Artigo Original

Evaluation of refractive status and optical components in eyes of school-aged children born prematurely

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RESUMO

Objectivos: Avaliar a função visual e determinar os fatores associados ao desenvolvimento de erros refrativos nas crianças em idade escolar que nasceram prematuramente.
Material e métodos: Foram incluídas 117 crianças com idade gestacional <37 semanas nascidas entre 1 de Janeiro de 2006 e 31 de Dezembro de 2007. Para análise estatística, foram divididas em grupos de acordo com a idade gestacional e peso ao nascimento (PN). Todas realizaram um exame oftalmológico completo e a medição dos componentes óticos.
Resultados: Não foi observado aumento estatisticamente significativo de erros refrativos nas crianças que nasceram mais prematuramente ($p>0.05$), embora o valor do equivalente esférico fosse maior para as crianças com PN <1500 g ($p=0.042$). Verificou-se maior número de casos de estrabismo nas crianças com PN <2000 g ($p=0.036$). Quanto aos componentes óticos, observou-se que as crianças mais prematuras tinham olhos com câmara anterior mais estreita, curvatura corneana maior e comprimento axial menor. Verificou-se ainda que a miopia nas crianças com PN <2000 g era causada por um aumento da curvatura corneana, enquanto naquelas com PN >2000 g se devia a um comprimento axial maior. As crianças com antecedentes de ROP tinham maior prevalência de erros refrativos quando comparadas com aquelas que não tiveram ROP ($p=0.004$).
Conclusões: As crianças que nasceram mais prematuramente e aquelas com história de ROP parecem apresentar um risco aumentado de desenvolver erros refrativos e estrabismo, que podem persistir ao longo da vida. Nestas crianças, o erro refrativo parece ser mais influenciado pela curvatura corneana do que pelo comprimento axial.

Palavras-chave
Prematuridade; baixo peso ao nascimento; erro refrativo; componentes óticos; retinopatia da prematuridade.

ABSTRACT

Purpose: To evaluate the visual function and determine the factors associated with the development of refractive errors in school-aged children born prematurely.
Material and methods: One hundred and seventeen children with gestational age less than 37 weeks that were born between 1 January 2006 and 31 December 2007 were included. For

statistical purpose, participants were divided into groups according to gestational age and birth weight (BW). All made a complete ophthalmic examination and measurement of optical components.

Results: There was no statistically significant increase of refractive errors in children born more prematurely (p>0.05), although the value of the spherical equivalent was greater for children with BW <1500g (p=0.042). It was observed a higher number of cases of strabismus in children with BW <2000 g (p=0.036). Regarding optical components, it was observed that infants born more prematurely had eyes with shallower anterior chamber, steeper corneal curvature and shorter axial length. It was also found that myopia in children with BW <2000g was caused by an increase of the corneal curvature, while in those with BW >2000 g was due to an increased axial length. Children with ROP had more prevalence of refractive errors compared with those without ROP (p=0.004).

Conclusions: Children born more prematurely and those with ROP appear to be at increased risk of developing refractive error and strabismus, which can persist throughout life. In these children, refractive error seems to be most affected by corneal curvature than by axial length.

Keywords

Prematurity; low birth weight; refractive error; optical components; retinopathy of prematurity.

INTRODUCTION

Advances in neonatology care and increasing survival rates have been associated with an increasing number of prematurely born infants[10]. Preterm birth can inflict a host of challenges on the developing ocular system. Numerous reports conducted so far have shown that children born prematurely or with low birth weight (BW) are at high risk of developing ophthalmic problems in infancy and childhood and later in life[1,4,11,13,14]. Retinopathy of prematurity (ROP) is a well-known threat to the vision of preterm infants[15]. Apart from the immediate devastating complications of ROP, it is likely that preterm birth may also lead to abnormal development of the eyes, with increasing rates of impaired visual acuity, refractive errors, amblyopia and strabismus[9,10,17]. However, the risk factors for the development of refractive errors in premature infants have not been fully investigated. Moreover, most studies were focused on preschool aged children. Studies of the refractive status of school-aged children who were born prematurely remain limited[1,10].

The investigation of refractive errors and optical components in children born prematurely could help to understand how prematurity affects the refractive status. Therefore, the purpose of our study was to evaluate the visual function of school-aged children who where born prematurely, and to determine the factors associated with the development of refractive errors in these children.

MATERIAL AND METHODS

The study sample included all children of premature birth (gestational age (GA) less than 37 weeks) who were born between January 1, 2006, and December 31, 2007, and were admitted to the Neonatal Intensive Care Unit of Pedro Hispano Hospital (PHH), Portugal. Of the 227 eligible children, 117 were given parental permission and were enrolled in the study. This study was performed in the Department of Ophthalmology of PHH between March 1 and August 31, 2015, when the participants' age ranged between 7 and 9 years. Written, informed consent was obtained from the parents of the study participants. The study protocol conformed to the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of PHH.

