# Evaluation of Strabismus and Refractive Status in Premature Infants at Risk for Retinopathy of Prematurity

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**Purpose:** The aim of our study was to evaluate strabismus and refractive aspects in premature infants at risk of developing retinopathy of prematurity.
**Material and method:** All infants with gestational age less than 34 weeks and birth weight below 2000 g who were born or transferred to the Neonatology Intensive Care Unit or who were hospitalized in the Premature Neonatology Clinic of Tîrgu Mureş between January 2008 and March 2009, were enrolled in a prospective study regarding the development of strabismus and refractive errors. Patients were subdivided in three groups: group A – prematures without retinopathy of prematurity, group B – prematures with spontaneously regressed retinopathy of prematurity and group C – prematures with laser treated retinopathy. The first examination was performed at 4 to 6 weeks after birth, followed by others depending on eye fundus appearance, until complete vascularization of retina, or involution of retinopathy occurred. Complete ophthalmological assessment took place at 6 months, and 3 years.
**Results:** Of the 240 eyes of 120 premature infants included in our study, the incidence of retinopathy was recorded in 20%. At 3 years follow-up, the overall incidence of myopia was 6.3%, hyperopia was noticed in 85%, astigmatism in 8.75%, while strabismus appeared in 11.3% of the studied eyes. The incidence of myopia, astigmatism and strabismus was higher in eyes with retinopathy of prematurity, particularly in laser treated eyes, while higher hyperopia appeared in eyes without retinopathy.
**Conclusions:** Premature babies with retinopathy of prematurity have higher rates of strabismus and refractive errors, particularly myopia. Long-term follow-up of these babies is mandatory for early detection and treatment of these ocular problems.

**Keywords:** astigmatism, hyperopia, myopia, preterm infants, strabismus

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## Introduction

Retinopathy of prematurity (ROP) is not only one of the most common cause of blindness in children worldwide, but due to early or delayed complications it represents one of the major causes of visual loss. In addition to the complications in the acute phase of ROP (especially retinal detachment), the following complications may occur after 1 to 30 years:

A. Structural complications:
- late retinal detachment;
- macular dragging with macular heteropia;
- retinal folds;
- lattice like degeneration;
- retinal tears.

B. Functional complications:
- strabismus;
- nistagmus;
- refractive errors;
- amblyopia;
- decreased visual acuity;
- visual field changes;
- secondary glaucoma.

due to these complications, careful follow-up of prematures with risk of ROP is required, on regular basis, more frequently for the youngest children and at least once per year for older ones.

## Material and method

During January 2008 – January 2012 all preterm infants born or transferred to the Neonatology Intensive Care Unit, as well as those admitted to the Tîrgu Mureş Premature Neonatology Clinic and presented risk of developing ROP underwent screening. Among them, those who were born between January 2008 and March 2009 were evaluated in terms of strabismus and refractive errors at the age of 6 months, and 3 years.

In our study, the eligibility criteria were:
- premature newborns with gestational age (GA) ≤34 weeks and birth weight (BW) ≤2000 g,

and as exclusion criteria we used:
- premature newborns with GA >34 weeks and/or BW >2000 g;
- premature newborns with GA ≤34 weeks and BW ≤2000 g who have missed one or more follow-up controls;
- preterm infants with congenital anomalies;
- on term newborn.

According to the presence and severity of ROP disease, the study population was divided into three groups, as follows:
- group A – prematures without ROP;

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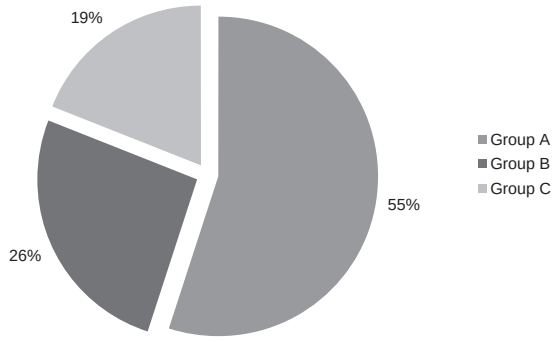


