ECRONICON OPEN ACCESS

EC OPHTHALMOLOGY
Research Article

Cross-Sectional Refractive Outcome, Ocular Abnormalities, and Intraoucular Pressure among Severe Preterm and Term Malay Children without Retinopathy of Prematurity

Alshaarawi Salem*, Shatriah I, Wan Hazabbah and Zunaina E

Department of Ophthalmology, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

***Corresponding Author**: Alshaarawi Salem, Department of Ophthalmology, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia.

Received: March 16, 2017; **Published:** April 06, 2017

Abstract

Purpose: To evaluate the refractive errors, ocular abnormalities, and introcular pressure in severe preterm and term Malay children aged 8 - 16 years old.

Design: Comparison cross-sectional study.

Participants: Children aged 8 to 16 years old at follow up visit at Hospital universiti sains Malaysia of risk factor of prematurity.

Methods: Detailed eye examination, including subjective retinoscopy, ocular movement (EOM) assessment, Snellen chart for distance (Reichert, NY, USA), Slit lamp biomicroscopy (Clement Clarke International, UK) with 90D and 78D lenses (Volk, USA), Goldman applanation tonometer.

Results: The mean spherical equivalent for the right eye was -1.42 (2.63) diopter in the severe preterm group, whilst in the term group was -0.48 (0.79) diopter. In the left eye, the spherical equivalent for severe preterm patients was -1.23 (2.56) diopter and for term group was -0.33 (0.7) diopter. There was no statistically significant difference of spherical equivalent in the right eye and left eye between severe preterm and term patients (Table 4.2.8). Intraocular pressure was noted to be lower in the severe preterm group (14.28 mmHg) compared to term group (16.00 mmHg). This difference was statistically significant with p = 0.04 (Table 4.2.6).

Conclusion: This study showed that Intraocular pressure was statistically significant in preterm children compared to term Malay children aged 8-16 years old.

Keywords: *Ocular Abnormalities; Severe Preterm; Malay Children; Retinopathy of Prematurity*

Introduction

A preterm child is defined as a child born at less than 37 weeks of gestation [1,2]. The causes of preterm birth are elusive and unknown in most situations; many factors appear to be associated with the development of preterm birth, making the reduction of preterm birth a challenging proposition. [1] defined premature delivery as that occurring before 37 completed weeks of gestation, starting from the first day of the last menstrual period.

Severe preterm or early preterm delivery is defined as babies born at 32 weeks or less of gestation. The earlier a baby is born, the less likely he or she is to survive. Those who do survive are at high risk of lifelong health problems, of which the ophthalmic complications include retinopathy of prematurity, myopia, amblyobia, strabimus and optic nerve abnormalities [3-5].

Both prematurity and low birth weight have been associated with an increase incidence of ophthalmic disorders such as refractive errors, strabismus, and amblyopia. While ample literatures exist on screening of retinopathy of prematurity, very little has been written about screening programmes for long term follow up for these infants [6].

In a study by Cooke., *et al*. [7] on visual impairment at 7 years of age in severe preterm children as opposed to full term children, it was observed that these preterm children were more likely to wear glasses due to poor visual acuity as well as reduced stereopsis and strabismus, but they showed no significant decrease in the contrast sensitivity. It was also demonstrated that although these children had no major neurodevelopmental sequelae, they had an increased prevalence of visual impairment at an early age (Primary school-going age). This was associated with visual, perceptional, motor and cognitive defects. In contrast, O' Connor., *et al*. [8] stated that low birth weight children have significant deficit in both visual acuity and contrast sensitivity.

Furthermore, studies of refractive state among premature infants are difficult to compare, because of methodological variation, like differences at age in examination, factors associated with refractive error cohort size. Most of the subjects included in the studies were older than 3 months of age, and measurements only started after that specific age. Consequently, information about concurrent early longitudinal changes in refractive state of the eye of premature infants is sparse.

However, certain cross sectional studies reported that rates of myopia ranged from 5% [9] through 22.4% [10] to more than 70% [11], depending upon the presence and severity of ROP and the age at time of examination.