All participants underwent a complete ophthalmic examination. Distance visual acuity was tested monocularly using a Snellen letter chart. Best corrected visual acuity (BCVA) was expressed as a decimal notation. Cover and cover-uncover tests were performed to detect strabismus. Stereoscopic vision was examined with Randot Stereo Test (400 to 20 seconds of arc). The refractive status was determined by cycloplegic retinoscopy, 30 minutes after the instillation of 1% cyclopentolate eye drops 3 times at a 10-minute interval. All refractions were performed by one of two examiners (RG or AM). Refractive error was recorded in the form of spherical equivalent (SE). Astigmatism was recorded as negative cylinder value. Anterior segment examination with a slit lamp and indirect fundoscopy after pupillary dilatation were also performed in all children. The optical components, including anterior chamber depth (ACD), central corneal thickness (CCT), and corneal curvature (CC) were measured by Sirius® Scheimpflug tomography, and axial length (AL) was obtained by Zeiss IOL Master® biometer .

Medical records were reviewed to collect data regarding child's birth and medical history, including GA, BW, and the presence and stage of ROP. The infants examined for the presence of ROP included those falling within the criteria for the ROP screening program[19]: infants born before 32 weeks' GA and/or infants with BW below 1500 g. ROP was categorised by the stage of maximum severity in the acute phase, and was performed according to The International Classification of Retinopathy of Prematurity[12].

To analyse the refractive changes and the associated factors, participants were divided into groups according to their GA (<30 weeks, 30-<35 weeks, and ≥35 weeks) and BW (<1000 g, 1000-<1500 g, 1500-<2000 g, and ≥2000 g). Regarding their refractive status, they were divided into 3 groups: myopia (defined as SE less than -0.50 D), hyperopia (as a SE more than +0.50 D), and emmetropia (as a SE between -0.50 e +0.50 D). In children with symmetric eye refraction, we have chosen the information in the right eye for further data analysis. In children who had different refractive status or different stages of ROP between the right and the left eye, the information on the eye with more advanced disease was chosen for analysis.

Statistical analysis was performed with software IBM SPSS® version 21.0. A p-value of <0.05 was considered statistically significant. Independent samples t-test and one-way ANOVA were used for comparing mean values of continuous variables between the groups of the study. The chi-square test was used to examine the associations between categorical variables.

RESULTS

The total study population included 117 children. There were 63 (53.8%) boys and 54 (46.2%) girls. The mean age was 7.79±0.62 years (37 children at 7, 67 at 8, and 13 at 9 years of age). The average GA was 32.43±3.30 weeks (with a range from 25 to 36 weeks) and average BW was 1799±696 g (ranging from 490 to 3100 g). Forty-nine children (41.9%) were born before the GA of 32 weeks and/or weighed less than 1500 g at birth. Thirteen children (26.5% of those eligible for screening) had documented ROP, including 4 (30.8%) at stage 1, 3 (23.1%) at stage 2, and 6 (46.1%) at stage 3. Two children received laser treatment for ROP. The mean GA was 28.38±2.29 weeks and mean BW was 948±297 g in the ROP group comparing with 29.43±2.02 weeks (p>0.05) and 1194±263g (p=0.002), respectively, in the non-ROP group.

Tables 1 and 2 summarise the characteristics of visual function and optical components of the study participants divided according their GA and BW.

The mean visual acuity was not significantly different between the study groups (p>0.05), although children with GA <30 weeks and BW <1000g had the lowest values. There was also no statistically significant increase of refractive

Table 1 | Comparison of gestational age groups in terms of visual function and optical components.

	<30 weeks (n= 29)	30-<35 weeks (n=43)	≥35 weeks (n= 45)	*p*
BCVA	0.94±0.10	0.97±0.08	0.97±0.08	0.314
SE (D)	0.80±1.05	0.89±1.82	0.59±2.10	0.715
Astigmatism (D)	-0.74±0.57	-0.53±0.37	-0.72±0.82	0.258
Amblyopia	2 (6.9%)	2 (4.7%)	4 (8.9%)	0.733
Strabismus	4 (13.8%)	3 (7.0%)	2 (4.4%)	0.330
Stereopsis (")	71.79±91.37	45.64±39.12	43.64±24.46	0.070
ACD (mm)	2.94±0.33	3.08±0.28	3.09±0.25	0.077
CCT (μm)	548.34±30.65	546.11±33.24	555.33±32.99	0.406
CC (D)	44.80±1.62	43.93±1.34	43.17±1.21	<0.001
AL (mm)	22.01±0.85	22.68±0.79	22.76±0.96	0.001

Table 2 | Comparison of birth weight groups in terms of visual function and optical components.