Fig. 1. Incidence of strabismus at 6 months

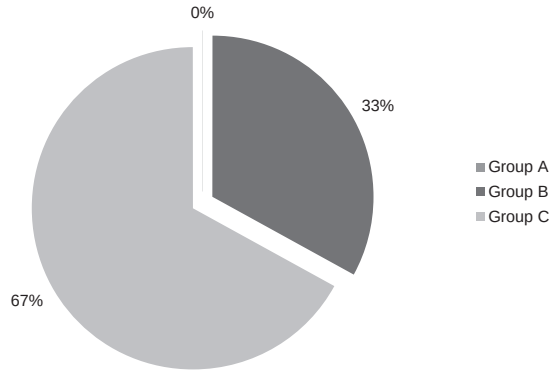


Fig. 2. Incidence of myopia at 6 months

– group B – prematures with spontaneously regressed ROP;
– group C – prematures with laser treated ROP.

Follow-up assessment included orthoptic exam, cycloplegic refraction (skiascopy and autorefractometry) and ophthalmoscopy.

The clinical data were evaluated using the chi-square test. Differences were considered to be statistically significant for p values smaller then 0.05.

## Results

Our lot of premature babies evaluated until the age of three years included 120 children (240 eyes), representing 82.75% of all prematures who were born between January 1, 2008 and March 31, 2009 (145 newborns) and presented risk for developing ROP. From a total of 240 eyes, 48 eyes (20%) have developed various stages of ROP, while the rest of 192 eyes (80%) did not have any type of retinopathy of prematurity. From the eyes with ROP, in 75% of our cases, ROP regressed spontaneously, while 25% of them required laser therapy. Therefore, the overall incidence of laser treated eyes was 5% with a positive result after treatment – a regression of active ROP.

### The first assessment (at 6 months)

Ophthalmologic examination at 6 months revealed an overall strabismus incidence of 11.3% (27 eyes). Among them, 55% (15 of 27 eyes) were eyes without ROP, 26% (7 of 27 eyes) were patients with spontaneously regressed ROP and 19% (5 of 27 eyes) were cases with laser treated ROP (Figure 1).

Myopia occurred in 5% (12 eyes), with an incidence of 0% in eyes without ROP, 33% (4 of 12 eyes) in those with spontaneously regressed ROP and 67% (8 of 12 eyes) in those with laser treated ROP (Figure 2). Mean equivalent spheric (MES) of myopia was –1.00 D for those with spontaneously regressed ROP, and –7.625 D for the laser treated group.

Hyperopia occurs with an overall incidence of 86.3% (207 of 240 eyes). The highest incidence of hyperopia was found in the group without ROP (94.8%, 182 of 192 eyes). For the regressed ROP group, the incidence of hyperopia was 69.4% (25 of 36 eyes), while hyperopia wasn't noticed in patients with laser treated ROP.

### The second assessment (at 3 years)

At the age of 3 years, we recorded strabismus in 10.8% of the eyes (26 of 240 eyes). The incidence slightly decreased in those without ROP – 6.8% (13 of 192 eyes) and had slightly increased in patients with regressed ROP – 22.2% (8 of 36 eyes), while in the treated group it remained constant – 41.7% (5 of 12 eyes)(Figure 3 and 4). Regarding the type of strabismus, 92.6% (25 of 27 eyes) had conver-

