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CLINICAL STUDY

RetCam image analysis of the optic disc in premature infants

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Abstract

Purpose **To evaluate the correlation between optic disc parameters and birth weight or gestational age in premature infants.**

Methods **RetCam fundal images were taken of 97 premature infants who needed screening for retinopathy of prematurity and who had no ischemic brain injury. The images were taken at a postmenstrual age of 36 weeks and analyzed. The optic disc cup to disc ratio, optic disc area, rim area, and cup to disc area ratio were calculated using image analysis. We evaluated the relationship between these optic disc parameters and gestational age or birth weight.**

Results **The optic cup to disc ratio was less than 0.15 in 139 eyes (71.6%) and 0.5 or more in six eyes (3.1%). The optic cup disc area ratio was less than 0.05 in 146 eyes (75.3%) and 0.3 or more in four eyes (2.1%). On evaluating the association between optic disc parameters and gestational age or birth weight, optic disc cup to disc ratio, optic disc area, rim area, and cup to disc area ratio did not show significant relationships.**

Conclusion **The optic disc parameters of premature infants had no correlation with birth weight and gestational age.**

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Keywords: birth weight; gestational age; optic nerve head; premature infant

Introduction

Glaucoma is known as the second leading cause of blindness and visual impairment globally and is the major cause of blindness in both eyes in some groups.[1,2] Evaluation of the optic disc shape is important for early diagnosis and for assessing the progression of glaucoma.[3] Therefore, many studies have been conducted that predict changes in optic disc shape in glaucoma and reveal the factors affecting these changes.

Some studies have demonstrated a difference between the optic disc shape of low birth weight premature babies and that of full-term babies. Reports have also shown that infants of low birth weight and low gestational age tend to have a significantly large cup to disc (CD) ratio as older children.[4–6] By analyzing the optic disc shape of children approximately 12 years of age, a recent study showed that intrauterine growth retardation in premature babies affects the increase in CD ratio, which can be a risk factor for glaucomatous optic nerve change.[7] Other studies reported that the CD ratio significantly increased in premature babies with ischemic brain lesions compared with normal babies.[8–10] These studies show that the optic disc shape can change because of several factors at birth. However, there are limitations in the previous studies investigating the relationship of optic disc shape and premature infants, because most of these have examined the optic disc shape in children approximately 10 years of age.

In this study, an attempt was made to photograph and analyze the optic disc parameters during screening for retinopathy of prematurity (ROP) in premature infants using a digital fundus camera. We also analyzed the relationship between optic disc parameters and birth weight or gestational age in premature infants.

Materials and methods

Digital fundus images of premature infants undergoing routine screening for ROP at Chonnam National University Hospital from October 2008 to December 2010 were studied. All infants were examined in the neonatal intensive care unit. The pupils were dilated with cyclopentolate 0.2% and phenylephrine

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1%, instilled 30–45 min before screening. Proparacaine 0.5% was instilled before examination. After routine screening for ROP with an indirect ophthalmoscope, digital fundus images of the optic nerve head in both eyes were taken with an 80-degree lens using a digital fundus camera (RetCam Clarity Medical Systems Inc, Pleasanton, CA, USA). The images of the optic nerve head at postmenstrual age (PMA) of 36 weeks were then analyzed. Premature infants with ischemic brain lesions were excluded.

The images taken were analyzed with Image J software (National Institutes of Health, Bethesda, MD, USA). The boundary of the optic disc and cup in each picture was marked by carefully delineating their outlines with a cursor, and the vertical optic disc CD ratio was then calculated by measuring the distance between the upper and lower poles of the disc and the cup boundary in pixels. The optic disc area, rim area, and CD area ratio were calculated using image analysis.[8] Conversion of the figure measurement from pixels to mm was carried out according to the formula presented in a previous study, and 0.0176 mm/pixel was applied to the 80-degree lens used in this study; twisting or distortion of pictures which can be caused by a camera were ignored.[8,11]

Gestational age and birth weight were investigated retrospectively using medical records. We evaluated the relationship of the optic CD ratio, CD area ratio, the disc area, and rim area with gestational age or birth weight. Further, because Plus disease (dilatation and tortuosity of retinal arteries and veins on the optic nerve head) in ROP can obscure and underestimate the optic CD ratio, the subjects were divided into two groups according to the presence of pre-plus or Plus disease. Group 1 had no pre-plus and Plus disease with or without ROP, whereas Group 2 had pre-plus or Plus disease with ROP.[12]

This study was approved by the Chonnam National University Hospital institutional review board, and the research adhered to the tenets of the Declaration of Helsinki.

