Optic Disk Size and Optic Disk-to-Fovea Distance in Preterm and Full-Term Infants

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Purpose. Few studies have assessed optic disk and retinal morphology in infants. Here the optic disk and optic disk-to-fovea distance were measured in preterm and full-term infants in vivo.

Methods. Optic disk (OD) dimensions and the center-to-center distance between the OD and the macula were measured using digital imaging in infants undergoing routine ophthalmic examinations. Postmenstrual age of the mother at the time of examination ranged from 32 to 50 weeks. From each image, the OD-to-fovea distance (ODF) and the OD height (ODH) and OD width (ODW) were measured.

Results. In 51 retinal images from 51 infants, mean ± SD values obtained were 4.4 ± 0.4 mm (ODF), 1.41 ± 0.1 9 mm (ODH), and 1.05 ± 0.13 mm (ODW). These dimensions did not change significantly over the age range studied. The mean value for the ratio between ODF and mean OD diameter (ODF/DD) was 3.76.

Conclusions. Results of this in vivo study suggest that though the optic nerve head diameter increases by more than 50%, only limited growth occurs at the highly organized area of the posterior pole from birth to adulthood. This study discusses the finding of a large-angle kappa in infants and the use of a disk macula/disk diameter ratio in the diagnosis of optic nerve hypoplasia. (*Invest Ophthalmol Vis Sci.* 2006;47:4683–4686) DOI:10.1167/iovs.06-0152

Until recently, in vivo assessment of the optic nerve head and its relationship to the fovea has not been possible during infancy, when the eye is growing particularly rapidly. The few measurements that have been obtained have come from postmortem studies.[1] The latter are subject to shrinkage artifact, and measurements are underestimated by more than 10%.[1] Recently developed digital imaging that permits the sequential imaging of the posterior pole has opened new opportunities for the investigation of developmental changes in optic disk and macula during infancy.[2,3]

Studies to date have suggested that during ocular growth, the distance between the optic disk and the macula grows disproportionately less than the overall increase in globe dimension.[4,5] With the use of digital imaging, we undertook an in vivo study in infants to measure optic disk size and its distance from the fovea.

Materials and Methods

Digital fundus images were selected randomly from infants undergoing routine screening for retinopathy of prematurity and larger infants assessed for other clinical indications at St. Mary's Hospital (London, UK). The 80° or 130° lens of a digital fundus camera was used (RetCam; Massie Laboratories, Dublin, CA). Images contained no patient-identifiable information of any nature at any time, and the study was performed in accordance with the tenets of the Declaration of Helsinki II. Eyes with congenital abnormalities, retinopathy of prematurity, and intraocular inflammation were excluded from all analyses.

All infants were examined in the neonatal intensive care unit. Infants' pupils were dilated with 2.5% phenylephrine and 0.5% cyclopentolate eye drops. Before examination, topical anesthesia (proxymetacaine 0.4%) was instilled in both eyes, and an eyelid speculum used. Contact lens coupling fluid (Viscotears; Novartis, Basel, Switzerland) was applied to the cornea, and the camera lens was placed on it.

Images were analyzed with software (Paint Shop Pro version 7.02; www.jasc.com). For each image, the macula was identified by Isenberg's five stages of macular development, as follows: 0, no pigmentation; 1, pigmentation of the macula; 2, partial annular reflex; 3, complete annular reflex; 4, foveolar pit; 5, foveolar light reflex.[6] Images that were out of focus, decentralized, or without a discernible macula were not used (43 macula images were used).

Points were marked at the superior, inferior, nasal, and temporal edges of the OD and of the macula (Fig. 1). Distances between them, measured in pixels, were calculated using the Pythagorean theory (neglecting any distortion caused by the projection of the camera). Optic disk height (ODH) was measured using the distance between the superior and inferior points on the disk, and optic disk width (ODW) was measured using the temporal and nasal points. The position of the center of the optic disk was calculated as the mean of the four points marked on the perimeter. The position of the fovea was calculated in the same way using the points on the perimeter of the macula. The optic disk center to fovea (ODF) distance could then be measured.

The optic disk was defined by the inner border of the scleral rim surrounding the nerve tissue. Conversion from pixels to millimeters was based on the manufacturer's calibration of 0.03 mm/pixel for a 130° field-of-view lens scaled appropriately for the field widths of lenses used in the present study: 0.0176 mm/pixel (80° lens) and 0.0306 mm/pixel (130° lens; RetCam; Massie Laboratories). In adult eyes, the correction can be applied to correct optic disk measurements for refractive error when the parameters of axial length, keratometry, and ametropia are known.[7–9] In infants these calculation are more challenging because gaining the aforementioned measurements is difficult and the eye is continuing to grow. Although assumptions are made to calculate optic disk measurements— globe diameter, radius of geometric center to retinal surface, angle subtended from fovea to optic disk—the quantitative differences in optic disk measurements from independent studies has not been solely attributed to calibration factors.[10]

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Submitted for publication February 9, 2006; revised April 26 and June 6, 2006; accepted September 11, 2006.

