye was chosen at random from each subject. The line of best fit was calculated: eye length=0.966×$\log_e$(age)+18.270 (r^2=0.479, r=0.692, P≤0.001; Figure 2).

No statistical difference was noted between both eyes. Non-linearity across age groups was found (P=0.411) showing faster axial length growth during the first 10mo with a decline in the rate of growth afterwards.

DISCUSSION

Currently, no large study has examined the ocular axial length of healthy pediatric subjects without intraocular pathology in either eye up to the age of 7y. Only six studies have measured axial length in healthy children. Table 3 lists the studies, their findings, and the limitations to each of the studies when compared to this study. The authors have attempted to reach out to all aforementioned authors to make a collaborative data set, though access to these data sets were not available.

Previous studies have also evaluated changes in corneal curvature[6,15], endothelial cell density[16-17], lens changes[18], as well as retinal surface changes[19] in children. Limitations in these studies include small cohorts and contralateral eye pathology[10-14]. Based on our large series of healthy pediatric subjects, we have derived a logarithmic regression model for axial length growth of pediatric eyes with a graph template for clinical use (Figure 3). This model shows that both eyes grow at similar rates. Although it is well known that axial length increases significantly during the first few years of life[20-21], normative data from young children less than 2 years of age is scarce because healthy children do not generally undergo routine ultrasonography.

This study shows an increase in axial length over time. The most significant increases in axial length occur during the first 10mo of age, at which point axial length continues to increase, though at a decreased rate. The logarithmic regression model (Figure 2) shows this trend.

Axial length is of essential value when calculating the power of intraocular lenses (IOLs). IOL power continues to be a topic of debate among pediatric ophthalmologists partly because of the scarcity of reliable model of axial length in the pediatric population. The main challenge when deciding IOL power is the future change in refraction due to growth associated changes in axial length, anterior segment, and corneal power[7,15,22]. During childhood there is a decrease in corneal

Table 2 Comparisons of regression models for all patients *n*=330 eyes

Equation	Model summary					Parameter estimates			
	r^2	*F*	df1	df2	Significance	Constant	b1	b2	b3
Linear	0.442	128.943	1	163	0	20.203	0.038		
Logarithmic	0.479	149.973	1	163	0	18.270	0.966		
Quadratic	0.469	71.505	2	162	0	19.795	0.071	0.000	
Cubic	0.478	49.075	3	161	0	19.474	0.113	-0.002	1.130E-5
Growth	0.442	128.872	1	163	0	3.006	0.002		
Exponential	0.442	128.872	1	163	0	20.202	0.002		
Logistic	0.442	128.872	1	163	0	0.049	0.998		

Table 3 Summary of prior studies measuring pediatric axial lengths in normal children

Authors	Subjects	Age range	Findings	Limitations
Herrera *et al*[9]	93	4-16y	Axial length of 23.19±1.13 mm (range, 19.89-25.74 mm).	Axial length was not divided by age.
Gordon *et al*[11]	148	Infants to 36y	Axial length has the greatest length increase until 2y. Significant decrease in the axial length rate increase is present until age 15.	Small cohort of pediatric subjects. Premature infants were included.
Mutti *et al*[4]	222	3 and 9mo	Average increase in axial length of 1.2±0.51 mm between the ages of 3 and 9mo.	Only data from two time points: 3 and 9mo. A scan performed with closed eyelid.
Pennie *et al*[12]	20	<12mo	Axial length rate increase may vary between anterior and posterior segments.	Small cohort.
Sampolesi *et al*[13]	18	2-72mo	Axial length increases mostly during year 1 and 2 as compared to adults.	Small cohort of patients.
Youn *et al*[14]	10, 79	<2y, 2-7y	Average axial length change from birth until age 2y was 21.31±0.97 mm. From 2-7y was 22.04±0.92 mm.	Small cohort at younger ages and no trend throughout the two groups, age groups were wide ranging.

curvature and increase in axial length. Furthermore, the IOL' effective position may affect the long-term refractive outcome. No study to date has evaluated if IOL axial location changes as the eye grows. One study has shown that there is a likelihood of IOL to dislocate in pediatric eyes due to the relatively small size of the capsule when compared to adult eyes[23]. Another factor that significantly impacts IOL calculations in children is the decrease in corneal curvature that occurs early in life[7,15,22]. Currently, IOL calculations are performed using later generation algorithms such as the SRK-T, Hoffer-Q, and Holladay II equations. These formulas have historically been based on adult normative data and may lead to refractive errors when applied to the pediatric population due to assumptions made in the formulas like that of the corneal curvature. The current series provides the largest data set to date on axial length growth in the normal pediatric eyes and may help pediatric cataract surgeons during preoperative evaluation in children in the amblyopic age range.

The most common long-term refractive error following pediatric cataract surgery has been shown to be due to a myopic shift due to axial length increase[24-26]. These studies have shown that the patients who underwent cataract surgery at a younger age had a greater average myopic shift in postoperative refraction of approximately 6.00 diopters when compared to those who had cataract surgery at an older age[27]. This model may help determine proper lens power based on predicted axial growth and may assist in the prevention of amblyopia post-operatively[28].

There have been many new advances in understanding different disease states that affect eyes of pediatric patients. With a global focus on diagnosing and preventing progressive axial myopia[29-31] and changes in choroidal thickness[9,32], having a normative model for pediatric axial lengths may enhance the ophthalmologists' ability to diagnose and monitor such diseases.

Pathologic axial myopia may lead to visually threatening complications. These may include: amblyopia, retinal detachment, retinal schisis, staphyloma, tilted optic nerve head, and subretinal neovascularization. An axial length growth model may allow earlier diagnosis and treatment. Atropine therapy and other investigational therapies may be tailored based on the growth curve. Other applications for the new model may include the diagnosis and management of patients with congenital glaucoma. This algorithm and chart will be of indispensable use for monitoring pediatric glaucoma. As glaucoma damage in the pediatric population results in elongation in axial length, monitoring change in axial length when compared to normative values can give the ophthalmologist another tool in their decision making and treatment algorithm for this blinding disease.

Limitations to our study include its retrospective nature and a lack of other data points that are currently used to calculate

IOL powers. These include keratometry, anterior chamber depth, lens thickness, and white-to-white distance.

The current study presents the largest series of bilateral ocular axial lengths without intraocular pathology. This data may aid in the diagnosis and management of multiple diseases including IOL power calculation in the pediatric population, pathologic myopia, and congenital glaucoma. Further studies are needed to evaluate refractive outcomes after pediatric cataract extraction and IOL implantation using this model.

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