Developmental Changes in Anterior Corneal Astigmatism in Tohono O’odham Native American Infants and Children*

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ABSTRACT

Purpose: To describe change in corneal astigmatism in infants and children of a Native American tribe with a high prevalence of astigmatism.

Methods: Longitudinal measurements of corneal astigmatism were obtained in 960 Tohono O’odham children aged 6 months to 5.8 years. Change in corneal astigmatism (magnitude (clinical notation), J0, J45) across age in children with high astigmatism (≥2 diopter (D) corneal astigmatism) or low/no astigmatism (<2 D corneal astigmatism) at their baseline measurement was assessed.

Results: Regression analyses indicated that early in development (6 months to <3 years), astigmatism magnitude decreased in the high astigmatism group (0.37 D/year) and remained stable in the low/no astigmatism group. In later development (3 to <8 years), astigmatism decreased in the high (0.11 D/year) and low/no astigmatism groups (0.03 D/year). In 52 children who had data at all three of the youngest ages (6 months to <1 year, 1 to <2 years, 2 to <3 years) astigmatism decreased after infancy in those with high astigmatism (p = 0.021), and then remained stable from age 1–2 years, whereas astigmatism was stable from infancy through age 1 year and increased from age 1–2 years in the low/no astigmatism group (p = 0.026). J0 results were similar, but results on J45 yielded no significant effects.

Conclusions: The greatest change occurred in highly astigmatic infants and toddlers (0.37 D/year). By age 3 years, change was minimal and not clinically significant. Changes observed were due primarily to change in the J0 component of astigmatism.

Keywords: Astigmatism, children, longitudinal, native American, refractive error

INTRODUCTION

A high prevalence of astigmatism has been documented among preschool- and school-age members of several Native American tribes,1–8 including the Tohono O’odham of southern Arizona.9–12 Recent reports of data from Tohono O’odham infants show a high prevalence of astigmatism, which decreases in the second year of life.12,13 This pattern is similar to that seen in Caucasian, Asian, and Hispanic infants: astigmatism is prevalent in infancy,14–28 but longitudinal studies indicate that the amount of astigmatism decreases significantly after the first year of life.17,18,21,23,28–31 However, cross-sectional data has shown that the initial decrease in prevalence of astigmatism after infancy in Tohono O’odham children is followed by an increase in prevalence by age 2 years to the level we see in Tohono O’odham preschool and school-age children.12,13

The purpose of the present study was to longitudinally examine change in corneal astigmatism in infants and young Tohono O’odham children.

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The present study focuses on corneal astigmatism, as astigmatism in Tohono O’odham children arises primarily from the anterior cornea. Longitudinal data will allow us to describe change in astigmatism over the course of early development and determine the extent to which these changes can be predicted in individual children.

MATERIALS AND METHODS

Subjects

Subjects were children who were recruited for participation between September 2005 and May 2010. Children aged 6 months through to first grade were eligible to participate, although analyses only included data obtained between 6 months and <8 years of age. Children were recruited from the Women, Infants and Children clinics, from the Tohono O’odham Early Childhood Head Start program, from the Tohono O’odham community, and from kindergarten and first grade classrooms on the Tohono O’odham reservation. Once enrolled, follow-up was attempted yearly (within 1-year age windows: 1 to <2 years, 2 to <3 years, 3 to <4 years, 4 to <5 years, 5 to <6 years, 6 to <7 years, and 7 to <8 years, with attempts to maintain at least a 6 month separation between follow-ups) until either the child graduated first grade or the study ended (May, 2010). This research followed the tenets of the Declaration of Helsinki and was approved by the Tohono O’odham Nation and by the Institutional Review Board of the University of Arizona. Parents provided written informed consent prior to testing.

Apparatus

IK4 Keratometer

The infant keratometer (IK4) has been previously described in detail. Briefly, it consists of a single-ring (200 mm diameter) keratoscope with 12 infrared light emitting diodes (LEDs) and a central green fixation light attached to a custom telecentric telephoto lens designed for use with a Sony TRV460 Digital-8 camcorder (Sony Electronics Inc, San Diego, CA). The instrument records the infrared image, and allows visualization of the dark pupil. Digital recording allows for extraction of individual frames for analysis. Custom software was written to isolate each frame, permit quality control, and if appropriate, image analysis to determine corneal power in the principal meridians. Previous studies have shown good agreement between IK4 and Retinomax K-Plus2 (Nikon Inc, Melville, NY) keratometry measurements of young children.