The most extensive work has been done by Fledelius [12,13], with two decades worth of occulometric and refractive data on premature infants. This study was a 7 - 10 year follow-up of children. They were screened for regressed ROP and concurrent myopia. It was shown that the incidence of myopia was 25% in those with regressed ROP as opposed to those without regressed ROP.

Fledelius [14] performed a cohort study on preterm babies without ROP, and found that a disproportionate number of these subjects had persistent myopia even up to the age of 18 years. This type of myopia is known as myopia of prematurity (MOP), and it has an early onset. The hallmark of MOP is arrested development of the ocular anterior segment and presence of retinopathy of prematurity.

MOP has the characteristics of a relatively high corneal curvature, shallow anterior chamber, and thick lens with an axial length that is a shorter than would be expected for the dioptric value. This is in contrast to myopia not associated with prematurity, which is attributable to increase in axial length [10].

Methods

Study and Population

A list of severe preterm names and addresses was taken from the Medical Record Office, Hospital Universiti Sains Malaysia, Kubang Kerian. The patients were recruited from the medical record office, Neonatology wards, Labour room and postnatal wards, and pediatric wards. The eligible names and addresses were selected according to inclusion and exclusion criteria which approved according to patient's files. Non probability sampling method was applied to select the subjects. Selected subjects were called to the Ophthalmology Clinic, either by phone or direct home visit.. Severe preterm subjects who meet the inclusion and exclusion criteria were recruited in this study.

Questionnaire

The questionnaire was prepared to find the eligible volunteer based on selection criteria. The questionnaire was designed to enquire the general medical and ocular history, the status of Malay and contact number.

A detailed ocular examination were performed on all children. Monocular distant visual acutiy (VA) was tested on 6 meter using Snellen chart (Reichert, NY, USA).

Presenting visual acuity was assessed with spectacle correction, if worn and recorded as a letter read correctly. Acycloplegia was induced with cyclopentolat 1% (one drop) and tropicamid 1% (one drop each) repeated after 5 min, after instaling amethocaine 1% (one drop). Retinoscopy and refined subjectively using the crossed-cyl technique was performed.spherical equivalent refraction (SER) was calculated from these readings using the fomula SER = spher + 0.5 cylinder.

Ocular movement (EOM) assessment, Slit lamp biomicroscopy (Clement Clarke International, UK) with 90D and 78D lenses (Volk, USA), Auto Tonometer (Air Puff) (Depew. N.Y. USA) have been used.

Statistical Analysis

The latest version of SPSS 18 was used. Mean and standard deviation of all parameters were described either in mean and standard deviation (SD) for skewed data. Categorical variables were described in frequency and percentage. Independent t-test were used to compare mean of refractive errors, ocular abnormalities, and intraocular pressure between severe preterm and term Malay children.

Results

Table 1 shows the demographic data of severe preterm group. Majority of patients were born in between 30 - 32 weeks of gestational i.e. 37.5% male and 34.38% were female, whilst the majority of the patients (37.5% male and 25% were female) were born with birth weight ranging between 1000-1499 gram. On the other hand, no cases of retinopathy of prematurity have been recruited in this study according to inclusion and exclusion criteria.

	Severe Preterm			
	Male		Female	
	n	(%)	n	(%)
Gestational Age (Week)				
• 24-26	3	(9.4)	1	(3.13)
• 27-29	3	(9.4)	2	(6.25)
• 30-32	12	(37.5)	11	(34.4)
Birth Weight (g)				
• 500-999	6	(18.7)	3	(9.4)
• 1000-1490	12	(37.5)	11	(34.4)
Presence of ROP				
• Yes	0	(0.0)	0	(0.0)
• No	18	(56.2)	14	(43.7)

32 severe preterm and 32 terms patients were recruited in the study. The mean age and standard deviation (SD) for severe preterm patients were 9.81 (2.60) years old respectively, whilst for the control groups were 11 (2.41) years.

