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Ocular changes in premature infants

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ABSTRACT

Introduction: This article aimed to review the literatures on visual impairments and ocular changes in premature infants with low birth weight and gestational age.
Methods: Five electronic databases including: PubMed, Web of Science, Science direct, Ovid, and Scopus were searched. Original articles published until 2015 describing preterm infants were reviewed. Repetitive and derivative articles were excluded.
Results: Out of 100 unique, potentially relevant articles, 42 studies that addressed and met the inclusion criteria were evaluated.
Conclusion: Prematurity affects ocular structures (from anterior to posterior segment) and functions. Premature infants are at risk of myopization. Concerning the changes in premature infants, a significant increase is found in axial length, intraocular pressure, and central corneal thickness; moreover, high incidence of retinal changes is reported as a result of prematurity. On the other hand, visual acuity, tear, electroretinogram, and visual evoked potential responses decrease with prematurity. The most common ophthalmic disorders in preterm infants are myopia and retinopathy of prematurity, which could affect life quality due to reduced visual acuity.

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Introduction

Preterm birth is the birth of an infant at less than 37 weeks of gestation (1). Preterm birth is the most common cause of mortality among infants worldwide (2). The reported prevalence of prematurity among infants with less than 28 weeks gestational age (GA) is 33% (3). According to the results of a study, retinopathy of prematurity (ROP) was reported in 26.2% of premature infants (4). Premature infants are at risk for cerebral palsy, developmental delays, and vision and hearing problems (5). Preterm infants are more likely to sustain abnormalities of visual system, which lead to reduced vision (6). Ophthalmic complications of prematurity include refractive error, strabismus, abnormal retinal vessels or ROP, visual loss due to reduced development of visual cortex, cortical visual impairments, and some rare, late-onset problems such as glaucoma, retinal detachment, and phthisis (6). In the late 1940s, ROP was initially reported to be the most common ocular abnormality in preterm infants (2,7). The existing evidence presented that >50% of neonates with <1000 g birth weight (BW) show some degree of ROP (8). Possible risk factors for ROP are as follows: low oxygen level, low GA and BW, hyperglycemia, low insulin-like growth factor, loss of nutrients, neonatal infections (particularly fungal), genetic factors, low blood levels of vitamin E, and light exposure

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(9,10); however, low BW (LBW) and GA are the main risk factors for ROP. With respect to genetics as a predisposing factor, ROP occurs more often in white infants, as compared to black ones and in males rather than females (2). Since premature infants have lower serum levels of vitamin E, the role of vitamin E in ROP was also considered (7). Development of cryotherapy and laser photocoagulation in the 1980s and 1990s were considered effective modalities in preventing blindness. It has been suggested that intravitreal bevacizumab could be helpful in ROP therapy and could reduce both the myopia and astigmatism in premature infants. Blindness was significantly more common in preterm male infants (11), which may be secondary to cicatricial ROP or intracerebral hemorrhages (12). The first phase of ROP is initiated during the first 30–32 weeks, and the second phase, which is characterized by retinal neovascularization, begins approximately within the first 32–34 weeks of postmenstrual age (7). Ocular changes in premature infants lead to various eye size problems and cause refractive errors in preterm infants (13). Since most of the previous studies discussed changes in the retina and the refractive state of the eye, this study aimed to provide an accurate and comprehensive summary of the ocular changes in preterm infants.

Methods

Data sources and searches

The data were retrieved from the electronic databases including PubMed, Web of Science, Science direct, Ovid, and Scopus. In addition, we handsearched the reference lists of review and original articles. The following keywords were used for our search: 'prematurity', 'ocular', 'eye', 'premature infants', and 'preterm infants'. Using the same search parameters, all the identified journals, which were published from 1960 up to 2015, were manually searched.

Study selection

The study selection process is illustrated in Figure 1. Eligibility assessment was performed by one of the authors through reviewing the titles and abstracts. Thereafter, the full-text versions of 42 articles were reviewed independently by two authors. The inclusion criteria included studies discussing ocular changes in prematurity, all the relevant studies except for case reports, cohort studies in which follow-up was completed, studies in which participants did not have any comorbidities, and all the studies published up to 2015.