For statistical analysis, the result was tested using an independent *t*-test and Spearman's correlation using SPSS Version 17.0 (SPSS Inc., Chicago, IL, USA); a *P*-value less than 0.05 was considered significant.

Results

A total of 194 images of the left and right eyes of 97 infants (47 male and 50 female) were assessed. The mean gestational age was 30.3 ± 2.8 weeks (range, 26.1–35.7 weeks) and the mean birth weight was 1475.7 ± 480.3 g (range, 770–2480 g). The mean PMA at which digital fundus images were taken was 36.1 ± 1.1 weeks (range, 35.3–36.6 weeks).

Among all the infants studied, the optic CD ratio was less than 0.15 in 139 eyes (71.6%) and 0.5 or more in 6 eyes (3.1%). The optic cup disc area ratio was less than 0.05 in 146 eyes (75.3%) and 0.3 or more in 4 eyes (2.1%) (Figure 1).

We found that 116 eyes of 58 infants had no pre-plus and Plus disease (group 1) and 78 eyes of 39 infants had pre-plus or plus disease with ROP (group 2). Gestational age and birth weight were 30.9 ± 2.8 weeks and 1560.0 ± 473.9 g in group 1 and 29.3 ± 2.5 weeks and 1347.1 ± 464.2 g in group 2, respectively. There were statistically significant differences between groups ($P < 0.01$, $P < 0.01$). Between the two groups, the optic disc CD ratio (0.13 ± 0.13, 0.12 ± 0.12), optic disc CD area ratio (0.05 ± 0.08, 0.05 ± 0.07), optic disc area (1.10 ± 0.23 mm^2, 1.10 ± 0.22 mm^2), and rim area (0.95 ± 0.22 mm^2, 1.02 ± 0.21 mm^2) did not show significant differences (Table 1).

In the correlation between optic disc parameters and birth weight or gestational age, the relationships between optic disc CD ratio ($R = -0.02$, $P = 0.75$; $R = -0.07$, $P = 0.36$), CD area ratio ($R = -0.04$, $P = 0.63$, $R = -0.12$, $P = 0.08$), optic disc area ($R = -0.06$, $P = 0.43$; $R = -0.13$, $P = 0.08$), and rim area ($R = -0.09$, $P = 0.22$; $R = -0.01$, $P = 0.91$) were not significant (Figure 2).

Discussion

To date, most studies on optic disc shape have focused on glaucomatous optic nerve change in adult glaucoma

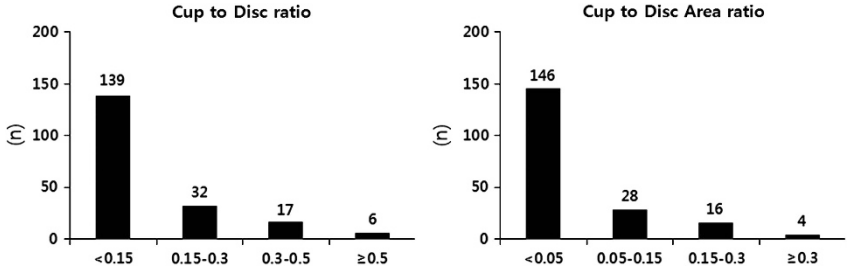

Figure 1 Distribution of premature infants by optic disc cup to disc ratio and cup to disc area ratio.

patients, as it is widely known that changes in optic disc shape are the characteristic findings of glaucoma.[3] However, few studies have been conducted on the optic disc shape of newborn babies because the examination is difficult, and a high-quality retinal image device for infants has been developed only recently. Therefore, many previous studies have analyzed the optic disc shape of children aged around 10 years and assessed the relationship between optic disc shape and gestational age or birth weight.[5–7,9,10] Fledelius[6] stated that the optic disc CD ratio was significantly larger in children with a birth weight of less than 2000 g than in full-term babies, but there was no significant difference between children with a birth weight less than 2000 g and those with a birth weight less than 1500 g. Hellstrom *et al*[4,5] reported that optic disc and rim area were significantly small in children around 7 years of age with an average premature birth of 27 weeks compared with full-term babies, but there was no difference between the two groups in optic disc CD area ratio. Recently, in a study on 12-year-old children, Samarawickrama *et al*[7] reported that the optic disc CD ratio of babies with intrauterine