With reference to Table 2 the mean spherical equivalent (SE) for the right eye was -1.42 (2.63) in the severe preterm group, whilst in the term group -0.48 (0.79). In the left eye, the SE for severe preterm patients was -1.23 (2.56) and for term group was -0.33 (0.7). There is no statistically significant difference of spherical equivalent right eye and left eye between severe preterm and term patients.

Spherical equivalent (D)	Mean (SD)	Mean diff (95% CI)	t-stat (df)	p-value
Right eye				
• Severe preterm	-1.42 (2.63)	0.95 (-0.04, 1.93)	1.94 (36.50)	0.06
• Term	-0.48 (0.79)			
Left eye				
• Severe preterm	-1.23 (2.56)	0.90 (-0.04, 1.84)	1.91 (35.57)	0.06
• Term	-0.33 (0.70)			

Table 2: *Comparison of the spherical equivalent between severe preterm and term groups.*

Visual acuity at 6/6 reported the maximum percentage in both groups and both eyes i.e. in severe preterm group right eye (50%) and (50%) left eye, whilst term group (25%) right eye and (23%) left eye. , following by 6/7. to 6/9 and 6/12 to 6/18.

With reference to Table 3 5 (16.0%) of severe preterm subjects were having tropia in the right eye and 6 (19.0%) in the left eye, whilst all the subjects in the term group had an essentially normal of ocular motility.

Strabismus findings	Severe Preterm		Term	
	n	(%)	n	(%)
Tropia (near and/or distance fixation)				
• Right eye	5	(16.0)	0	(0.0)
• Left eye	6	(19.0)	0	(0.0)

Table 3: *Strabismus findings in severe preterm and term groups.*

All the subjects in the severe preterm group had an essentially normal eyelid (Table 4) and conjunctiva, whilst 2 (6.0%) of term subjects were having conjunctivitis and 1 (3.13%) had chalazion. Cornea and lenticular opacity was found normal in both groups. Hence 100% normalcy was noted in both groups involving the right eye and left eye. Fundus examination in the severe preterm group revealed increasing cup disc ratio in 2 subjects (6.25%) in both the right eye and left eye.

Ocular findings	Severe Preterm		Term	
	n	(%)	n	(%)
Eyelid and conjunctiva anomalies				
• Right eye	0	(0.0)	2	(6.2)
• Left eye	0	(0.0)	1	(3.1)
Cornea and/or lenticular opacity				
• Right eye	0	(0.0)	0	(0.0)
• Left eye	0	(0.0)	0	(0.0)
Fundus (increase cup disc ratio, retina scaring)				
• Right eye	2	(6.2)	0	(0.0)
• Left eye	2	(6.2)	0	(0.0)

Table 4: *Eye lid, anterior and posterior segments findings in severe preterm and term groups.*

Table 5 shows that intraocular pressure (IOP) was noted to be lower in the severe preterm group (14.28 mmHg) compared to term group (16.0 mmHg). This difference was also statistically significant with P = 0.04.

IOP (mm Hg)	Mean (SD)	Mean diff (95% CI)	t-stat (df)	p-value
• Severe preterm	14.28 (2.77)	-1.69 (-3.37, .01)	-2.01 (56.43)	0.04
• Term	16.00 (4.00)			

Table 5: *Comparison of intraocular pressure between severe preterm and term groups.*

Discussion

Our study aimed to evaluate refractive errors, ocular abnormalities, and introcular pressure in severe preterm and term Malay children.

There is currently no on data refractive errors, ocular abnormalities, and introcular pressure among severe preterm and term malay children in Malaysia. On the other hand, no study has been done to see whether severe preterm show a similar refractive errors, ocular

abnormalities, and introcular pressure with term children as compared to other studies done elsewhere. In our study, we studied these parameters in a population of severe preterm or had born less than 32 weeks at hospital university sains Malaysia, Kubang Kerian, 16150, Kelantan.

This study was comparison a cross sectional study, the population of children aged 8-16 years old and the total number of male subjects in both case and control group was higher than the total number of female subjects. The sampling method used was random sampling. The study population age ranged from 8 to 16 years. The mean age and standard deviation for severe preterm group were 9.81 (2.60) years old. While for the control group (term subjects), the mean were 11 (2.41) years. Majority of patients in the severe preterm group were born between 30 to 32 weeks of gestation, with the birth weight range between 1000 to 1499 grams.

