Refractive and Biometric Status of Children Born Premature without Retinopathy of Prematurity
(Status Refraksi dan Biometri Kanak-kanak Dilahirkan Pramatang Tanpa Retinopati Pramatang)

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ABSTRACT
A cross-sectional study was undertaken to determine the refractive and biometric status of premature children without Retinopathy of Prematurity (ROP) and full term children. Fifty eight children between the ages of 3 and 7 years (32 children born premature without ROP and another 26 children born full term and normal) were examined. Refractive error, corneal curvature, axial length, anterior chamber depth and crystalline lens thickness were determined. The results revealed that children between the age of 3 and 7 years were emmetropic, irrespective of whether they were born premature without ROP or full term. However, children born premature without ROP had significantly steeper corneas ($t = 3.14, p = 0.0349$), shorter axial lengths ($t = 3.18, p = 0.0313$) and thicker crystalline lens ($t = 3.31, p = 0.0256$) compared to children born full term within the same age group. This study suggests that compensation in ocular parameters can occur to maintain emmetropia, mainly by adjustment of axial length and corneal curvature.

Keywords: Axial length; corneal curvature; crystalline lens thickness; premature without retinopathy of prematurity; refractive error

INTRODUCTION
Refractive errors are common in the neonatal period following full term and preterm birth. Full term infants usually have hyperopia and astigmatism which reduces rapidly during the first year of life (Saunders et al. 2002). This process of emmetropisation was found to be complete in 82% of full term infants by 12 months of age (Ingram et al. 1991).

Some studies have reported that premature infants who do not develop ROP demonstrate a normal pattern of refractive development (Fledelius 1996a; Pennefather et al. 1997; Saw & Chew 1997). Other studies have shown that there is an increase risk of developing significant refractive errors particularly myopia among these premature infants without ROP (Fledelius 1996b).

The underlying mechanism for the increased incidence of myopia in premature children is not well understood. It has been suggested that myopia is probably the normal refractive state in infants before full term with the eye becoming more hyperopic in early infancy (Fledelius 1992). Compared with the eye of the full term baby, this type of myopia (myopia of prematurity) has been shown to have steeper corneas (Cook et al. 2003; Fledelius 1992, 1996), shorter axial length, shallow anterior chamber and thick crystalline lens (Fledelius 1992). Other studies have found that axial length measurements do not differ much in children born premature without ROP and those born full term (Koraszewska-Matuszewska et al. 1993; Zadnik et al. 1993). Crystalline lens thickness has also been shown to be almost the same for children born premature or full term.
(Garner et al. 1995; Zadnik et al. 1993). The hallmark of myopia of prematurity is the arrested development of the ocular anterior segment (Fledelius 1981).

Previous studies have reported different patterns of development of refractive error among premature infants without retinopathy. Differences in refractive error found in children born prematurely without ROP from previous studies could be due to differences in study design, for example age of patients, methods used and gestational ages. Although similar data is available from studies done overseas, no data is available from the local Malaysian population. Knowing the pattern of refractive development of infants born premature without retinopathy would help the clinician in the management of visual status of the premature children.

In children born full term, it has been shown that emmetropisation occurs by the age of 1 year (Ingram et al. 1991). It has also been shown that myopia tends to develop and progress in children born full term after the age of 7 years (Jobke et al. 2008; Robinson 1999; Twelker et al. 2009). The onset of myopia after the age of 7 years is more likely to be associated with near work. Therefore between the ages of 3 and 7 years, all the ocular components develop is well coordinated to maintain emmetropia in normal full term children. Some studies have shown that premature children without ROP may have a normal pattern of development, while other researchers have shown that some premature children without ROP have myopia. Although the premature eyes are smaller (having shorter axial length), myopia can be expected if the other ocular components (like the corneal curvature, anterior chamber depth, and crystalline lens thickness) development did not compensate for the shorter axial length (or emmetropisation did not occur).

The aim of the present study was to determine the refractive and biometry status of children born premature without ROP and children born full term of between 3 and 7 years of age.