	<1000 grs (n= 17)	1000-<1500 grs (n= 28)	1500-<2000grs (n= 21)	≥2000 grs (n=51)	*p*
BCVA	0.92±0.12	0.97±0.06	0.95±0.11	0.97±0.07	0.314
SE (D)	0.65±1.13	1.50±1.97	0.36±0.90	0.54±2.03	0.715
Astigmatism (D)	-0.74±0.60	-0.54±0.45	-0.75±0.66	-0.65±0.70	0.258
Amblyopia	1 (5.9%)	2 (7.1%)	2 (9.5%)	3 (5.9%)	0.733
Strabismus	2 (11.8%)	3 (10.7%)	3 (14.3%)	1 (2.0%)	0.330
Stereopsis (")	88.75±118.54	50.00±35.78	38.50±18.93	45.31±31.54	0.070
ACD (mm)	2.88±0.35	2.96±0.27	3.19±0.21	3.11±0.26	0.077
CCT (µm)	549.00±26.82	554.92±33.37	544.79±33.09	550.73±34.03	0.406
CC (D)	45.11±1.78	44.43±1.22	43.39±1.50	43.32±1.20	<0.001
AL (mm)	21.80±0.96	22.22±0.66	22.83±0.58	22.85±0.95	0.001

errors or need of wearing glasses (p>0.05) in children born extremely premature compare to those of modest prematurity, although it has been found that the value of the SE was greater for children with BW <1500 g compare to those with BW ≥1500 g (1.17 vs 0.49, p=0.042). The cylinder power was not significantly different between the study groups (p>0.05).

Evaluation of the refractive status showed 8 cases of myopia, 67 cases of hyperopia, and 42 cases of emmetropia. No significant difference was found in GA and BW among these three refractive groups (p>0.05). The average BCVA was found to be significantly poorer (p=0.003) and the degree of astigmatism was highest (p=0.029) in the myopia group compared to the other two refractive groups.

Amblyopia was not more frequent in children born with greater prematurity in comparison to those less premature. There was, however, a statistically increased number of cases of strabismus in children with BW <2000 g (p=0.036) and worse stereoscopic vision in children with GA <30 weeks and BW <1000 g (p<0.05). Among those failing stereopsis test, 30.8% had amblyopia in clinical diagnosis, and 15.4% had strabismus (esotropia).

Children with a history of ROP had a higher number of refractive errors (p=0.004) and need of wearing glasses (p = 0.029) when compared with those without ROP. There was no increase in the prevalence of myopia in the ROP group. There was also no significant increase in the incidence of strabismus in these patients (p>0.05).

Regarding the optical components, it was observed that extremely premature children had shallower ACD, steeper CC and shortest AL than children with lower degree of prematurity. All GA and BW groups showed a similar CCT.

Comparing the three refractive groups with respect to the optical components, it was found that in children with lowest BW (<2000 g) myopic eyes had a steeper CC and hyperopic eyes a flatter curvature; AL was similar between these groups. On the other hand, myopic eyes of children with more modest prematurity (≥2000 g) had greater AL and similar CC comparing to those eyes with hyperopia or emmetropia. ACD was higher in all myopic eyes irrespective of BW. Table 3 summarises the detailed characteristics of optical components of the three refractive groups according to the BW.

Table 3 | Comparison of optical components among the three refractive groups.

Refractive error	BW < 2000 g			BW ≥ 2000g		
	ACD (mm)	CC (D)	AL (mm)	ACD (mm)	CC (D)	AL (mm)
Myopia	3.39±0.15	46.28±1.80	22.61±0.50	3.36±0.13	43.82±1.04	25.33±1.77
Hyperopia	2.91±0.28	43.94±1.53	22.19±0.90	3.03±0.25	43.38±1.23	22.56±0.64
Emmetropia	3.11±0.29	44.64±1.50	22.25±0.70	3.17±0.25	43.16±1.18	22.91±0.59
p	0.004	0.024	0.526	0.039	0.631	<0.001

Table 4 | Ocular parameters according to the stage of ROP.

Parameter	Without ROP n=36	ROP Stage 1 n=4	ROP Stage 2 n=3	ROP Stage 3 n=6	*p*
GA (weeks)	29.43±2.02	30.75±0.96	27.33±2.52	27.33±1.75	0.018
BW (g)	1193±263	1209±268	968±202	764±238	0.003
SE (D)	0.83±1.00	1.19±0.47	1.91±5.31	2.10±2.85	0.310
Astigmatism (D)	-0.62±0.53	-0.50±0.29	-0.67±0.52	-0.63±0.52	0.971
ACD (mm)	2.93±0.27	2.96±0.25	3.13±0.59	2.77±0.42	0.518
CC (D)	44.30±1.39	44.94±2.21	46.57±1.82	45.22±1.70	0.141
AL (mm)	22.30±0.70	21.87±1.36	21.83±0.79	21.28±0.98	0.060

To further evaluate the influence of ROP and the severity of ROP on ocular development, we compared the refractive status and optical components between the different ROP stages and non-ROP groups (table 4). Significantly smaller GA and BW were found in the children with ROP stage 2 and 3 ($p<0.05$). The SE tend to be higher with more advanced ROP stage, although no statistically significant difference was found ($p>0.05$). The degree of astigmatism was found to be similar regardless of the presence and the extent of ROP. There was no significant difference for optical components values between the different stages of ROP ($p>0.05$), although eyes with more advanced ROP appeared to have a tendency to shallower ACD, steeper CC and shorter AL.