Data extraction and quality assessment

Two researchers extracted the data from the included articles. Study design and outcomes concerning refraction error, strabismus, visual acuity (VA), intraocular pressure, axial length (AXL), cornea, tear, pupil, retinae, visual evoked potential (VEP), electroretinography, and cortical visual impairments were extracted from all the included articles. Studies were evaluated for the inclusion criteria, accurate recruitment of participants, accurate measurement to minimize exposure to bias, precise evaluation of outcomes to minimize bias, and identification of confounding factors and bias (Table 1).

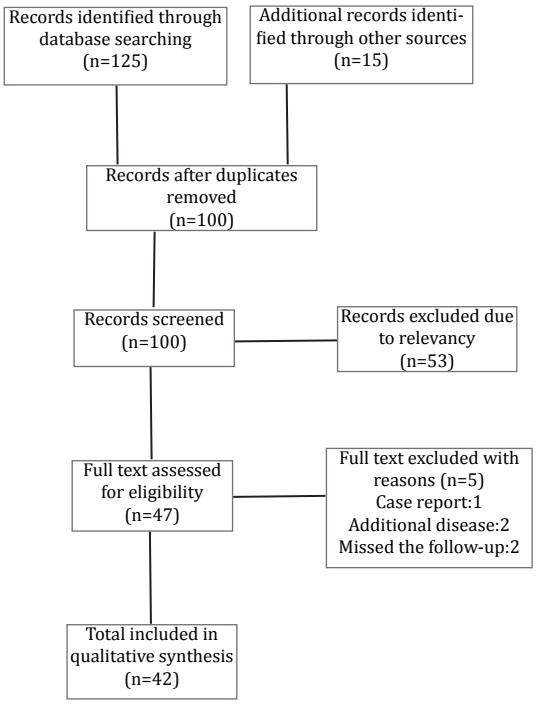

Figure 1. study selection process.

Results

Most studies reported that ROP could have diverse effects on ocular structure and function through refractive error, AXL, retinae, strabismus, intraocular pressure, cornea, and vision. Findings of the relevant studies are discussed in discussion section and also were summarized in Table 2.

Discussion

Refractive error

Preterm birth affects the process of emmetropization through arrested development of the anterior segment (14,15), or mechanical restriction as a result of biological stress secondary to retinopathy (15). Mohammadzadeh et al. stated that refractive error is the most common ophthalmic disease in low birth weight children, and myopia is the most refractive error (16). High incidence of myopia in premature infants could be related to preterm birth, ROP, or disease treatment (13). In a cohort study performed on LBW infants, the mean

Table 1. Quality assessment of included studies.

Cross sectional study Author Year	**Describe the setting, locations, and relevant dates**	**Given the eligibility criteria**	**Clearly define all outcomes, exposures and predictors**	**Clearly define all potential confounders, and effect modifiers**	**Bias**
Acar D (2015)	Yes	Yes	Yes	Yes	Yes
Rudanko S (2003)	Yes	Yes	Yes	No	Yes
Laws D (1994)	Yes	Yes	Yes	Yes	No
Spierer A (1994)	Yes	Yes	Yes	No	No
Remon L (1992)	Yes	No	Yes	Yes	No
Heravian J (1990)	Yes	Yes	Yes	Yes	No
Autzen T (1989)	Yes	Yes	Yes	Yes	Yes
Talylor M (1987)	Yes	Yes	No	Yes	Yes
Norcia A (1985)	No	Yes	Yes	Yes	No
Hittner H (1979)	Yes	Yes	Yes	Yes	No
Cohort study	**Accurate recruitment of study participants**	**Accurate measurement of exposure to minimum bias**	**Accurate measurement of outcome to minimum bias**	**Identification of confounding factors**	**Completed follow up**
Bin-Khathlan AA (2014)	Yes	Yes	Yes	No	Yes
Hsieh CJ (2012)	Yes	Yes	Yes	Yes	Yes
Chen T (2010)	Yes	Yes	Yes	No	Yes
Ng P (2008)	Yes	Yes	Yes	No	Yes
O'Connor A (2006)	Yes	Yes	Yes	No	Yes
O Connor A (2006)	Yes	Yes	Yes	No	Yes
Kirwan C (2005)	Yes	Yes	Yes	No	Yes
Cook A (2003)	Yes	Yes	Yes	Yes	Yes
Saunders K (2002)	Yes	Yes	Yes	Yes	Yes
Schalij-Delfos (2000)	Yes	Yes	Yes	No	Yes
Theng J (2000)	Yes	Yes	Yes	No	Yes
Friedman C (2000)	Yes	Yes	Yes	No	No
Holmstrom G (1999)	Yes	Yes	Yes	Yes	Yes
Holmstrom G (1998)	Yes	Yes	Yes	Yes	Yes
Fledelius HC (1996)	Yes	Yes	Yes	No	Yes
Theo SL (1995)	Yes	Yes	Yes	No	Yes
Lue CL (1994)	Yes	Yes	Yes	No	Yes
Pike M (1994)	Yes	Yes	Yes	Yes	No
Tucker SM (1992)	Yes	Yes	Yes	Yes	Yes

