

Comparative study of visual dysfunctions in 6–10-year-old very preterm- and full-term-born children

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Abstract

Purpose To compare visual dysfunction between very preterm-born (VPB) children with no retinopathy of prematurity (no-ROP) at 6–10 years of age and age- and sex-matched full-term-born controls.

Methods This is an observational, prospective study that included 30 children, 6–10 years of age, born \leq 32 weeks of gestation, with no-ROP, and 30 age- and sex-matched full-term-born controls, conducted

from January 2015 until August 2015. All children underwent complete ophthalmic evaluation. Main outcome measures include visual functions (best corrected visual acuity (BCVA), color vision, and stereoacuity), ocular alignment, refractive errors, and the presence of amblyopia and nystagmus.

Results Mean BCVA of the right eyes was 0.04 ± 0.08 logMAR for VPB children and 0.02 ± 0.05 logMAR for the full-term children ($P = 0.075$). Mean BCVA for the left eyes was 0.07 ± 0.09 logMAR for VPB children and 0.02 ± 0.05 logMAR for the full-term children ($P = 0.014$). Refractive errors were slightly higher though not statistically significant in VPB children compared to full-term children ($P = 0.125$). The incidence of myopia and hypermetropia was 16.7 and 40%, respectively, in VPB children and 10 and 23.3%, respectively, in full-term children. Anisometropia found only in VPB children with an incidence of 16.7%. Amblyopia found in 10% of VPB children compared to 3.3% in full-term children. Strabismus was found equally in 10% of each group.

Conclusion VPB children with no-ROP are at an increased risk of developing decreased BCVA at least in one eye and anisometropia compared to age-matched full-term controls.

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Keywords Visual dysfunctions · Very preterm ·
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Introduction

Advancements in perinatology and neonatology care over the last decades led to marked improvement in the survival rates of very immature infants [1]. With this increase in survival rate of preterm infants, ophthalmic dysfunctions are expected to upsurge and long-term ophthalmic care would be indispensable. Visual dysfunction can involve visual acuity, color discrimination, pupil reactivity, ocular movement, and refractive errors. Insult to the developing eyes and visual pathways can be induced by the immature retinal vascularization combined with unstable oxygenation and circulation [2]. Preterm birth is believed to pose an impact on the developing ocular system, which become manifest in various pathological range and significance [3].

Though retinopathy of prematurity (ROP) is considered the major ocular problem in children born prematurely, premature birth per se may herald an increased risk of abnormal refractive development and other ocular problems in infancy and early childhood [4]. In premature children, vision is compromised due to an increased incidence of strabismus, refractive errors, and cerebral vision impairment. In addition to the significant impact on visual function, there is a crucial influence on other developmental aspects of childhood, including educational and psychological issues [3]. Most existing studies on this subject have not been able to identify whether ocular morbidity is a consequence of premature birth by itself or secondary to ROP. The extent to which preterm children with no-ROP are at risk of developing ocular morbidities and imperfect ophthalmic development is not fully uncovered yet [2]. Prematurely born children are considered at high risk to develop a wide range of ophthalmic disorders [5–15]. These disorders include deficits of visual acuity [9], color vision [10, 16], and refractive errors [5, 6, 15, 17]. Children with a low birth weight are also more likely to develop strabismus [11, 12] and severe visual impairments as a result of either damage to the posterior visual pathway [11, 13] or due to association with retinopathy of prematurity [14].

Identifying the extent of visual dysfunction and ocular morbidities in very preterm-born infants provides useful information for planning future follow-up, with the required medical, social, and educational services.

The purpose of this study is to compare visual dysfunction between very preterm-born (VPB) children with no-ROP at 6–10 years of age and age- and sex-matched full-term-born controls.

Methods

Design

This is an observational prospective case–control study. The study was performed at a University Hospital, Al-Khobar, Kingdom of Saudi Arabia, between January 2015 and August 2015. The study was reviewed and approved by the Dammam University Institutional Review Board and was carried out in accordance with the tenets of the Declaration of Helsinki, and a written informed consent was obtained from the parents of the participants in the study.