Procedures

Video keratoscope images were obtained for each child’s right eye using the IK4. Infants and toddlers sat on a parent’s lap and measurements were obtained while the parent and tester directed the child’s attention towards the center green fixation light (the only visible light against the black disk of the keratometer). Older children were asked to fixate on the center green light in the display. Videos of approximately 15–30 seconds in length were recorded during which the tester viewed the monitor of the IK4’s camcorder and aligned the reflected images of the circle of twelve infrared LEDs around the perimeter of the child’s pupil, moving the instrument forward or backward until the reflected ring of lights was in sharp focus. Videos were later converted to images and only quality (centered and in focus) images were used in the analyses (see Supplementary Appendix – available online). Children aged 3 years and older also completed an eye examination including cycloplegic autorefraction and autokeratometry (Nikon Retinomax K-Plus 2).

Data Processing

Detailed information on data processing, including image analysis, identification of outliers, quality control methods, assessment of calibration over time, and methods of correcting for shifts in instrument calibration over time are provided in the Supplementary Appendix (available online). In general, processing of data used custom image analysis software for determination of keratometry powers associated with the steepest and flattest anterior corneal curvatures. These corneal powers were then decomposed, using the Fourier method of Thibos, into the power vectors M, J0, J45. The many observations generated for each patient encounter were reduced to point estimates for the keratometry of the subject at that point in time. For each subject encounter, the mean and median for M, J0, and J45 across observations were determined.

Data Analysis

Longitudinal Analysis: Change in Corneal Astigmatism in Children aged 6 months through 7 years

For longitudinal analyses, comparisons were made between children classified as having high astigmatism (≥2 D corneal astigmatism) or low/no astigmatism (<2 D corneal astigmatism) at their baseline (first) assessment. Longitudinal measures were fitted using a linear mixed model (LMM). Each independent LMM included an anterior corneal astigmatism...
component as the dependent variable and an astigmatic indicator variable (high vs. low/no astigmatism groups), follow-up (time), and astigmatic indicator by follow-up as interactions, were included as fixed covariates. Subject and follow-up were included in the LMM as random effects to adjust for correlation associated with serial encounters within subjects. The inclusion of the astigmatic by follow-up interaction term allowed us to test if the rate of development or slope over time differed by baseline astigmatism status.

In order to determine if any observed change with age was occurring primarily early in development (age ≤3 years) vs. later in development (age >3 years), additional longitudinal analyses using the same methods as described above were conducted on two sub-groups: subjects with at least 2 measurements at age ≤3 years (234 subjects, 520 encounters) and subjects with at least 2 measurements at >3 years of age (661 subjects, 1681 encounters).

Longitudinal Analysis: Change in Corneal Astigmatism from Infancy through age 2 years
This repeated measures analysis of variance (RMANOVA) analysis included only children for whom we had data for the three youngest age groups (6 months to <1 year, 1 to <2 years, and 2 to <3 years). Comparisons were made between the high astigmatism group (≥2.00 D corneal astigmatism) and the low/no astigmatism group (<2.00 D corneal astigmatism).

RESULTS

Subjects
A total of 1688 subjects were enrolled in the study and participated in at least one testing session between the ages of 6 months and <8 years. Data from 27 children were excluded from analysis for the following reasons: strabismus (16), ptosis (3), nystagmus (1), hemangioma (1), exudates (1), Down syndrome (1), cataract (1), blepharophimosis (1), autism (1), and asymmetric optic nerves (1). Of the remaining 1661 subjects, corneal astigmatism measurement was successfully obtained within at least one age window for 1546 subjects (93%), providing 3154 total observations. At least two measurements were obtained from 960 subjects (2568 observations).