MATERIALS AND METHODS

SUBJECTS

Two groups of Malay children between 3 and 7 years were investigated. One group consisted of children born premature and the second group consisted of those born full term. The recruitment of all subjects was on voluntary basis. The inclusion criteria for children born premature were gestation period of 28 to 32 weeks, birth weight below 2.0 kg, no ROP and other systemic or ocular complications. In the case of full term infants, the inclusion criteria were gestation period of 36 weeks or more, birth weight of greater than 2.0 kg, and no other systemic or ocular complications.

Thirty-two children born premature without retinopathy of prematurity (ROP) were examined. The children were recruited from the Pediatric Clinic at Universiti Kebangsaan Malaysia (UKM). These children were born at the Kuala Lumpur Maternity Hospital and had been on follow-up at the UKM Pediatric Clinic since birth. These children were confirmed not to have any retinopathy of prematurity or its signs by the pediatric ophthalmologist since birth.

Another group of twenty-six children who were born full term were also examined. The mean age of these children were matched with the mean age of those born premature without ROP. The children were recruited from the Pediatric Clinic at UKM and from kindergartens around Kuala Lumpur. These children also had no reported ocular problems or any neurological disorders.

Prior to participation in the study, written informed consent was obtained from all parents. Approval from the Research Committee of the Faculty of Allied Health Sciences, Universiti Kebangsaan Malaysia was obtained, which also looked into the ethical aspects of the study.

LOCATION OF EXAMINATION

All optometric examinations were conducted at the Optometry Clinic, Universiti Kebangsaan Malaysia.

METHOD

All optometric examinations were performed by the same examiner. Visual acuity was first measured using either a Snellen chart or a Sheridan Gardiner chart. Distance static retinoscopy was performed using a Neitz streak retinoscope. In static retinoscopy, the refractive state is determined while the patient fixates a distance object (to relax accommodation). This would reveal the refractive error subjectively. A working lens of +1.50D (for a working distance of 67 cm) was placed in a trial frame and the child asked to fixate a spot light at a distance of 6 m. Refractive error was then determined by observing and neutralising the movement of the reflex.

This was followed by cycloplegic refraction using 1% cyclopentolate. Cycloplegic refraction was performed in order to reveal the full refractive error. This was followed by measurement of corneal curvature and refraction with a Nikon Auto Ref Keratometer NRK-8000. Lastly, axial length, anterior chamber depth and crystalline lens thickness was determined using the Teknar Ophthasonic A-Scan III. Before subject data was collected, repeatability and validity of the Nikon Auto Ref Keratometer NRK-8000 was done. It was found that the Nikon Auto Ref Keratometer NRK-8000 has good repeatability (r = 0.9458) and good validity (r = 0.9755) when compared to subjective refraction. All measurements were performed on the right eye only.

RESULTS

All analysis was done using the unpaired t-test. Table 1 shows the parameters measured in the two study groups. It can be seen that the mean age of children in the two groups are similar and statistically not significantly
different. Similarly, the visual acuity in decimal of both groups was 0.9 (equivalent to almost 6/6 Snellen acuity). Noncycloplegic and cycloplegic refraction also shows no statistically significant difference. The refraction data shown is the mean spherical equivalent. Similarly, anterior chamber depth shows no statistically significant difference between the two groups. The only statistically significant difference is in the crystalline lens thickness, axial length and corneal curvature. Premature children without ROP have thicker crystalline lenses, shorter axial lengths and steeper cornea compared to children born full term and normal.

**DISCUSSION**

This study showed that children born full term and premature without ROP between the ages of 3 and 7 years are emmetropic. However, premature children without ROP have thicker crystalline lenses, shorter axial lengths and steeper cornea compared to children born full term and normal.

Several longitudinal studies on full term infants show that eye refraction changes with age and there is a trend towards emmetropia (Ehrlich et al. 1995; Wood et al. 1995). This is also seen in the present study.