Definitions

The WHO defines preterm birth as any birth before 37 completed weeks of gestation. Preterm neonates are subclassified according to gestation duration at delivery into extreme preterm if born less than 28 weeks of gestation or very preterm if born between 28 and 31 + 6 days of gestation (like our selected population) or late preterm if born between 32 weeks and 36 weeks + 6 days.

Subjects

This study included children 6–10 years old who were born \leq 32 weeks of gestation in University Hospital at Al-Khobar, Saudi Arabia, and a control group of full-term children, born in the same hospital in the same period of time. Subjects' data were obtained from the hospital records. Out of one hundred VPB subjects born between 2004 and 2009, we were able to reach only 42 children.

The complete ophthalmologic examination was done for all the subjects. The main outcome measures were: (1) the best corrected visual acuity (BCVA) using E charts at 6 m distance (decimal acuity was converted to logMAR units), (2) color vision using Ishihara isochromatic color plates, (3) stereoacuity using Lang stereo test II, (4) strabismus assessed by cover, cover–uncover, and alternating cover tests, (5)

anterior segment examination using slit lamp, (6) funduscopy, (7) cycloplegic refraction using cyclopentolate hydrochloride 1%. Refractive errors were converted to the spherical equivalent (spherical equivalent = spherical refractive value + half the cylindrical refractive value). Significant refractive error was considered if hypermetropia was $\geq +3$ diopters (D), myopia ≥ -1 D, or astigmatism ≥ 1 D, (8) anisometropia ≥ 2 D, (9) presence of amblyopia, which was defined as a difference of at least two lines in BCVA between the eyes with BCVA in the amblyopic eye ≤ 0.2 logMAR that could not be explained by structural abnormalities in the eye, and (10) nystagmus and cataract were determined. Ametropia was corrected with glasses, and subjects with strabismus underwent orthoptic and anti-amblyopic therapy as indicated.

Statistical methods

All categorical variables were represented by the frequency with percentage, and it was analyzed by using Chi-square and Fisher exact test. Continuous data were presented by mean with standard deviation and median for abnormal data, and it was analyzed by using independent t test and Mann–Whitney U test. In all analyses, $P < 0.05$ was considered statistically significant. All statistical analyses were performed using SPSS for Windows Statistical software, Version 20.0

Results

A total of 72 subjects were examined: 42 of them were VPB children, and 30 were full-term children. Eight children with retinopathy of prematurity, three children with cerebral pathologies with inability to determine their visual acuity, and one child with congenital cataract were excluded.

Eleven of the VPB children were either twins or triplets. All full-term subjects were singleton births. Table 1 summarizes demographic criteria for both VPB and full-term children.

Visual acuity and refractive values of VPB and full-term children are presented in Table 2. Refractive errors were higher in the VPB children than in the full-term children, with no statistically significant difference ($P = 0.125$). The incidence of myopia was 16.7%

in the VPB children and 10% in full-term children. Hypermetropia was more common than myopia in both groups. It was found in 40% of VPB children and 23.3% of the full-term children. Astigmatism (≥ 1 D) was found in eight (27%) of the VPB children and six (20%) of the full terms. Five (16.7%) of the VPB children had anisometropia compared to none of the full-term children ($P = 0.020$). Neurologic morbidities that included mainly motor disabilities were found in also 5 of the VPB children and none of the full-term children ($P = 0.020$) (Table 3). There was no statistical correlation between anisometropia and neurologic morbidities ($P = 0.29$).

Amblyopia was found in three (10%) of the VPB children and one (3.3%) of the full-term children. Strabismus was almost equally found in the VPB children group and full-term children (Table 3).

Color vision defects were present in two (6.25%) of the VPB children group, while none of the full-term children had the problem with color vision. Two (6.25%) of the VPB children had defects in stereopsis (Lang stereo test II: 0 and 200). All the full-term children had full stereopsis. None of the VPB nor the full-term children presented with nystagmus. Fundus examinations were normal for all subjects.