Longitudinal Analyses
Change in Corneal Astigmatism between ages 6 months and <8 years
This analysis is based on 2568 corneal astigmatism measurements (subject encounters) from 960 subjects who contributed to the final longitudinal dataset. The average follow-up was 2.09 (standard deviation, SD, 1.01) years duration (from baseline to last encounter), ranging from 0.13–4.59 years. Of the sample of 960, 475 (49%) had two encounters, 349 (36%) had three encounters, 110 (11%) had four encounters, 25 (3%) had five encounters, and one subject (<1%) had 6 encounters. Children were classified as having high astigmatism (≥2 D corneal astigmatism) or low/no astigmatism (<2 D corneal astigmatism) at their baseline measurement. Analyses were conducted for data across the full age range (6 months to <8 years), and sub-group analyses were conducted restricting data to <3 years (analysis of change early in development) and restricting data from 3 to <8 years (analysis of change later in development). An overall summary of results is shown in Table 1.

1) Full age range (6 months to <8 years). Analysis of clinical notation astigmatism data indicated that the difference in change with age (slopes) between high and low/no astigmatism groups neared statistical significance (p=0.09). Both high and low/no astigmatism groups showed a small but significant decrease in astigmatism with age (−0.05 for the high astigmatism group, p<0.001 and −0.02 D/year for the low/no astigmatism group, p<0.003). Analysis of J0 data indicated that the high and low/no astigmatism groups significantly differed in change in astigmatism (slope) with age. Those with high astigmatism showed a small but borderline statistically significant decrease in corneal astigmatism occurring at a rate of −0.01 D/year (p=0.054). The low/no astigmatism group did not show significant change in astigmatism with age (+0.01 D/year). Analysis of J45 data indicated that the high and low/no astigmatism groups did not significantly differ in change in astigmatism (slope) with age: both showed a small but statistically significant decrease in astigmatism at a rate of −0.03D/year (p<0.001).

2) Early changes (6 months to <3 years). Analysis of clinical notation astigmatism data indicated that there was a significant difference in change in astigmatism (slope) between the high and low/no astigmatism groups (p=0.001). Those with high astigmatism had a significant decrease in astigmatism (−0.37 D/year, p<0.001), whereas there was no significant change in the low/no astigmatism group (+0.05 D/year). Analysis of J0 data also indicated that high and low/no astigmatism groups significantly differed in change in astigmatism (slope) with age. Those with high astigmatism showed statistically significant decreases in corneal astigmatism occurring at a rate of −0.20 D/year (p<0.001). The low/no astigmatism group showed a small but significant increase in astigmatism with age (0.06 D/year,
TABLE 1. Longitudinal analysis summary: Results of separate analyses conducted for magnitude of astigmatism in clinical notation (CN Mag), J0, and J45 measures, and for the full age range (6 months to <8 years of age, top section), early development (6 months to <3 years, middle section), and for later development (3 to <8 years, bottom section). Results indicate whether change in the high astigmatism group (≥2.00 D astigmatism at baseline) significantly differs from 0, whether change in the low/no astigmatism group (<2.00 D astigmatism at baseline) significantly differs from 0, and whether change in the high astigmatism group significantly differs from the low/no astigmatism group.

<table>
<thead>
<tr>
<th>Age range</th>
<th>n</th>
<th>Measure</th>
<th>High astigmatism</th>
<th>Low/no astigmatism</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Change per year (D)</td>
<td>Significance (p value)</td>
</tr>
<tr>
<td>6 months to &lt;3 years</td>
<td>234</td>
<td>CN Mag</td>
<td>−0.37 0.001</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>J0</td>
<td>−0.20 0.001</td>
<td>0.001</td>
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<tr>
<td></td>
<td></td>
<td>J45</td>
<td>+0.03 ns</td>
<td>0.001</td>
</tr>
<tr>
<td>3 to &lt;8 years</td>
<td>661</td>
<td>CN Mag</td>
<td>−0.11 0.001</td>
<td>0.001</td>
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<tr>
<td></td>
<td></td>
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<td>−0.04 0.001</td>
<td>0.001</td>
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<tr>
<td></td>
<td></td>
<td>J45</td>
<td>−0.05 0.001</td>
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ns, not statistically significant; CN Mag, magnitude of astigmatism in clinical notation; D, diopters

$p = 0.003$). Analysis of J45 data indicated that high and low/no astigmatism groups did not significantly differ in change in astigmatism (slope) with age: neither showed a significant change in astigmatism with age (high astigmatism group +0.04 D/year, the low/no astigmatism group −0.02 D/year).