Disclosure: **D.J. De Silva**, None; **K.D. Cocker**, None; **G. Lau**, None; **S.T. Clay**, None; **A.R. Fielder**, None; **M.J. Moseley**, None

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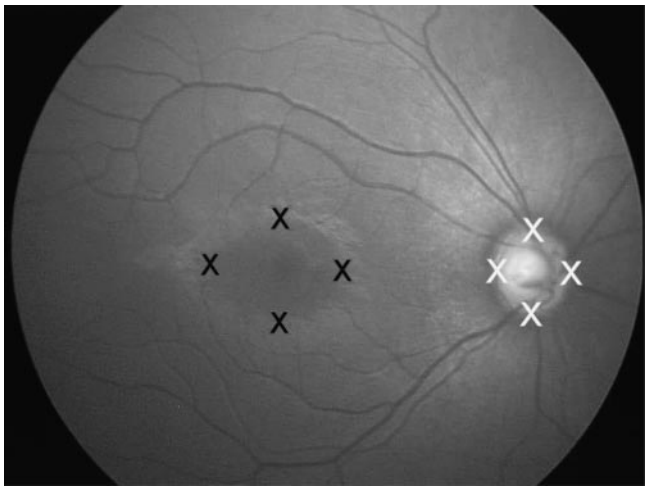

FIGURE 1. Fundus photograph using a digital fundus camera (Retcam 130) with markers denoting superior, inferior, nasal, and temporal points of the disk and macula.

RESULTS

Fifty-one images of left and right eyes from 51 infants were assessed. Of the infants, 55% (28) were boys and 45% (23) were girls. Only one eye was included for each infant, and the best-quality image was selected from right and left eyes. Mean gestational age was 30.1 ± 4.7 weeks (range, 23–40 weeks), and mean birthweight was 1153 ± 470 g (range, 440-3050 g). Mean postmenstrual age of the mother at measurement was 37.3 ± 3.3 weeks (range, 32.2–48.9 weeks).

Mean ± SD values obtained were: ODH, 1.41 ± 0.19 mm; ODW, 1.05 ± 0.13; ODF, 4.4 ± 0.4 mm (Figures 2–4). Longitudinal measurements were obtained from a subset of eight infants; dimensions did not change significantly over the age range studied (9 weeks). The mean value for the ratio between ODF and mean OD diameter (ODF/DD) was 3.76. A summary of the results, including Isenberg's stage of macular development and optic disk appearance, are shown in Table 1. The "indistinct" disk margin refers to a change at the optic disk rim that did not represent a scleral ring or a double-ring sign. These changes might have represented other disk morphology, such as tilted disks.

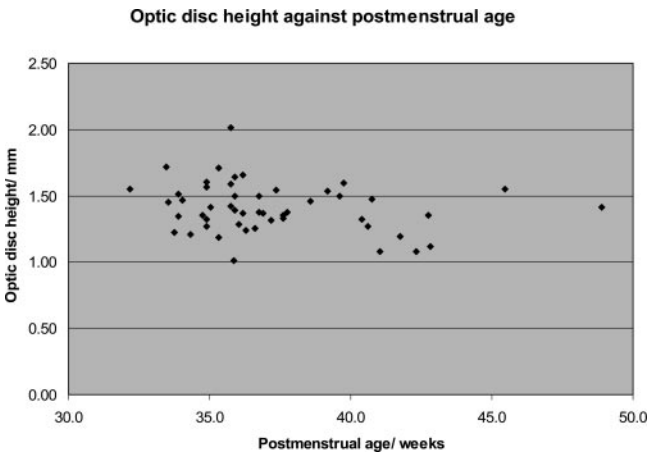

FIGURE 2. Optic disk height as a function of postmenstrual age.

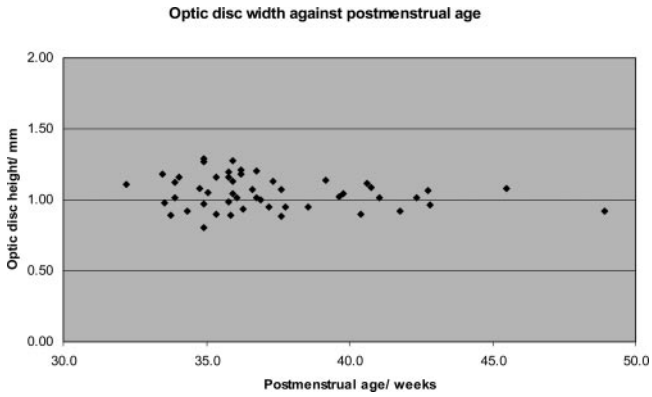

FIGURE 3. Optic disk width as a function of postmenstrual age.