Discussion

The present study shows fairly good BCVA of VPB children that ranged from 0.3 to 0.0 logMAR in either eye; however, mean BCVA of the left eye was significantly lower than that of full-term children ($P = 0.014$), while none of the VPB children had BCVA less than 0.7 logMAR. This reduction in distance visual acuity in at least one eye in VPB children in this study was due to anisometropia. Our results are in line with O'Connor et al. [18] who reported no significant long-term effect on visual acuity in children with no or regressed, mild ROP. However, it contradicts results of other studies that supported the concept that premature birth per se may carry a greater risk of reduced visual acuity compared to full-term children [10, 19–22]. The extent to which ocular development is disturbed by premature birth by itself in children with no-ROP is not well established yet [2]. The prevalence of functionally low vision in children 5–15 years is 1.52/1000 that was mainly attributed to retinal lesions followed by amblyopia

Table 1 Demographic data of participants

	VPB children (<i>n</i> = 30)	Full-term children (<i>n</i> = 30)
Gender		
Male	15 (50%)	16 (53%)
Female	15 (50%)	14 (47%)
Age (years)	8.13 ± 1.48	7.70 ± 1.58
Mean gestational age (weeks)	29.5 ± 1.55 (ranged 25–31)	39.8 ± 1.00 (38–41)
Mean birth weight (Kg)	1.1 ± 0.24	2.9 ± 0.29

Table 2 Visual acuity and refractive values of VPB and full-term children

	VPB (30 children)	Full term (30 children)	<i>P</i> value
Mean visual acuity (logMAR)			
OD	0.04 ± 0.08	0.02 ± 0.05	NS
OS	0.07 ± 0.09	0.02 ± 0.05	0.014*
Spherical equivalent (mean, D)			
OD	1.97 ± 3.0	1.91 ± 2.1	0.930
OS	2.14 ± 3.1	1.78 ± 2.0	0.598
Cylindrical power (mean, D)			
OD	− 0.64 ± 1.0	− 0.46 ± 0.5	0.392
OS	− 0.71 ± 0.8	− 0.51 ± 0.5	0.298

**P* value < 0.05 is considered statistically significant

[23]. Larsson et al. [19] reported lower distance visual acuity in the preterm-born children in contrast to full-term ones despite the good overall visual outcome in the prematurely born children. Darlow et al. [20] reported a distant visual acuity less than 0.4 in the worse eye in 15% and the better eye in 5% of children with no-ROP. Holmström et al. [21] found that 2.5% of the preterm infants (including ROP cases) had poor vision (< 0.3) at the age of three and a half. Dowdeswell et al. [10] obtained low levels of distant visual acuity in the preterm children (including ROP

cases) compared to the full-term ones. It has been suggested that exposure of the premature eye to the extrauterine environmental factors would affect metabolism and overall function of the developing, immature eye [6].

Strabismus prevalence in full-term preschool and elementary school children is reported to range from 1.6 to 4.3% [23–25]. Strabismus in our study was almost equally found (10%) in the preterm children and full-term children groups. The increased rate of strabismus in full-term children could be due to high prevalence of hypermetropia that could be inherent to the sample selection. Strabismus rate in this study is relatively higher than the rate by Holmström et al. [17] and Bin-Khathlan et al. [15] who observed strabismus rates of 5.9 and 7.2%, respectively, in preterm children with no-ROP or neurologic complications. Nevertheless, strabismus rate in our study is lower than several studies that showed an increased prevalence of strabismus in prematurely born children [3, 11–14]. Fledelius [26] reported an overall frequency of strabismus to be 17.8% in prematurely born children, compared to 5.9% in full-term children.

The prevalence of amblyopia in normal preschool and school-aged children is 3.9–4.1% [23, 25]. In this study, amblyopia was detected in three (10%) of the preterm children, who had anisometropia, compared

Table 3 Frequency of strabismus, amblyopia, and refractive error in VPB and full-term children

	VPB (30 children)	Full term (30 children)	<i>P</i> value
Esotropia	3	2	0.640
Exotropia	1	1	0.999
Amblyopia	3	1	0.301
Neurologic morbidities	5	0	0.020*
Anisometropia	5	0	0.020*
Myopia (≥ − 1 D)	5	3	0.448
Hypermetropia (≥ 3 D)	12	7	0.165
Astigmatism (≥ 1 D)	9	5	0.222

**P* value < 0.05 is considered statistically significant

to one (3.3%) of the full terms who had accommodative esotropia. The frequency of amblyopia in preterm children is slightly higher than the reported rate that ranged from 1.4 to 7.7% [2, 27, 28].