We noted that the preterm group showed a trend of being more myopic compared to the term group. The spherical equivalent was -1.42 (2.63) in the right eye and -1.23 (2.56) in the left eye in the severe preterm group, while the spherical equivalent was -0.48 (0.79) in the right eye and -0.33 (0.70) in the left eye in the term group.

The myopic trend observed in our preterm group was consistent with other published tudies in preterm children [10,11,15,16]. Pohland., *et al*. [15] reported that myopia is a frequent finding in preterm children. The etiology of myopia of prematurity is yet to be explained according to Pohland., *et al*. [15]. The known factors that cause myopia in term patients are changes in the lens, corneal curvature, refractivity of the media and axial length of the eye.

Pohland., *et al*. [16] hypothesized that myopia was caused by excessive elongation of the optic axis in myopic preterm infants without ROP. They explained that deficiency of the bone mineral produces dolichocephalic deformation of the skull in preterm infants, and as a result the frontal axis was shorter and the biorbital diameter got narrowed. Consequently the optic axis became elongated in preterm children [15].

In a study conducted by Quinn., *et al.* [11], the proportion of eyes with myopia in the preterm population was increased compared to term children. However, the degree of myopia was related to retinopathy of prematurity, whereby eyes with moderate or acute-phase retinopathy of prematurity demonstrated increased prevalence of high myopia. There was a 28% increase in myopia in preterm children for every 100 gram decrease of birth weight. The odds of high myopia increased by 49% by age five and a half years with every 100 gram decrease in birth weight The risk of developing myopia in preterm children with severe acute phase ROP was 36 times higher than those preterm children who did not have ROP [11].

Cross sectional studies conducted by O'Connor., *et al.* [10] and Quinn., *et al.* [11] which reported that the degree of myopia was directly proportional to the severity of retinopathy of prematurity. However, we did not observe any statistically significant difference in spherical equivalence between the severe preterm and term groups in our study. This is probably because we did not include children with history of retinopathy of prematurity in our study.

Differences in refractive error found in children born prematurely without ROP from previous studies could be due to difference 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.

Poor visual acuity is a common problem affecting preterm individuals with very low birth weight [17]. We documented that only 50 % of our preterm children had visual acuity 6/6, while 78.1% of term children displayed visual acuity of 6/6. Our results are consistent with several similar studies which are summarized in the next few paragraphs.

A study was conducted by Cooke., *et al*. [7] to determine the prevalence of ophthalmic impairments in very preterm compared with term infants. Their study population consisted of 2 groups; 297 children aged 7 years old and born before 32 weeks of gestation were assessed while the control group consisted of 210 term infants. They reported that preterm patients showed poorer visual acuities (< 6/9)

compared to the term controls, and this result was statistically significant. ($p = 0.007$ for left eye, $p = 0.002$ for right eye). Furthermore, the number of preterm children (12.8%) wearing spectacles for myopia was significantly higher than the term children (4.3%, $p = 0.002$). Strabismus was also noted to be significantly more in the preterm group ($p < 0.001$) [7].

O'Connor., *et al.* [18] conducted a study to determine the visual functions of preterm children aged 10 to 12 years of birth weight less than 1701 gram. The results were compared to a group of term children. There was a significant reduction in visual acuity in the preterm compared to the term group in this study. In all cases the study cohort had a lower median acuity and a greater spread of values ($p < 0.001$). However, the median acuity of the study cohort was equal to or better than 0.0 logMAR (that is, within the normal range). Despite, this in the low birth weight cohort there were 55 (18.8%) cases with binocular acuity below 0.0 with no known ocular pathology. However, 35 of these cases were less than one line below 0.0 which could reflect the normal acuity variation. Moreover, 51.9% low birth weight children with no retinopathy of prematurity (similar to the preterm population in our study) had visual acuities worse than 6/9 compared to 6/6 in the control group [18].