However, there are conflicting reports in premature infants. Some report that premature infants are generally hyperopic (Cook et al. 2003; Ton et al. 2004), and many of them subsequently become myopic (Page et al. 1993). However, some researchers report myopia, astigmatism and anisometropia as a common finding in premature children in the first few months of life, because of failure of emmetropisation (Fledelius 1992; Laws et al. 1992; Rodriguez et al. 1996). Shapiro et al. (1980) failed to find a significant change in refraction or a trend toward emmetropia in premature children aged between 6 months and 3.5 years. A study by Saunders et al. (2002) has shown that infants born prematurely without ROP achieve emmetropisation by 6 months of age. The authors suggest that in the absence of ROP the emmetropisation process is often able to correct the abnormal refractive errors associated with preterm birth. The present study is in agreement with the results of Saunders et al. (2002).

For children between the ages of 3 and 7 years, corneal curvature is significantly steeper in children born premature without ROP compared to those born full term. These children also have significantly shorter axial lengths and significantly thicker crystalline lens. Axial length to corneal radius of curvature ratio (AL/CR) was determined as shown by Grosvenor and Scott (1994). It was found that the AL/CR ratio for children born premature without ROP and children born full term was 2.90. Grosvenor and Scott (1994) have shown that if the AL/CR ratio is close to 3.00, this shows that the eye tends to be emmetropic. A steeper cornea, thicker crystalline lens but a shorter axial length shows that there is coordinated eye growth to maintain emmetropia. This is also consistent with Atkinson et al. (1996) notion that there is coordinated growth of the eye.

The results of this study show that in children born fullterm and premature without ROP, emmetropisation probably occurred to maintain emmetropia. It was also seen that premature children without ROP between the ages of 3 and 7 years, had steeper corneas, thicker crystalline lens but shorter axial lengths compared to children born full term in the same age group. The shorter axial length probably compensated for the steeper corneal curvature and thicker crystalline lens by way of coordinated eye growth to maintain emmetropia in premature children without ROP. The results from this study are in agreement with other studies. Since emmetropisation does occur in premature children without ROP and children born full term, the mechanism and trend of refractive error development is probably similar. Clinicians managing refractive error of children whether born premature without ROP or full term have to look out for and be vigilant about genetical and environmental factors that might contribute to refractive error development.

**TABLE 1. Comparison of measured parameters in children born prematurely without ROP and born full term between the age of 3 and 7 years**

<table>
<thead>
<tr>
<th>Tested parameters</th>
<th>Premature without ROP (mean ± SD) (n=32)</th>
<th>Full term and normal (mean ± SD) (n=26)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual acuity (decimal)</td>
<td>0.900 ± 0.138</td>
<td>0.899 ± 0.124</td>
<td>0.942</td>
</tr>
<tr>
<td>Age (years)</td>
<td>5.23 ± 0.94</td>
<td>5.71 ± 1.46</td>
<td>0.1570</td>
</tr>
<tr>
<td>Noncycloplegic retinoscopy (D)</td>
<td>-0.02 ± 0.51</td>
<td>+0.09 ± 0.88</td>
<td>0.5910</td>
</tr>
<tr>
<td>Cycloplegic refraction (D)</td>
<td>+0.03 ± 0.72</td>
<td>+0.06 ± 0.74</td>
<td>0.8522</td>
</tr>
<tr>
<td>Anterior chamber depth (mm)</td>
<td>3.32 ± 0.50</td>
<td>3.50 ± 0.38</td>
<td>0.1320</td>
</tr>
<tr>
<td>Crystalline lens thickness (mm)</td>
<td>3.61 ± 0.18</td>
<td>3.41 ± 0.41</td>
<td>0.0230*</td>
</tr>
<tr>
<td>Axial length (mm)</td>
<td>21.85 ± 0.76</td>
<td>22.32 ± 0.88</td>
<td>0.0350*</td>
</tr>
<tr>
<td>Corneal curvature (mm)</td>
<td>7.58 ± 0.27</td>
<td>7.74 ± 0.30</td>
<td>0.0360*</td>
</tr>
</tbody>
</table>

* statistically significantly different using the unpaired t-test.
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REFERENCES