Bich D (1992)	Yes	Yes	Yes	Yes	No
Gallo J (1991)	Yes	Yes	Yes	No	No
Autzen T (1991)	Yes	Yes	Yes	No	Yes
Isenberg S (1990)	Yes	Yes	Yes	No	Yes
Nissenkorn (1983)	Yes	Yes	Yes	No	Yes
Case-control study	**Focusing a clearly question**	**Accurate recruitment of cases**	**Accurate selection of controls**	**Accurate measurement of exposure to minimum bias**	**Considering confounding factors**
Uva M (2011)	Yes	Yes	Yes	Yes	Yes
Heravian J (2011)	Yes	Yes	Yes	Yes	No
Larsson E (2003)	Yes	Yes	Yes	Yes	No
Isenberg S (1998)	Yes	Yes	Yes	Yes	Yes
Gallo J (1993)	Yes	Yes	Yes	Yes	No
Brown A (1986)	Yes	Yes	Yes	Yes	No
Fledelius H (1982)	Yes	Yes	Yes	Yes	No
Fledelius H (1981)	Yes	Yes	Yes	Yes	No

Table 2. Findings of included articles.

Study	Study design	Region	Sample	Age	Findings
Acar D (2015)	Cross sectional	Turkey	470	35.94±4.00 W	Both IOP and CCT values were found to be significantly higher in premature infants.
Bin-Khathlan AA (2014)	Cohort	Saudi Arabia	360	27±2.50 W	Esotropia and exotropia were diagnosed in 20% and 11% in premature infants, respectively.
Hsieh CJ (2012)	Cohort	Taiwan	109	30.40±2.04 W	The incidence and magnitude of significant refractive errors increased with severe ROP and with age.
Heravian J (2011)	Case Control	Iran	40	unavailable	Electroretinography can be applied to detect retinal anomaly and any disturbances in photoreceptors.
Uva M (2011)	Case Control	Italy	33	31±3.00 W	IOP measurements were slightly greater than in full-term newborns because of an increased CCT.
Chen T (2010)	Cohort	Taiwan	108	29.32±2.86	Comparison of refraction and optical components showed that the degree of myopia and astigmatism was higher in the ROP group. The degrees of myopia and astigmatism were higher in the ROP group than in the non-ROP group.
Ng P (2008)	Cohort	China	104	29.8 W	The IOP was significantly and negatively associated with postconceptional age.
O Connor AR (2006)	Cohort	United Kingdom	293	10-12 Y	There was a 1 diopter sphere shift in the MSE towards myopia over the 10–12 year period. Although those with severe ROP had the largest eyes, there was no significant association between birth weight and axial length.
O'Connor A (2006)	Cohort	United Kingdom	Unavailable	Unavailable	Premature infants, who are not routinely followed up, have a high risk of developing treatable refractive errors and strabismus.
Kirwan C (2005)	Cohort	Ireland	35	31W	Premature infants have thick corneas and small corneal diameters.
Cook A (2003)	Cohort	United Kingdom	68	29.4±1.87 W	Premature were myopes and became hyperopes towards the age. Premature infants has shorter AXLs, shallower anterior chambers, and more highly curved corneas.