Table 1 Patient demographics and comparisons of optic disc parameters between group 1 and group 2

	Total	*Group 1 (without pre-plus or plus)*	*Group 2 (with pre-plus or plus)*	P-*value*[a]
Number of eyes	194	116	78	
Gestational age (weeks)	30.3 ± 2.8	30.9 ± 2.8	29.3 ± 2.5	<0.01
Birth weight (g)	1475.7 ± 480.3	1560.3 ± 473.9	1347.1 ± 464.2	<0.01
Cup to disc ratio	0.13 ± 0.13	0.13 ± 0.13	0.12 ± 0.12	0.493
Cup to disc area ratio	0.05 ± 0.08	0.05 ± 0.08	0.05 ± 0.07	0.820
Disc area (mm^2)	1.10 ± 0.22	1.10 ± 0.23	1.10 ± 0.22	0.946
Rim area (mm^2)	0.98 ± 0.22	0.95 ± 0.22	1.02 ± 0.21	0.054

[a] Independent *t*-test.

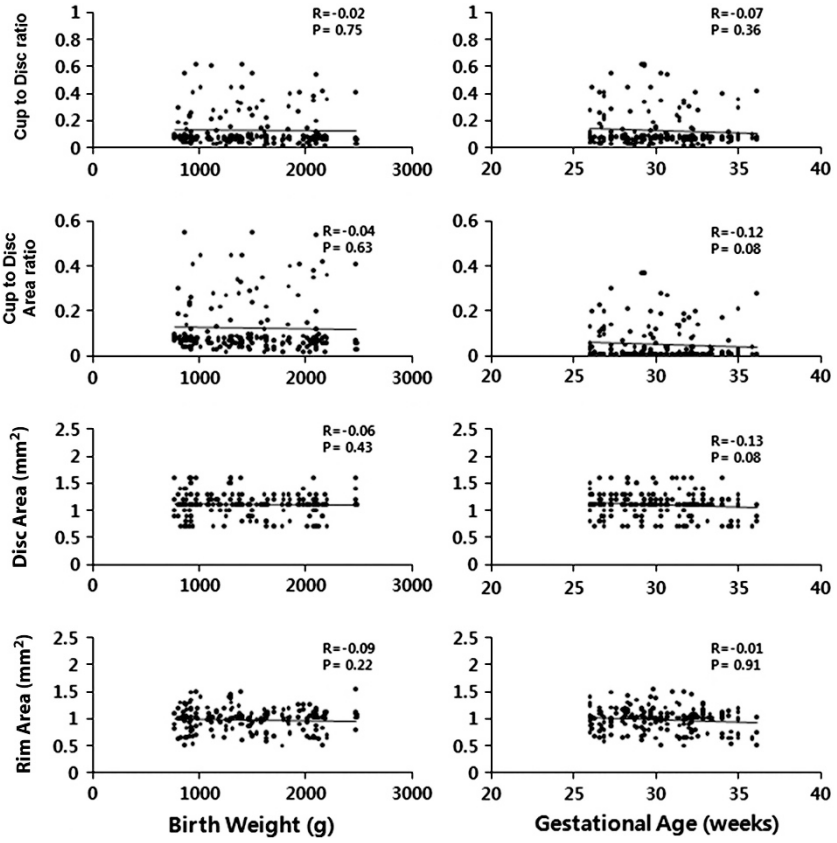

Figure 2 Relationship between optic disc parameters and birth weight and gestational age in premature infants.

growth retardation was significantly higher compared with the normal group, which meant that intrauterine growth retardation could be a future risk factor for glaucoma. Other studies reported that the optic disc CD ratio increased significantly in babies with an ischemic brain lesion.[9,10] However, these studies analyzed the optic disc shape of children older than 7 years and could not show the optic disc shape of newborn babies at that time.