Prematurely born children are at an increased risk of developing amblyogenic factors such as anisometropia, refractive errors, and strabismus [9, 17, 19, 20, 29]. In the current study, five (16.7%) of the preterm children had anisometropia while none of the full-term children were anisometropic. The frequency of anisometropia (≥ 2 D) in our studied group of preterm children is relatively high compared to the previously reported values. Anisometropia prevalence in full-term (6-year-old) children is reported to be 1.6% [30], while anisometropia rate in school-aged preterm children including children with ROP was 13.7% [31, 32] and 4.2% in children with no-ROP [32].

Comparing the results of the refractive states of the preterm children with previous studies is limited by methodological variations and epidemiological features such as the age of the subjects. During such judgements, cutoff levels of refractive errors must also be taken into consideration as the majority of the studies use different cutoff criteria for refractive definitions.

Emmetropization is a process that guides the ocular growth in full-term neonates who commonly exhibit high levels of hypermetropia and astigmatism toward the optimal refractive state [33]. Saunders et al. [4] documented emmetropization process in preterm children in the absence of ROP that corrects most of the refractive errors secondary to prematurity by the age of 6 months. Emmetropization in preterm infants, who tend to be more myopic and astigmatic at birth than their full-term peers, has been highlighted in several studies that revealed ocular development of preterm children soon catches up with that of normal children in the same age group [34, 35]. Nevertheless, at the age of 4 years 19% of the preterm children may still develop clinically significant risk of abnormal refractive changes [4]. In our study hypermetropia (≥ 3 D) was the most prevalent refractive error occurring in 40% of preterm-born children and 23.3% of the full-term children. However, myopia occurred in 16.7% of preterm-born children and 10% of the full-term children. The findings of our study vary from the results by Tuppurainen et al. [8] who reported hypermetropia (≥ 2 D) in 22.4%, myopia

(≥ 1 D) in 8.6%, and astigmatism (≥ 1 D) in 12.1% of 5-year-old children born at a gestational age of less than 32 weeks. Nevertheless, the high rate of hypermetropia can be explained by faulty emmetropization [36] or the possibility of having shorter axial length of the globe that can occur in preterm children with no-ROP [2, 37, 38]. The prevalence of hypermetropia in full-term children in our study was within the reported range of rates in randomly selected full-term children of the same age group that varied between 14.3, 19.1, and 22.6% [2, 8, 39].

In the current study, astigmatism in at least one eye was found in 30% of the preterm children and 20% of the full-term children. The prevalence of astigmatism was reported to be significantly more common in the preterm children compared to full-term ones [9, 29]. The increase in astigmatism risk in preterm children could be attributed to an arrest in the normal process of emmetropization with some disturbances in ocular growth.

In this study, two of the preterm children (twins) had defect in color vision (Ishihara isochromatic color plates test results: 25/38 and 20/38) and it was associated with full vision and negative family history of color blindness. All of the full-term children had full color vision. Color vision defect is described in preterm children independently of any obvious ocular pathology [10]. The possible increased risk of subtle damage of the visual system in the preterm-born babies is attributed [10]. A previous study suggested that the newborns in intensive care units are at risk of exposure to prolonged and relatively intense illumination that may damage the retinal cones with subsequent development of deficits in color vision and spatial contrast sensitivity [40].

An important limitation in this study is the relatively small sample size that may account for the lack of significant association between preterm birth and the development of refractive errors.

In conclusion, hypermetropia and amblyopia were more commonly encountered in VPB with no-ROP children than full-term-born children; however, this was not supported sufficiently statistically. There is a strong and clear link between VPB with no-ROP and the risk of decreased best corrected visual acuity at least in one eye and anisometropia compared to age-matched full-term controls. With the results presented above, it could be stated that a screening program by an ophthalmologist for VPB children should be

considered at an early age. Yet, in order to achieve more accurate results, the scope of this research should be expanded using larger samples.

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Compliance with ethical standards

Conflict of interest None of the authors have any proprietary interests or conflicts of interest related to this submission.

Informed consent Informed consent was obtained from the parents of all participants.

Research involving human participants This study was reviewed and approved by the Dammam University Institutional Review Board and was conformed to the tenets of the Declaration of Helsinki.

Statement on the welfare of animals This study does not contain any studies with animals performed by any of the authors.

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