(3) Later changes (3 to <8 years). Analysis of clinical notation astigmatism data indicated that there was a significant difference in change in astigmatism (slope) between high and low/no astigmatism groups ($p = 0.001$). Both groups had a significant decrease in astigmatism (−0.11 D/year, $p < 0.001$ for the high astigmatism group, −0.03 D/year $p < 0.012$, for the low/no astigmatism group). Analysis of J0 data also indicated that high and low/no astigmatism groups significantly differed in change in astigmatism (slope) with age. Those with high astigmatism showed small but statistically significant decreases in corneal astigmatism occurring at a rate of −0.04 D/year ($p < 0.001$). The low/no astigmatism group did not show significant change in astigmatism with age (−0.01 D/year). Analysis of the J45 data indicated that high and low/no astigmatism groups did not significantly differ in change in astigmatism (slope) with age: both showed a small but statistically significant decrease in astigmatism at a rate of −0.05 D/year ($p < 0.001$) for the high astigmatism group and −0.03 D/year ($p < 0.001$) for the low/no astigmatism group.

RMANOVA: Change in corneal astigmatism from infancy through age 2 years

This analysis included 52 children who were recruited into the study prior to age 1 year ($n = 239$), and for whom we had data at all three of the youngest ages (6 months to <1 year, 1 to <2 years, 2 to <3 years). RMANOVAs were used to compare change in corneal astigmatism (clinical notation, J0, and J45) over time between children classified as having high astigmatism (≥2D corneal astigmatism) or low/no astigmatism (<2D corneal astigmatism) at their baseline measurement. Mean change by amount of baseline astigmatism is plotted in Figure 1 and mean astigmatism across age is summarized in Table 2.

Results of the RMANOVA on magnitude of corneal astigmatism (clinical notation) yielded a significant main effect of age ($p < 0.05$) and a significant interaction between age and amount of baseline corneal astigmatism ($p < 0.004$). When subjects were separated by amount of baseline astigmatism, astigmatism decreased after 6 months to <1 year of age to 1 to <2 years of age in the high astigmatism group ($p = 0.021$), and then remained relatively stable with a modest non-significant decrease from age 1 to <2 years to age 2 to <3 years, whereas astigmatism was stable from 6 months to <1 year of age to 1 to <2 years of age in the low/no astigmatism group, with an increase from 1 to <2 years to age 2 to <3 years ($p = 0.026$).

Results of the RMANOVA on J0 yielded only a significant interaction between age and amount of baseline corneal astigmatism. The pattern was similar to that described above for clinical notation. Astigmatism decreased from 6 months to <1 year of age to 1 to <2 years of age in the high astigmatism group ($p = 0.009$), and then remained relatively stable with a modest non-significant decrease from age 1 to <2 years to age 2 to <3 years, whereas astigmatism was stable from 6 months to <1 year of age to 1 to <2 years of age in the low/no astigmatism group (non-significant), with an increase from age 1 to <2 years to age 2 to <3 years ($p = 0.002$). Results of the RMANOVA on J45 yielded no significant effects.
DISCUSSION

The results of the present study provide the first longitudinal data on corneal astigmatism in Native American infants and young children who are members of a tribe with a high prevalence of refractive astigmatism. Results indicated that early in development (6 months to <3 years of age), corneal astigmatism tends to decrease in children with high corneal astigmatism. However, although there was a decrease in astigmatic power in the highly astigmatic infants and toddlers, the majority (80%) still had astigmatism ≥2.00 D at their last measurement prior to 3 years of age. These data suggest that children in this age range who are prescribed spectacles should be evaluated frequently for appropriateness of prescription and continued need for spectacles. Astigmatism was relatively stable in infants and toddlers with initially low to moderate corneal astigmatism. Only 13% of these children developed astigmatism ≥2.00 D by the time they completed their last measurement prior to age 3 years.