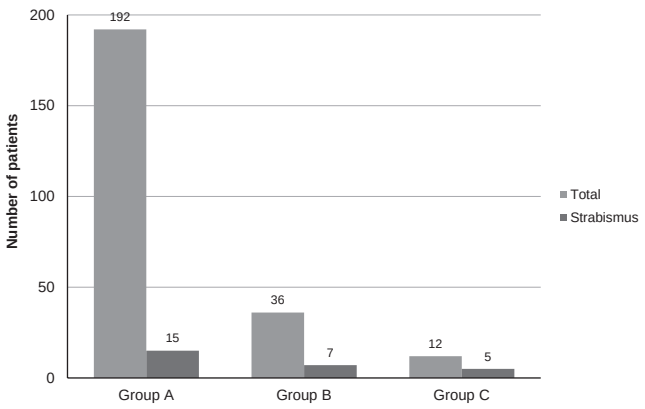


Fig. 3. Incidence of strabismus at 6 months

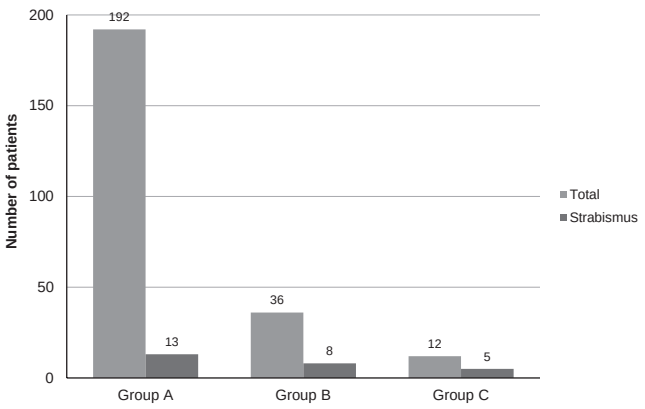


Fig. 4. Incidence of strabismus at 3 years

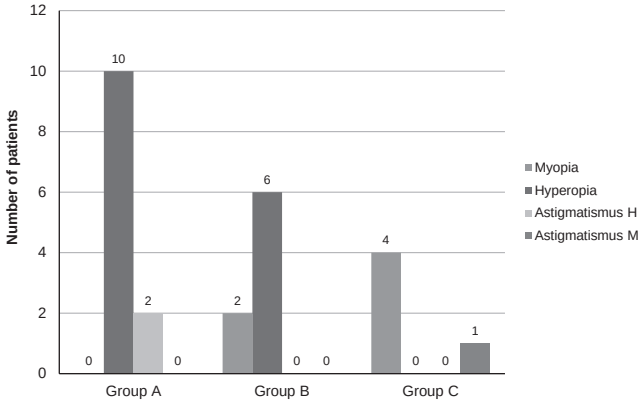


Fig. 5. Association of strabismus with refractive errors

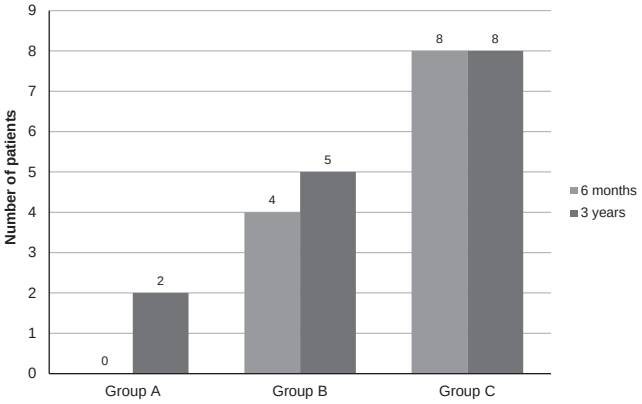


Fig. 6. Incidence of myopia at 6 months and 3 years

gent strabismus, while divergent strabismus was present in 7.4% of cases (2 eyes).

Regarding the association of strabismus with refractive errors, we noticed a close correlation between them. Thus, in patients without ROP and in those with regressed ROP hyperopia prevailed (83.3% and 75% respectively), while myopia was frequently associated with strabismus in the laser treated group (80%) (Figure 5).

The incidence of myopia at the age of three has slightly increased compared to values recorded at 6 months, to 6.3% (15 of all studied eyes). In patients with regressed ROP we found an increased incidence of myopia (13.9%, 5 of 36 eyes) compared to that at 6 months, while for those without ROP or who received laser treatment it remained constant (1% and 66.7% respectively) (Figure 6). Mean equivalent spheric of myopia was –0.75 D in patients without ROP, –1.00 D for spontaneously regressed ROP cases and –8.00 D in laser treated infants.

At the age of three, 85% (204 eyes) had hyperopia, the incidence being slightly smaller compared to the incidence at 6 months, both in the group without ROP (93.8%, 180 of 192 eyes) and in the group with regressed ROP (66.7%, 24 of 36 eyes). At this age, we haven't found any case of hyperopia among those with laser treated ROP (Figure 7).