In 1997, Powls., *et al*. have examined the visual impairment of very low birth weight children in UK and compared it with normal birth-weight controls. The study population was aged between 11 and 13 years. Monocular visual acuity and strabismus were components of visual testing in this study group. It was observed that very low birth weight children had poorer vision (< 6/9) (38%) than their term peers (23 %). The number of children wearing spectacles for myopia was significantly higher than in the very low birth weight group compared to the normal birthweight group (31% vs. 19%, $p = 0.02$). Visual acuity was both distant (6 metres) and near (0.3 metres) was poorer in the very low birth weight children than in their controls. Overall, there were more very low birth weight children than controls with impaired visual acuity (6/12 or worse) for both measures ($p < 0.05$) [19].

Both our studied groups, the preterm and term children demonstrated normal ocular motility. In contrast to our findings, Bendentto [20] reported that out of 87 Italian children, who were born less than 32 weeks, 5.7% had abnormal ocular motility and 94.3% had normal ocular motility [20].

We documented 5 (16.0%) preterm children who had tropia in the right eye, and 6 (19.0%) demonstrated tropia in the left eye. There was no tropia observed in the term children. Zacharias., *et al.* [21] have observed that strabismus was seen in 12.7% of a population of 5-years-old with birth weight less than 1 816 gram.

Similarly, a prevalence strabismus of 12.5% was reported by Moller (1970) in a group of 640 premature infants. In 1976, Fledelius demonstrated heterotropia in 22.5% of a group of 302 preterm infants, as opposed to only 5.9% in a control population composed of 237 full-term babies [22].

We noted the external eye examination was fairly normal in both groups, with a negligible number in the term group having chalazion and ptosis (6.25% in the right eye and 3.13% in the left eye). Furthermore, all subjects had normal cornea, with a normal transparent lens. Hence 100% normalcy in terms of gross morphology of the eyes was noted in both groups. However, there were 2 (6.25%) subjects in the preterm group had increasing cup disc ratio.

We observed that the intraocular pressure was significantly lower in the severe preterm group (14.28 mmHg) compared to the term group (16.0 mmHg). This is in accordance with some studies mentioned below. Based on the PubMed search on the keywords of 'intra-ocular pressure and preterm children', we were unable to find relevant studies describe intraocular pressure among preterm children aged 8 to 16 years as in our study.

On the other hand, Ng PC., *et al.* [23] conducted a study in Hong Kong to establish a normative range of intraocular pressure in 104 preterm infants with a median (interquartile range) gestational age of 29.8 (28.7 – 30.9) weeks and birth weight of 1208 (1049 – 1370). They also identified important perinatal factors that could affect the intraocular pressure during the early weeks of neonatal life. It was observed that with every one week increase in post-conceptional age, there was a statistically significant reduction in the IOP by -0.11

mm Hg. There was no significant difference in longitudinal measurements of IOP between the left and right eyes (p = 0.27) and the mean spherical equivalent discrepancy of measurement between the two eyes was 0.22 (0.20) mmHg [23].

Tucker., *et al*. in 1992 examined 70 premature infants 25 to 37 weeks' post-conceptional age during their first week of life. They reported that no significant correlation was found between intraocular pressure and gestational age or birth weight [24].

Conclusion

In conclusion no differents have been observed in refractive errors among severe preterm children were born at 32 weeks or less of gestation and term children. However, staitisically significant was noted in intraocular pressur with P value (p = 0.04) between severe preterm and term children aged 8 - 16 years old.

Bibliography

1. Silvia S G and Eve R. "Lowbirth weight, Preterm, and small for gestational age babies in Scotland, 1981-1984". *Journal of Epidemiology and Community Health* 45.3 (1991): 207-210.

2. World Health Organization. "The incidence of low birth: An update weekly Epidemiol Record" 59 (1984): 205-211.

3. Gallo JE., *et al*. «A population based study of ocular abnormalities in premature children aged 5 to 10 years". *American Journal of Ophthalmology* 111.5 (1991): 539-547.

