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 10 mo of life. After 36 mo, 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. 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. However, only a few small studies have been performed to evaluate the axial length in healthy pediatric patients without ocular disease in either eye. 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 12 mo 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). One-way ANOVA was performed to calculate the mean difference of axial length among the age groups.
ANOVA showed a statistically significant difference in the mean axial lengths between each of the age groups \( (P<0.001) \).

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 × loge(age) + 18.270 \( \left( r^2 = 0.479, r = 0.692, P \leq 0.001, \right. \) 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.

Axial length development in children

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

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 \( (P<0.001) \).

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 \( (P = 0.25, 95\%CI: -0.01 \text{ to } 0.04) \). 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.

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. During childhood there is a decrease in corneal...
curvature and increase in axial length. Furthermore, the IOL’s 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 of IOL to dislocate in pediatric eyes due to the relatively small size of the capsule when compared to adult eyes.

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 amblyopia post-operatively, there is a need for new models to predict axial growth and may assist in the prevention of amblyopia post-operatively. 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 amblyopia post-operatively, there is a need for new models to predict axial growth and may assist in the prevention of amblyopia post-operatively.

Table 2 Comparisons of regression models for all patients

<table>
<thead>
<tr>
<th>Equation</th>
<th>$r^2$</th>
<th>$F$</th>
<th>df1</th>
<th>df2</th>
<th>Significance</th>
<th>Parameter estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linear</td>
<td>0.442</td>
<td>128.943</td>
<td>1</td>
<td>163</td>
<td>0</td>
<td>20.203 0.038</td>
</tr>
<tr>
<td>Logarithmic</td>
<td>0.479</td>
<td>149.973</td>
<td>1</td>
<td>163</td>
<td>0</td>
<td>18.270 0.966</td>
</tr>
<tr>
<td>Quadratic</td>
<td>0.469</td>
<td>71.505</td>
<td>2</td>
<td>162</td>
<td>0</td>
<td>19.795 0.071 0.000</td>
</tr>
<tr>
<td>Cubic</td>
<td>0.478</td>
<td>49.075</td>
<td>3</td>
<td>161</td>
<td>0</td>
<td>19.474 0.113 -0.002 1.13E-5</td>
</tr>
<tr>
<td>Growth</td>
<td>0.442</td>
<td>128.872</td>
<td>1</td>
<td>163</td>
<td>0</td>
<td>3.006 0.002</td>
</tr>
<tr>
<td>Exponential</td>
<td>0.442</td>
<td>128.872</td>
<td>1</td>
<td>163</td>
<td>0</td>
<td>20.202 0.002</td>
</tr>
<tr>
<td>Logistic</td>
<td>0.442</td>
<td>128.872</td>
<td>1</td>
<td>163</td>
<td>0</td>
<td>0.049 0.998</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Authors</th>
<th>Subjects</th>
<th>Age range</th>
<th>Findings</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herrera et al</td>
<td>93</td>
<td>4-16y</td>
<td>Axial length of 23.49±1.13 mm (range, 19.89-25.74 mm).</td>
<td>Axial length was not divided by age.</td>
</tr>
<tr>
<td>Gordon et al</td>
<td>148</td>
<td>Infants to 36y</td>
<td>Axial length has the greatest length increase until 2y. Significant decrease in the axial length rate increase is present until age 15.</td>
<td>Small cohort of pediatric subjects. Premature infants were included.</td>
</tr>
<tr>
<td>Mutti et al</td>
<td>222</td>
<td>3 and 9mo</td>
<td>Average increase in axial length of 1.2±0.51 mm between the ages of 3 and 9mo.</td>
<td>Only data from two time points: 3 and 9mo. A scan performed with closed eyelid.</td>
</tr>
<tr>
<td>Pennie et al</td>
<td>20</td>
<td>&lt;12mo</td>
<td>Axial length rate increase may vary between anterior and posterior segments.</td>
<td>Small cohort.</td>
</tr>
<tr>
<td>Sampolesi et al</td>
<td>18</td>
<td>2-72mo</td>
<td>Axial length increases mostly during year 1 and 2 as compared to adults.</td>
<td>Small cohort of patients.</td>
</tr>
<tr>
<td>Youn et al</td>
<td>10, 79</td>
<td>&lt;2y, 2-7y</td>
<td>Average axial length change from birth until age 2y was 23.19±0.97 mm. From 2-7y was 22.04±0.92 mm.</td>
<td>Small cohort at younger ages and no trend throughout the two groups, age groups were wide ranging.</td>
</tr>
</tbody>
</table>

predicted axial growth and may assist in the prevention of amblyopia post-operatively. 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 and changes in choroidal thickness, 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 axial length when compared to normative values can give 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.

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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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Conflicts of Interest: Bach A, None; Villegas VM, None; Gold AS, None; Shi W, None; Murray TG, None.

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