Astigmatism was most properly evaluated at the age of 3 years, by using the autorefractometry method, which gives more accurate values compared with skiascopy used at 6 months. The overall incidence of astigmatism noticed in our study was 8.8% (21 eyes). Among them, 68% were recorded in patients included in the group without ROP, 23% were observed in cases with regressed ROP and 9% in laser treated group (Figure 8).

## Discussions

### 1. Strabismus

For a baby younger than 6 weeks it is impossible to diagnose strabismus, due to the lack of coordination in the eye movements [1]. For a good visual development it is essential to correct strabismus during childhood by medical or surgical means. The rising of the incidence of strabismus in premature infants is confirmed by numerous studies [2,3,4], being attributed to the following distinctive or associated conditions:

– the presence of ROP [5,6];
– the rising incidence of refractive errors [7];
– associated neurological damage [8].

We found an incidence of strabismus of 11.3% at the first assessment (at the age of 6 months) and 10.8% at the second assessment (children aged 3 years). These percentages are similar to those reported by Schaffer et al. [9] and by Robinson et al. (11–12%) [10]. Other international studies showed higher incidence of strabismus

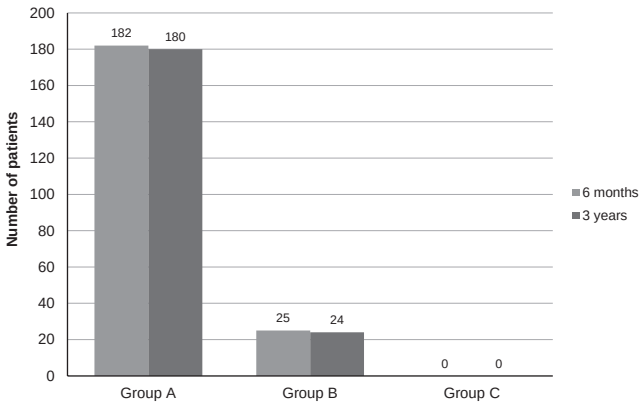


Fig. 7. Incidence of hyperopia at 6 months and 3 years

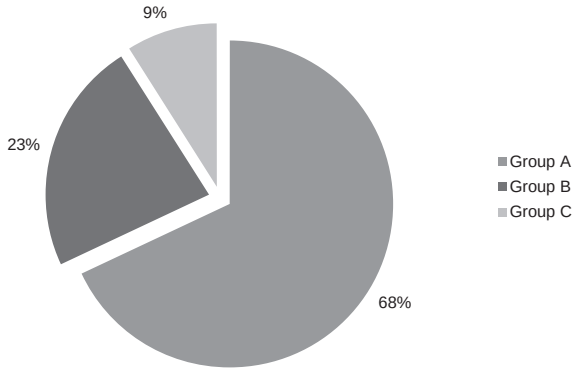


Fig. 8. Incidence of astigmatism at 3 years

(12.5–24.1%) among premature infants at risk for ROP [11,12,13].

Comparing the incidence of strabismus at 6 months and at 3 years in the ROP group (25%, respectively 27%) and within the non-ROP group (7.8% at 6 months and 6.8% at 3 years) a statistically significant association between the presence of ROP and the development of strabismus is ascertained ($p = 0.0007$). Therefore, ROP is a risk factor for strabismus appearance. This result is in concordance with other studies. Thus, Darlow et al. [6] found an incidence of strabismus of 19% in infants without ROP and 33% in those with ROP (a sample of 338 prematures). Bremmen et al. [5] reported an incidence of 3.78% strabismus in cases without ROP and 18.63% in ROP patients, while Cats et al. [18] showed that the incidence of strabismus ranged from 23–47% in infants with ROP compared with 10–20% for premature infants without ROP. Instead, Robinson et al. [10] reported a greater incidence of strabismus in the group without ROP (25%) compared with the ROP group (20%), hence no significant association between strabismus and ROP.