4. Keith CG and Kitchen WH. "Ocular morbidity in infants of very low birthweight". *British Journal of Ophthalmology* 67.5 (1983): 302-305.

5. Dowdeswell HJ., *et al*. "Visual deficits in children born at less than 32 weeks' gestation with and without major ocular pathology and cerebral damage". *British Journal of Ophthalmology* 79.5 (1995): 447-452.

6. Schalij-Delfos N., *et al*. "Long term follow up of premature infants: detection of strabismus, amblyopia, and refractive errors". *British Journal of Ophthalmology* 84.9 (2000): 963-967.

7. Cooke RW., *et al*. "Ophthalmic impairment at 7 years of age in children born very preterm". *Archives of Disease in Childhood - Fetal and Neonatal Edition* 89.3 (2004): F249-F253.

8. O'Connor AR., *et al*. "Educational attainment associated with ophthalmic morbidity in a low birth weight population". *British Orthoptic Journal* 58 (2001): 19-23.

9. Hungerford J., *et al*. "Ocular sequelae of preterm birth and their relation to ultrasound evidence of cerebral damage". *British Journal of Ophthalmology* 70.6 (1986): 463-468.

10. O'Connor AR., *et al*. "Strabismus in children of birth weight less than 1701g". *Archives of Ophthalmology* 120.6 (2002): 767-773.

11. Quinn GE., *et al*. "Prevalence of myopia between 3 months and 5½ years in preterm infants with and without retinopathy of prematurity". *Ophthalmology* 105.7 (1998): 1292-1300.

12. Fledelius HC. "Ophthalmic changes from age of 10 to 18 years. A longitudinal study of sequels to low birth weight.I. Refraction". *Acta Ophthalmologica (Copenh)* 58.6 (1980): 889-898.

13. Fledelius HC. "Pre-term delivery and subsequent ocular development. A 7-10 year follow-up of children screened 1982-84 for ROP. 3. Refraction. Myopia of prematurity". *Acta Ophthalmologica Scandinavica* 74.3 (1996): 297-300.

14. Fledelius HC. "Preterm delivery and the growth of the eye. An oculometric study of eye size around term-time". *Acta Ophthalmologica* 204 (1992): 10-15.

15. Pohland F. "Hypothesis: myopia of prematurity is caused bye postnatal bone mineral deficiency". *European Journal of Pediatrics* 153.4 (1994): 234-236.

16. Pohland F. "Prevention of postnatal bone demineralization in very low birth weight infants by individually monitored supplementation with calcium and phosphorus". *Pediatric Research* 35.1 (1994): 125-129.

17. Darlow BA., *et al*. "Prospective study of New Zealand infants with birth weight less than 1500 g and screened for retinopathy of prematurity: Visual outcome at age 7-8 years". *British Journal of Ophthalmology* 81.11 (1997): 935-940.

18. O'Connor AR., *et al*. "Visual function in low birthweight children". *British Journal of Ophthalmology* 88.9 (2004): 1149-1153.

19. Powls A., *et al*. "Visual impairment in very low birthweight children". *Archives of Disease in Childhood* 76.2 (1997): F82-F87.

20. Benedetto R. "Refractive error and ocular motility disorders in preterm babies with and without retinopathy of prematurity". *Ophthalmologica* 213.5 (1999): 295-299.

21. Zacharias L., *et al*. "Visual and ocular damage in retrolental fibroplasia". *American Journal of Ophthalmology* 53.2 (1962): 337-745.

22. Fledelius Hc. "Prematurity and eye: Ophthalmic 10-years old follow up of children low and normal birth weight". *Acta Ophthalmologica Supplement* 128 (1976): 3-245.

23. Ng PC., *et al*. "A Longitudinal Study to Establish the Normative Value and to Evaluate Perinatal Factors Affecting Intraocular Pressure in Preterm Infants". *Investigative Ophthalmology and Visual Science* 49.1 (2008): 87-92.

24. Tucker SM., *et al*. "Corneal diameter, axial length, and intraocular pressure in premature infants". *US National Library of Medicine* 99.8 (1992): 1296-1300.

Volume 6 Issue 2 April 2017