Our study investigated only premature infants who needed screening for ROP. At a PMA of approximately 36 weeks, no difference was seen in optic disc measurements on the basis of gestational age or birth weight. We assumed that the dilatation and tortuosity of retina vessels on the optic disc due to Plus disease or pre-pus disease could result in an underestimation of the optic CD ratio. However, there were no differences in any optic disc parameters between premature infants with and without Plus disease or pre-plus disease. Recently, a study on optic disc measurements in full-term infants was reported.[13] The study suggested that there were no differences in optic disc measurements between male and female infants and between low birth weight and normal birth weight infants. A study on optic disc morphology in premature infants using Retcam was reported in February 2013.[14] They investigated the ratio of the vertical to the horizontal diameter, CD ratio, and the presence or absence of a double ring and concluded that the vertical–oval form of the optic disc in premature infants correlates with a low birth weight and low gestational age and that the double ring sign was frequently found in infant optic discs. Whereas their study focused only on the optic disc shape and double ring sign, our study investigated many parameters of the optic disc, including optic CD ratio, CD area ratio, disc area, and rim area.

According to the previous studies and our study, there was no influence of birth weight and gestational age on optic disc cupping and disc rim area, reflecting the number of ganglion cell axons in premature and full-term infants; however, among children aged approximately 10 years, those with a history of low birth weight and gestational age had an optic disc with a larger cupping and smaller rim area. We believe that this is due to the difference between the time of physiological ganglion cell axonal loss and optic disc maturation. Studies on the normal development of the human optic nerve suggest that at least 70% of ganglion cell axons generated during the development (16–32 weeks of gestation) of the primary visual pathway are lost during fetal life.[15] An autopsy study has shown that the growth of the normal optic disc and nerve is 50% complete at 20 weeks of gestation, 75% complete at birth, and 95% complete before 1 year.[16] This is also in accordance with the findings of other studies that showed an absence of increase in optic disc area with age in a group of healthy children aged between 2 and 10 years.[17] The full-term infant spends the last months of gestation in the relatively stable environment of the uterus, whereas the premature infant spends the corresponding time period in a markedly different environment, with altered functional and metabolic requirements. It has been suggested that interference with physiological ganglion cell axonal loss causes excessive elimination of axons,[18] whereas the optic disc size increases until about 2 years of age. Therefore, a premature baby with a lower gestational age and birth weight may have large optic disc cupping and a small disc rim area after 2 years of age.

Recently, a case of postnatal increase in optic disc cupping with periventricular leukomalacia was reported.[19] The male infant was born at 24 5/7 weeks' gestation. At 20 weeks of age, retinal examination showed a CD ratio of 0.4 in both eyes. At 15 months of age, retinal examination showed enlargement of the optic discs and an increased CD ratio of 0.6 in the right eye and 0.7 in the left eye. Periventricular leukomalcia induced retrograde trans-synaptic degeneration of retinogeniculate axons. Therefore, the baby showed a visible increase in optic disc cupping. Similarly, excessive physiological axonal loss in premature and low birth weight infants could induce an enlarged cupping after about 2 years of age.

From our study and previous studies, it can be assumed that there is no difference in optic disc shape according to birth weight or gestational age, but optic disc cupping can change after about 2 years of age when the optic disc has nearly reached its maximum size. Prospective studies analyzing long-term changes in optic disc could facilitate our understanding of the growth of optic disc and cupping.

A limitation of this study is the possibility of measurement bias due to refractive errors that could have influenced the measurements. There are still arguments about the necessity and method of correcting refractive myopia. A study reported that refractive myopia is not associated with magnification. However, another study demonstrated that correction of optic disc measurements on fundus photographs is needed.[8,20] The problem is that using magnification correction formulas that have been used generally for adults is not appropriate for premature infants. We believe that a new correction method is required for future studies on optic discs in premature infants in order to be more delicate and meticulous. Further, a follow-up study after a PMA of 36 weeks is needed for the evaluation of serial optic disc change.

In conclusion, we analyzed the optic parameters targeting premature infants of GA less than 36 weeks. The optic disc parameters of premature infants have no association with birth weight and gestational age.

Summary

What was known before

- Some studies have shown that low birth weight and low gestational age influence the shape of the optic disc in older children approximately 10 years of age.
- However, these studies could not show the optic disc shape of newborn babies at that time.