DISCUSSION

We undertook an in vivo imaging study to assess dimensions of the optic disk and fovea in the infant. To date, few studies have assessed optic disk and macular morphology in infants, and those undertaken have been subject to artifacts arising from postmortem fixation.[1,6]

A random selection of infants undergoing screening for retinopathy of prematurity was assessed. Many of these infants were born prematurely and weighed less than 1.5 kg. It is unknown whether the development of the optic disk and macula in these infants was normal.

Previous studies assessing the dimensions of the optic disk and fovea in the infant include a postmortem study of the optic disk,[1] subjective observation of the posterior pole,[6] the use of digital neonatal fundus photographs,[11] and the use of digitized photographic images from older children who were born before term.[2,3] Table 2 summarizes reports of optic disk measurements in infants to date. Rimmer et al.[1] reported in postmortem infants younger than 40 weeks' gestation optic disk heights of 1.10 ± 0.21 mm and widths of 0.93 ± 0.15 mm. These measurements were taken from formalin-fixed eyes that had been collected over a 20-year period. Our results are consistent with these findings and take into account an estimated 13% nerve shrinkage induced by fixation. Measurements of optic disk height and width from clinical studies are larger than those of postmortem studies. Nerve shrinkage induced by fixation, a white flange of scleral tissue at the disk rim, and

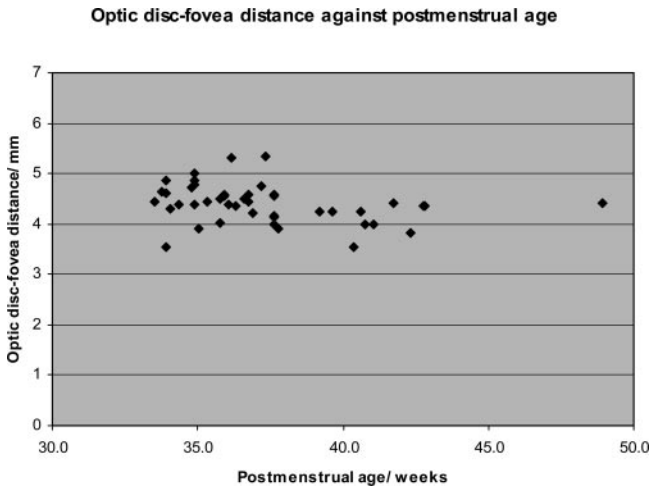

FIGURE 4. Optic disk-to-fovea distance as a function of postmenstrual age.

TABLE 1. Stage of Macular Development and Optic Disk Appearance

	Mean PMA, wk (range)	Mean Birth Weight, kg (range)	No. of Eyes (%)
Stage of macular development[6]			
0 = No pigmentation	0	0	0
1 = Pigmentation of the macula	36.1	0.750	1 (2.3)
2 = Partial annular reflex	36.0 (34.3–40.7)	0.993 (0.660–1.410)	10 (23.3)
3 = Complete annular reflex	36.4 (33.6–42.4)	1.231 (0.650–2.000)	18 (41.8)
4 = Foveolar pit	39.4 (34.9–48.9)	1.165 (0.440–3.050)	14 (32.6)
5 = Foveolar light reflex	0	0	0
Total	37.3 ± 3.3 (32.2–48.9)	1.153 ± 0.466 (0.440–3.050)	43
Optic disk appearance			
Scleral rim	37.7 (33.7–48.9)	1.193 (0.440–3.050)	12 (23.5)
No scleral rim	36.7 (33.6–41.7)	1.118 (0.660–1.410)	8 (15.7)
Double ring sign	36.9 (33.7–44.9)	1.091 (0.650–1.091)	15 (29.4)
Indistinct	—	—	16 (31.4)
Total	37.3 ± 3.3 (32.2–48.9)	1.153 ± 0.466 (0.440–3.050)	51

PMA, postmenstrual age.

magnification factors used to calculate disk size have been proposed to explain this discrepancy.[12] The scleral rim was excluded in our measurements of the optic disk.

Hellström et al.[2] assessed optic disk area, cup, and retinal vessels of children at 4.8 to 6.1 years who were born earlier than 29 weeks' gestation and reported morphologies different from those in full-term infants. These differences included small optic disk area, small optic disk rim, and increased tortuosity of the retinal arteries independent of retinopathy of prematurity.