In later development (age 3 years to <8 years), corneal astigmatism tended to decrease in children with initially high corneal astigmatism and in children with initially low or no corneal astigmatism, although a greater decrease was apparent in more astigmatic children. However, changes in astigmatism were generally small and would not be considered clinically significant. This is useful information for clinicians and parents with regard to recommending continued follow-up for children prescribed spectacles for astigmatism. However, other factors need to be considered in terms of follow-up recommendations, such as development and progression of myopia. We are currently examining a longitudinal dataset that will provide information on myopia in this population.

Finally, results of longitudinal analysis yielded significant effects in measurements of J0, but no significant effects of J45. These findings indicate that observed changes in corneal astigmatism are attributable mainly to changes in the magnitude of the J0 component. The findings that astigmatism is quite stable in this population once children reach 3 years of age and that the changes that do occur are primarily in the J0 component of astigmatism are valuable for clinical practice.
if future interventions, such as surgical interventions, are to be considered.

In a previous report, we observed that the cross-sectional prevalence of refractive astigmatism (right eye >2.00 D) was 30% in Tohono O’odham infants (6 months to <1 year of age), and was 23–29% at ages 2 through 7 years. However, prevalence was significantly lower (14%) in children 1 to <2 years of age. Thus, as in non-Native American populations, astigmatism decreases in the second year of life. In contrast, the prevalence of high astigmatism in Tohono O’odham children increases by age 2 years to a level near that seen in infancy and remains at that level until at least 8 years of age. A similar trend was observed in African American and Hispanic children: there was a significant decrease in prevalence of high astigmatism (>3.00 D) after infancy, and a subsequent increase through the preschool years, although the increase in prevalence observed did not reach the level seen in infancy as it did in Tohono O’odham children. In Tohono O’odham children prevalence of corneal astigmatism >2.00 D was found to be lower in the 1 to <2-year-old age group when compared with all other age groups through age 7 years, except the 6 to <7-year-old group, similar to the pattern seen with refractive astigmatism. The presence of this pattern of decreased prevalence in corneal astigmatism in the 1 to <2 year age range data confirmed that, as found in previous reports, astigmatism arises primarily from the anterior cornea in Tohono O’odham children.

The present longitudinal analysis provided some interesting insights into the cause of the unexpected pattern we observed in cross-sectional data from this population, i.e., the decrease in prevalence in the 1 to <2 year age range. The longitudinal analysis focused only on children aged 6 months through 2 years and suggests that the pattern of results observed in the cross-sectional data resulted from a combination of different developmental patterns observed in infants with high vs low/moderate astigmatism. Specifically, infants with high astigmatism in infancy tended to show reduced astigmatism in the second year of life (similar to that seen in other populations), whereas infants with low to moderate astigmatism in infancy tended to remain stable in the second year of life, followed by a slight increase in the third year of life. Taken together, and viewed cross-sectionally, these patterns combine so that it appears that overall astigmatism decreases in the second year of life and then increases again. This result illustrates the importance of longitudinal data in understanding change in individuals.

The present study has a number of strengths, including the large sample size, the use of the same instrument to obtain measurements of corneal astigmatism across the entire age-range tested, identification and inclusion of only the highest quality keratometric images in analysis, and reduction in bias in measurements caused by changes in instrument calibration over time. However, there are also limitations in the present study, such as the limited generalizability of data to other populations. Similar studies with other racial and ethnic populations will be required in order to determine how well these data generalize to other populations.

In conclusion, longitudinal data from this population has allowed us to better evaluate and understand patterns of change in astigmatism observed in individual infants and children. These data also suggest that high astigmatism that we have previously observed in preschool and school-age Tohono O’odham children is likely to have been present from infancy, and persist through critical early stages of visual development. While previous research has suggested that Tohono O’odham children with high astigmatism show, on average, significantly reduced best-corrected visual acuity, suggesting the presence of amblyopia, it also seems likely that this form of persistent visual degradation from such an early age may have more subtle effects on visual performance. Additional research on other aspects of visual performance, such as perception of form, motion, and reading, are currently underway.

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DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

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