Study	Study design	Region	Sample	Age	Findings
Rudanko S (2003)	Cross Sectional	Finland	125	23-36 W	Retinopathy of prematurity, optic atrophy, and cerebral amblyopia were the main diagnoses associated with visual impairment.
Larsson E (2003)	Case control	Sweden	217	10 Y	Significant refractive errors were 4 times more common in 10-year-old prematurely born children than in full-term controls.
Saunders K (2002)	Cohort	Ireland	59	31.6 W	Myopia and anisometropia were associated with prematurity. The early emmetropization process differed from that of the full term group.
Schalij-Delfos (2000)	Cohort	Netherland	130	Less than 37 W	Premature infants were known to have strabismus, amblyopia and refractive error in 5 years follow up.
Theng J (2000)	Cohort	Singapore	113	30.2 W	Premature babies with ROP had higher rates of myopia and strabismus than those without ROP.
Friedman C (2000)	Cohort	United state	93	27.2±1.8 W	Premature infants with ROP have lower mean serum inositol compared with those without ROP.
Holmstrom G (1999)	Cohort	Sweden	260	29 W	The overall incidence of subnormal vision and strabismus in children born prematurely was higher than in a full term population of the same age.
Holmstrom G (1998)	Cohort	Sweden	248	29 W	The risk of refractive errors is higher in preterm infants than in infants born at term, and also prematurely born infants without ROP do run an increased risk of having myopia and anisometropia.
Isenberg S (1998)	Case Control	United state	36	30-37 W	Reflex and basal tear secretion reduce in premature infants.
Fledelius HC (1996)	Cohort	Unavailable	88	31 W	There was a more curved cornea and a shorter axial length than expected from refractive value.
Theo SL (1995)	Cohort	Malaysia	113	32.1±2.5	Duration of oxygen therapy is significantly associated with development of ROP.
Laws D (1994)	Cross sectional	United kingdom	134	27±2.1 W	There is linear growth in axial length during the neonatal period in premature infants although axial length decreased with increasing stage of ROP.
Lue CL (1994)	Cohort	United state	87	Less than 30 W	Most of the premature infants with ROP have myopia and visual acuity is significantly poor in these patients.
Spierer A (1994)	Cross sectional	Israel	Unavailable	Unavailable	Intra ocular pressure is lower in premature infants.
Pike M (1994)	Cohort	Unavailable	42	35 W	Preterm cerebral insults may produce a variety of visual difficulties.
Gallo J (1993)	Case control	Unavailable	10	Unavailable	Higher keratometric diopter values were found in myopic premature children than in emmetropic full term children and myopic full term children.
Tucker SM (1992)	Cohort	Canada	70	25-37 W	Corneal diameter and total axial length showed parallel linear increases although no significant correlation were found between intra ocular pressure and gestational age.
Remon L (1992)	Cross sectional	Spain	152	Unavailable	The differences of central corneal thickness and peripheral corneal thickness between male and female babies and between right and left eyes were not statistically significant.
Bich D (1992)	Cohort	United state	81	30.4±1.5 W	Retinal function varies with dietary supply of omega 3 fatty acid in very low birth weight infants.
Gallo J (1991)	Cohort	Sweden	134	Less than 33 W	Children with a birth weight below 1000 g and a gestational age less than 30 weeks present the highest rate of regressed ROP.
Autzen T (1991)	Cohort	Denmark	13	Less than 33 W	There was no correlation between gestational age, birth length and weight and central corneal thickness.
Isenberg S (1990)	Cohort	United state	30	26 W	Mydriasis should not be considered indicative of a central nervous system disorder, and a pupil unresponsive to light should not be considered suggestive of blindness until a preterm infant reaches at least 32 weeks' postconceptional age.
Heravian J (1990)	Cross Sectional	Iran	50	Unavailable	VEP as an objective method can predict VA.
Autzen T (1989)	Cross Sectional	Denmark	30	Unavailable	There was no correlation between gestational age, birth weight, and CCT.