DISCUSSION

Ocular structures go through a continuous development and remodelling process before and after birth. Premature delivery may affect ocular development or later process of emmetropization[10,21]. Many reports analysing the refractive status and optical components in children born prematurely focused on children of preschool age[2,3,10,20]. It has been shown that prematurity may have a significant influence on optical components, including ACD, CC and AL, that are potential factors that contribute to the development of refractive errors in children born prematurely, which may persist through life[2,3]. Therefore, in this study, we enrolled a cohort of children aged between 7 and 9 years that were born prematurely, to evaluate the effect of preterm birth on long-term ocular refractive status.

In our study, there was no statistically significant correlation between BCVA or refractive error and the degree of prematurity. Amblyopia was also not more frequent in children born extremely premature in comparison to those less premature. There were, however, an increasing number of cases of strabismus in children with BW <2000 g. Holmström et al[11] also showed that children, at 10 years, born prematurely have a greater risk of strabismus than children born at term do.

O'Connor et al[16] studied the refractive status in children aged 10 to 12 years with a BW <1701 g, and both myopic shift and significant shorter AL were found. Simple cross-sectional studies comparing premature with full-term infants also revealed that premature infants are more prone to development of myopia from an early age and may remain myopic later on in childhood and adolescence. This is known as myopia of prematurity[3] secondary to arrest of ocular growth[5]. Chen et al[1] documented that premature children showed higher prevalence of myopia, hyperopia and astigmatism, compared with the control subjects. In our study, however, it was not verified a higher incidence of myopia or degree of astigmatism in children born extremely premature compare to those with modest prematurity.

Our analysis of optical components showed that children born extremely premature had shallower ACD, steeper CC and shorter AL than the other less premature children did. Regarding the kind of refractive error, we found that the development of myopia in children with BW <2000 g was justified by an increased CC, while in those with BW ≥ 2000 g was due to a greater AL. No significant difference in AL was found between myopic and hyperopic eyes in children with lowest BW. Fledelius[7] reported that 10-year-old preterm children had smaller globes than full-term children. He also found that AL of preterm globes was shorter than expected from their refractive state. Other studies also reported that CC may be influenced by prematurity, and preterm infants had a steeper CC than did full-term infants[1]. Friling et al[8] showed too that highest readings of CC were noted in the babies with the lowest BW and youngest postconceptional age. Fielder et al[6] postulated that lower extrauterine temperatures may impede corneal flattening in preterm infants.

In our study, 26.5% of children eligible for ROP screening program had documented ROP. The prevalence of ROP in our cohort was lower to that reported in other studies (prevalence >40%)[1,3]. This may be due to the retrospective analysis of medical records with loss of information and because many children were out of the hospital local area having lost the follow-up visits in our Ophthalmology Department. We observed that children with ROP had a higher number of refractive errors than children without ROP. Eyes of these children had shallower ACD, steeper CC and shorter AL, but there was no statistically significant difference compared with other children of less premature birth. Cook et al[3] also showed that eyes of premature infants have shorter AL, shallower ACD, and more highly curved corneas than eyes of full-term infants, and that these differences become more significant as the severity of ROP increases.

There were some limitations in our study. First, the data on birth history were collected retrospectively, as already mentioned. Another limitation was that our study groups only included children of premature birth and we didn't compare those groups with an age matched control group of full-term infants. Robaei et al[18] showed that even modest degrees of low BW (children with a BW of 1500 to 2499 g) and prematurity may be associated with increased ophthalmic morbidity.

In conclusion, our study demonstrated that school-aged children with preterm birth seem to have increased incidence of ophthalmic problems. Although it was not documented a higher incidence of refractive errors in children born more prematurely, the existence of ROP seems to be a risk factor for its development. In these patients, the refractive error is mainly attributable to anterior segment components, mostly CC, rather than to AL.

Patients born prematurely should be informed of the possible risks of ocular diseases that may accompany refractive and ocular component changes. The importance of long-term follow-up should be emphasized. Future studies will be needed to compare these results with a group of age matched full-term patients and to examine their refractive and visual function changes during their adolescence to adult ages.

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