What this study adds

- We evaluated the optic disc parameters of premature infants at birth. Our study shows that there is no difference in the optic disc parameters of premature infants according to birth weight or gestational age.

Conflict of interest

The authors declare no conflict of interest.

References

1 Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. *Br J Ophthalmol* 2006; **90**: 262–267.
2 Kingman S. Glaucoma is second leading cause of blindness globally. *Bull World Health Organ* 2004; **82**: 887–888.
3 Jonas JB, Budde WM. Diagnosis and pathogenesis of glaucomatous optic neuropathy: morphological aspects. *Prog Retin Eye Res* 2000; **19**: 1–40.
4 Hellström A, Hård AL, Svensson E, Niklasson A. Ocular fundus abnormalities in children born before 29 weeks of gestation: a population-based study. *Eye (Lond)* 2000; **14**: 324–329.
5 Hellström A, Hård AL, Chen Y, Niklasson A, Albertsson-Wikland K. Ocular fundus morphology in preterm children. Influence of gestational age, birth size, perinatal morbidity, and postnatal growth. *Invest Ophthalmol Vis Sci* 1997; **38**: 1184–1192.
6 Fledelius H. Optic disc cupping and prematurity. Large cups as a possible low birth weight sequel. *Acta Ophthalmol (Copenh)* 1978; **56**: 563–573.
7 Samarawickrama C, Huynh SC, Liew G, Burlutsky G, Mitchell P. Birth weight and optic nerve head parameters. *Ophthalmology* 2009; **116**: 1112–1118.
8 McLoone E, O'Keefe M, Donoghue V, McLoone S, Horgan N, Lanigan B. RetCam image analysis of optic disc morphology in premature infants and its relation to ischaemic brain injury. *Br J Ophthalmol* 2006; **90**: 465–471.
9 Jacobson L, Hård A-L, Svensson E, Flodmark O, Hellström A. Optic disc morphology may reveal timing of insult in children with periventricular leucomalacia and/or periventricular haemorrhage. *Br J Ophthalmol* 2003; **87**: 1345–1349.
10 Jacobson L, Hellström A, Flodmark O. Large cups in normal-sized optic discs: a variant of optic nerve hypoplasia in children with periventricular leukomalacia. *Arch Ophthalmol* 1997; **115**: 1263–1269.
11 De Silva DJ, Cocker KD, Lau G, Clay ST, Fielder AR, Moseley MJ. Optic disk size and optic disk-to-fovea distance in preterm and full-term infants. Invest. *Ophthalmol Vis Sci* 2006; **47**: 4683–4686.
12 International Committee for the Classification of Retinopathy of Prematurity. The International Classification of Retinopathy of Prematurity revisited. *Arch Ophthalmol* 2005; **123**: 991–999.
13 Kandasamy Y, Smith R, Wright IMR, Hartley L. Optic disc measurements in full term infants. *Br J Ophthalmol* 2012; **96**: 662–664.
14 Hackl S, Zeman F, Helbig H, Oberacher-Velten IM. Optic disc morphology in premature infants. *Br J Ophthalmol* 2013; **97**: 314–317.
15 Provis JM, Van Driel D, Billson FA, Russell P. Human fetal optic nerve: overproduction and elimination of retinal axons during development. *J Comp Neurol* 1985; **238**: 92–100.
16 Rimmer S, Keating C, Chou T, Farb MD, Christenson PD, Foos RY *et al*. Growth of the human optic disk and nerve during gestation, childhood, and early adulthood. *Am J Ophthalmol* 1993; **116**: 748–753.
17 Mansour AM. Racial variation of optic disc parameters in children. *Ophthalmic Surg* 1992; **23**: 469–471.
18 Lambert SR, Hoyt CS, Narahara MH. Optic nerve hypoplasia. *Surv Ophthalmol* 1987; **32**: 1–9.
19 Longmuir SQ, Brodsky MC. Postnatal optic disc cupping in a non-glaucomatous infant with periventricular leukomalacia: nosologic implications. *Br J Ophthalmol* 2012; **96**: 606–607.
20 Pach J, Pennell DO, Romano PE. Optic disc photogrammetry: magnification factors for eye position, centration, and ametropias, refractive and axial; and their application in the diagnosis of optic nerve hypoplasia. *Ann Ophthalmol* 1989; **21**: 454–462.