Study	Study design	Region	Sample	Age	Findings
Talylor M (1987)	Cross Sectional	Canada	75	22-42 W	The 22-23 week GA neonates had no identifiable waves. In all infants > 24 weeks a large negative wave is seen with a latency around 300 msec (N300). After 27 weeks GA a late positive wave was present (P400), but with more variable latency and morphology. Between 30 and 35 weeks GA a small positive wave (P200) was seen in over one-third of the neonates; this component was present in all infants > 36 weeks GA.
Brown A (1986)	Case Control	United state	Unavail-able	Unavailable	Visual acuity of infants at 39 to 40 weeks of gestational age was about 0.023 stripes per minute of arc, or 0.69 cycles per degree (20/866). Between 34 and 44 weeks of gestational age, visual acuity improved at the rate of 0.46 octaves per month.
Norcia A (1985)	Cross sectional	United state	197	1-53 W	This visual acuity estimate change from a mean of 4.5 c/deg during the first month to about 20 c/deg at 8- 13 months of age.
Nissenkorn (1983)	Cohort	Israel	155	Unavailable	Myopia were found in 50% of the premature infants with ROP, while only 16% myopic premature infants were found among those who did not have ROP.
Fledelius H (1982)	Case control	Denmark	70	Unavailable	Premature infants represent significantly lower value of corneal curvature radius.
Fledelius H (1981)	Case control	Denmark	137	Unavailable	As compared with low-birth-weight, full-terms show a significantly higher cumulated visual acuity score.
Hittner H (1979)	Cross sectional	United state	36	Unavailable	Keratometry demonstrated steeper corneal curvature in LBW populations, as compared to term newborns.

sphere equivalent was +0.67D±1.62 with 19% being myopic and 6.6% with high hypermetropia (13). On average, there was one diopter sphere shift in the mean sphere equivalent towards myopia (13). The mean J0 and J45 (power vector) was -0.04 and -0.03, respectively, and the cylinder power and its axis showed a little change (13). ROP increases the risk of anisometropia; although, ROP did not have an effect on presence of refractive errors in this cohort study (13). Prematurity and ROP can imperil emmetropization in infants (8). Steeper corneas and thicker lenses promote the focusing power of the eye leading to myopia. This myopia, which is not due to ROP, is of low degree and is referred to as 'myopia of prematurity' (17). Studies have shown that premature infants are more susceptible to all refractive errors including astigmatism, hypermetropia, and anisometropia than their term counterparts (17). Myopia associated with severe ROP progresses during the first 6 to 9 months of life and to a lesser extent thereafter, becoming relatively stable by around three years of age. However, mild myopia associated with prematurity has a later onset and progresses in severity until the teen age (8). At the age of five years, children with ROP were found to be bespectacled and have amblyopia and myopia more than non-ROP ones (18). Duration of oxygen supplementation and hospital stay were considered as important predictive factors for the development of amblyopia and refractive errors (18). Holström et al. (19,20) followed 248 infants for three and half years, and observed increased incidence of myopia, astigmatism, and anisometropia in premature infants. Different studies showed that the incidence of myopia was inversely associated with BW and GA, but positively with increased severity of ROP (5,13,21,22). Nearly all the premature infants with ROP of stage three or above were myopic; on the other hand, children with no ROP or stage one ROP showed similar prevalence of myopia, emmetropia, and hyperopia (5). Chen et al. reported that almost 70% of children had with-the-rule astigmatism, whereas oblique astigmatism was found in 25% of children, and less than 5% of children showed the against-the-rule astigmatism (5). Myopia group demonstrated the highest amount of astigmatism (-1.56 D), and emmetropia group showed the lowest amount of astigmatism (-0.80 D) (5). The probability of developing myopia or hypermetropia in preterm infants is higher than in term ones (23). Nissenkorn et al. indicated that premature infants are generally hyperopic, and subsequently become myopic (24). The incidence of myopia is significantly higher in infants with ROP, as compared to the ones without ROP (25). According to Fielder and Quinn study, myopia in premature infants is divided into three groups: 1) physiologic myopia; 2) myopia with preterm birth; and 3) ROP related myopia. (26). The prevalence of myopia differs and depends on following factors: preterm birth, low BW and GA, the severity of ROP, and emmetropization in early infancy (26). ROP was the main predictive factor for both astigmatism and anisometropia (27). O'Connor et al. proposed

two kinds of emmetropization in premature infants: 1) a gradual increase in refractive errors in those children with ROP treated in early childhood; and 2) the permanent refractive status in those with regressed ROP or without ROP (13). It was stated that myopia of prematurity tends to regress during the first year of life, resulting in emmetropic or hyperopic status; however, this shift does not occur with severe ROP. Arrested development of the anterior segment is the main cause of occurrence of myopia of prematurity. Low AXL to power ratio, shallow anterior chamber, and thick lenses are three basic characteristics of myopia of prematurity (28). Most premature infants become myopic as they grow, and ROP is the main cause of anisometropia. Amblyopia and with-the–rule astigmatism are more prevalent in premature infants, as compared to full term ones.