Published measurements of adult optic disk dimensions indicate a height of 1.88 ± 0.19 mm and a width of 1.77 ± 0.19 mm.[12] Quigley's measurements[12] were taken from postmortem eyes fixed in formaldehyde. These values are 51% greater than those found in this study, suggesting that optic nerve size increases after birth. Although our infants were mildly premature at examination, on average 37.4 ± 3.2 postmenstrual weeks, the measurements suggest a significant increase in optic disk diameter from birth to adulthood. Proposed mechanisms for the change in optic disk size include increases of neural elements, increases in ganglion axon size, and myelination of the optic nerve fibers.[13]

Most maculae were identified by the presence of an annular ring reflex (65.1%) or a foveolar pit (32.6%) (Table 1), and the appearance of the maculae was consistent with Isenberg's stages of development.[6] In the present study, we found a mean ODF of 4.4 ± 0.4 mm at a mean postmenstrual age of 38 weeks. With digitized photographic fundus images, William and Wilkinson[4] recorded a mean ODF of 4.9 ± 0.3 mm in adults. The increase in ODF distance from 4.4 mm to 4.9 mm from infancy to adulthood corresponds to an increase of 11%. In contrast, the increase in axial length from approximately 16 mm at full term to 23 mm in adulthood represents an increase of 44%.[5,14–16] However, the present study finds that ODF values increase by only 11% from infancy to adulthood, indicating proportionally less growth at the macular region. This is in agreement with the notion that most growth in the globe occurs in the equatorial region and that growth in the highly organized and visually critical region of the central retina is kept to a minimum.[15,17,18]

Although a number of studies have reported a high prevalence of exotropia in infants,[19–21] subsequent evidence has suggested this to be pseudotropia, resulting from a large-angle kappa.[22–24] One study reported a proportion of approximately 50% of exotropia in photographs of infants younger than 1 year; however, after correction for angle kappa, no eyes had true exotropia.[24] Angle kappa is defined as the angle between the pupillary axis and the visual axis, and it has been proposed that a large-angle kappa in infants is secondary to the temporal location of the fovea. However, our results offer an alternative hypothesis. We found a relatively large ODF distance in the newborn infant relative to the size of the eyeball. Most eyeball growth occurs anterior to the posterior pole. As the infant grows, the eyeball enlarges anteriorly, angle kappa is reduced, and the resultant pseudoexotropia diminishes.

Optic nerve hypoplasia (ONH) is a developmental anomaly of the optic nerve resulting in a reduced number of axons. Diagnosis may be made on the appearance of the optic disk as a ring of hypopigmentation and hyperpigmentation, described as the double-ring sign. In our study, a high proportion of eyes

TABLE 2. Summary of Optic Disk Measurements in Infants

Investigators	Type of Study	Mean Age at Examination (range)	Gestational Age (wk)	No. of Eyes	Horizontal Disk Diameter (mm)	Vertical Disk Diameter (mm)	Mean Disk Area (mm^2)
Rimmer et al.[1]	Postmortem	—	<40	20	0.93 ± 0.15	1.10 ± 0.21	0.82 ± 0.26
Hellström et al.[2]	Digital photographs	7 y (5.1–9.3)	27	50	Descriptive analysis	—	—
Hellström et al.[3]*	Digital photographs	4.8 y (3.1–9.1)	29.1	39	—	—	2.80 ± 0.46
Present study	In vivo digital photographs	2 wk (1–9)	30.1 ± 4.7	51	1.05 ± 0.13	1.41 ± 0.19	1.17 ± 0.26

* Data extrapolated from the assessment of preterm children.

was found to have the double-ring sign (23%; Table 1), suggesting that this appearance may be a normal stage of disk development. After birth, the optic disk enlarges by another 50% to reach adult proportions, and we hypothesize the growth of the disk lessens or abolishes the double-ring sign and a reduction in disk growth, as in ONH, results in the preservation of the double-ring sign.

ONH is characterized by a spectrum of severity, and the optic disk may have an almost normal appearance.[25] A number of investigations have been proposed to aid the diagnosis of ONH. These include ultrasonography, axial tomography, electrophysiologic testing, and calculation of the disk macula/disk diameter ratio (DM/DD). Two studies proposed a threshold DM/DD for the diagnosis of OHN in children 2 years of age: in Alvarez et al.[26] it is ≥3.00, and in Barr et al.[25] it is ≥3.70. In our study, the DM/DD ratio was 3.76 in healthy infants, higher than the threshold values suggested for the diagnosis of ONH. Our findings suggest substantial growth—51%— of the optic disk between term and adulthood in contrast to the ODF, which increases 11%. This suggests the DM/DD ratio will be high in the neonatal period in most healthy persons. If normal growth fails to occur, a high DM/DD ratio will result, consistent with a diagnosis of ONH.

This in vivo study of optic disk size and disk-to-macula distance in infants suggests that though the optic nerve head diameter increases by more than 50%, only limited growth occurs at the highly organized area of the posterior pole from birth to adulthood.

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