AXL

Although short AXL was reported by some studies, but AXL is expected to be larger in premature infants than term ones. The results of O' Conner study showed that there was no statistically significant relationship between ROP and AXL. Nonetheless, those with severe ROP had the largest eyes. Axial lengths were as follows: in preterm infant without ROP=22.51 mm, stage 1=22.41 mm, stage 2=22.39 mm, and stage 3/4=22.63 mm. In addition, there was no significant association between BW and AXL (13). Laws et al. (29) stated that severe ROP is associated with shorter AXL. AXL increase in a linear model at a rate of 0.16 mm per week, accordingly in four weeks, an infant's eyes grew by 0.64 mm (15).

Retina

Studies of retina in premature infants showed that topography of photoreceptors is affected by ROP, which consequently affects VA. Optic disc also gets involved in premature infants, and ROP is the main change in the retina. Law et al. (29) proposed two postulations: the retina in ROP (in premature infants) has dysfunctional abnormalities and affects eye growth; in addition, ROP can cease or delay the normal migration of the photoreceptors from the fovea, which causes a change in the microscopic topography of the central retina and consequently affect VA. This could change emmetropization mechanism. Macula is pigmented but undistinguishable on ophthalmoscopy up to 34 weeks postconceptional age (PCA). Macular annular reflex is differentiable by 36 weeks PCA, although the foveal light reflex is not clinically clear until 42 weeks PCA. The incidence of ROP is mostly observed in infants with lower GA and BW (25). Evidence showed that the highest incidence of ROP occurs at the 24 weeks of gestation, and the lowest ROP is found in the >32 weeks of gestation (30). Retinopathy of prematurity was significantly more common when mechanical ventilation continued for more than two weeks (11). Friedman et al. (31) in the United States have reported that oxygen therapy for more than 30 days was associated with ROP. Teoh et al. (32) in Malaysia demonstrated that infants receiving oxygen every day were at risk of ROP 1.156 times more than other neonates, and that oxygen therapy for more than 30 days resulted in a more than 90% chance of ROP. Sabzehi et al. also stated that oxygen therapy for more than five days is a risk factor in progress of the ROP (33).

Strabismus

Studies regarding strabismus indicate that ROP is the principal cause for high incidence of ocular misalignment; and, esotropia and pseudo-strabismus are more common among other ocular misalignments. ROP has widespread effects on ocular structure and function, including refractive errors, and also increase the risk of abnormalities of ocular alignment (strabismus) (8). At the age of five years, infants with ROP were found to have strabismus more than infants without ROP (18). Holström et al. followed 248 infants for three and half years and found increased incidence of strabismus in premature neonates, as compared to full-term ones (19,20). Bin-khaltan et al. diagnosed squint in 36 infants with a cumulative incidence of 14% and mean GA of 27 weeks (GA range: 23–34 weeks). Esotropia was diagnosed in 20% of the ROP group and 5.5% of the non-ROP group. Exotropia diagnosis was made in 4% of infants with an incidence of 11% and 2% in the ROP and non-ROP groups, respectively (30). Ocular misalignment is more prevalent in premature infants (BW< 1500 g or GA<34 weeks) compared with normal infants. The prevalence of strabismus was 25% and 9.8% in the ROP and non-ROP groups, respectively in three years of follow-up (25).

Intraocular pressure

Several studies have demonstrated higher intraocular pressure values in premature infants (34,35); however, lower intraocular pressure measures have also been reported (36). On the other hand, some studies reported that intraocular pressure appears to be normal in premature infants (37).

Cornea

Majority of studies found higher central corneal thickness (CCT) values in premature infants (34,35). Uva et al. observed a strong negative

correlation between PCA and CCT (35).

Researchers determined that the corneal thickness of premature newborns at three months of age decreased significantly (to the same level as full-term newborns) (38,39). A significant decrease in CCT has been found up to 40th weeks, with no significant decline in CCT after that point. Corneal hydration, corneal evaporation, and corneal remodeling were considered as possible factors responsible for decrease in CCT during the first week of life (35,39-41). Keratometry demonstrated steeper corneal curvature in LBW populations, as compared to term newborns (42-44).

Visual acuity (VA)

It has been stated that both VA and contrast sensitivity are reduced in premature infants due to ROP, retinal changes, and neurological factors. A correlation between reduced VA and low GA was also found. There was a significant difference between the mean VA of eyes with ROP and the eyes without ROP. Poor vision (<0.5 logMAR) was common in eyes with severe ROP, while good vision (>0.2 logMAR) was mostly observed in eyes without ROP. Effective factors for reduced VA include GA, BW, intraventricular hemorrhage, degree of ROP, cryotherapy, and spherical equivalent. Intraventricular hemorrhage, obvious neurological sequelae, and degree of ROP, particularly cryotreated ROP, were proved to be important factors affecting VA of the eyes. ROP may not be the only cause of impaired VA in prematurely born children, but neurological complications may have a considerable effect on this problem (20). The very low BW children had significantly poorer contrast sensitivity than normal BW ones. Measured preferential looking (PL) acuity as early as 32 weeks PCA was about 20/2000, which improved to about 20/400 at 42 weeks PCA, 20/150 at 57 weeks PCA, and 20/60 by 92 weeks PCA. Mature acuity (20/20) is achieved after three years of age (45).

Tear

Premature infants showed reduced tear secretion in both basal and reflex tears in comparison with full-term infants (46).

Pupil

Pupils of preterm infants (less than 31 weeks PCA) are only about 4 mm in diameter, and do not respond to light (47).

Electroretinography

Heravian et al. reported that retinal neurotransmitters have a major role in generating retinal responses. They also demonstrated that electroretinography (ERG) can be applied to detect retinal anomaly and any other disturbances in photoreceptors (48). The result of ERG shows significant immaturity in amplitude and implicit time at 36 weeks PCA. The response develops fast in healthy preterm infants, as by 57 weeks PCA, the amplitude and implicit time reach the adult values. Cone responses improved in the perinatal period. Cone response and 30 Hz flicker cone response approach the adult responses at 57 weeks PCA; however, rod responses mature at a slower rate. Rod response shows a reduction in amplitude at 34–36 weeks PCA. Even at 57 weeks PCA, substantial immaturity of the rod response is also present (49).

VEP

Studies showed that latency and VEP acuity decrease in premature infants. Flash VEPs have been incorporated from premature infants at 24 weeks PCA and only a long latency negative peak is declared (50). The latency of the positive peak reduces from about 220 msec at 34 weeks PCA to 190 msec at 40 weeks PCA, and to 120 msec by 52 weeks PCA. Transient pattern reversal VEPs have been recorded from premature infants at 30 weeks PCA and the results showed that the pattern reversal response comprises a single positive peak with a latency of about 330 msec. Latency declines to 240 msec by 40 weeks PCA and 125 msec by 53 weeks PCA. VEP as an objective method could be useful in prediction of VA (51). The earliest VEP acuity reports were from infants at 36 weeks PCA; at this age, VEP acuity is about 20/200. VEP acuity matures rapidly to about 20/60 at 57 weeks PCA and to 20/30 by 66 weeks PCA (52).

Cortical visual impairment

Cortical visual impairment is more prevalent among preterm infants, which might be associated with congenital infections or malformations and neurological disorders. Severe intraventricular hemorrhage is strongly associated with poor acuity. In cases with normal acuity outcomes, other visual problems such as strabismus or nystagmus may be present. Premature infants with cortical visual impairment have abnormal flash VEPs, pattern VEPs, or both (53).

Conclusion

In conclusion, the prevalence of visual impairment is more in preterm infants because of ROP and perinatal brain lesions. Myopia is a prevalent refractive error in premature infants due to large AXL. VA, VEP acuity, and contrast sensitivity decrease due to ROP. Esotropia is the most common form of strabismus in premature

infants. Corneal assessment illustrated that corneal curvature is steeper, and CCT is lower in premature infants, as compared to term infants. There was no statistically significant difference between male and female infants in any of the measured variables at any point of time. Careful evaluation of infants with GA of 32 weeks or less for any prematurity-induced ocular changes is recommended.

Conflict of Interest

The authors declare no conflict of interest.

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