In terms of therapy influence on strabismus development, our study shows that there is no significant association between the applied treatment and strabismus ($p = 0.124$).

Strabismus evaluation data across ages show that at 3 years, from the eyes without ROP, two eyes had no strabismus, while a case has yet occurred in infants with regressed ROP. All of the ROP treated children have developed a non-accommodative strabismus at the age of 6 months which remained constant even at 3 years. Accommodative strabismus (associated with hyperopia >3.00 D) was recorded with increased frequency in the non-ROP group. Instead, in the ROP group, non-accomodative strabismus prevailed in association with more frequent myopia and astigmatism aspects.

## 2. Refractive status

### *Myopia*

While in early childhood, there is a high incidence of hyperopia in babies born at term, and with eye growth emmetropia occurs [14], in premature infants there is usually an increased incidence of myopia [15].

Allistair et al. [16] reported that there are three types of myopia associated with prematurity:

1. physiological and temporary – lasting from birth until the age of 40–42 weeks, due to a smaller anterior chamber (CA), an increased corneal curvature and a wider crystalline lens. In utero, the flattening of the cornea occurs between 27–40 weeks, so in premature infants the lack of flattening translates into an increase in corneal refractive power.
2. myopia of prematurity – which appears due to failure of anterior segment development, being independent of the presence of ROP. Its features are: shorter ocular axis compared to the refractive power of the eye, smaller CA and more spherical crystalline lens.
3. myopia caused by severe ROP – it seems to be due mainly to structural changes than to applied therapy. It can occur in the whole range of strength, from lower myopia to very high myopia and appears to be stable in early childhood, unlike other types of myopia which are not related to prematurity.

Besides myopia, there are other refractive errors, such as astigmatism, anisometropia (the optical power difference between the two eyes is greater than 2.00 D), which can be found with higher frequency in pre-term infants compared to term babies [17]. In our study, the overall incidence of myopia was 5% at 6 months and 6.3% at 3 years. Holmstrom [2] reports similar incidences for myopia, 8% at 6 months and 10% at 30 months, while Tuppurainen et al. [12] have found an incidence of 8.6% at 6 months. Our study shows a major difference between children with and without ROP in terms of myopia incidence. Thus, for the group without ROP the incidence of myopia at 6 months and 3 years was 1%, while for the group with ROP (both regressed and treated cases) the incidence of myopia was significantly higher: 25% at 6 months and 27% at 3 years. Other studies [18,19] have reported an incidence of 29–50% for the ROP group and 10–15% for the group without ROP, while Robinson [10] in a british study from 1993 noticed an incidence of myopia of 27.5% for the ROP group and 8.8% for the non-ROP group.

By comparing the incidence of myopia between the group of patients with spontaneously regressed ROP versus the group with laser treated ROP, we observed higher values of incidence for the treated group: 66.7% vs. 11.1% (at 6 months) and 66.7% vs. 13.8% (at 3 years), hence a statistically significant association between myopia and laser treatment ($p = 0.0004$). Holmstrom et al. [2] also report an increased value for the incidence of myopia at laser treated patients, namely 40–50%, while Pozzi [20] reported 55.6%. As well, the association between myopia and laser treatment is sustained by the study of Hsieh et al. [21]. On the other side, Choi et al. assume that some structural changes rather than laser treatment are the main causes of myopia appearance [19].

Medium and high myopia (>3.00 D) was seen only at laser treated ROP group with a mean spherical equivalent refraction of –7.625 D at 6 months, and –8.00 D at 3 years. In patients with regressed ROP, mean spherical equivalent was –1.00 D at 6 months, value observed at 3 years as well. The correlation of refractive results in both groups of patients showed an increase in the amount of high degree myopia in laser treated eyes.

### *Hyperopia, astigmatism, anisometropia*

The incidence of hyperopia in our study was 86.3% at 6 months and 85% at 3 years. This increased incidence of hyperopia can be explained by the large number of eyes without ROP (192 of 240 eyes), which had a rate of 93.8%

hyperopia. Our result is similar to that found by Kamm et al. [22] (95%), but much higher than other studies, such as that of Darlow et al. [6], which show an incidence of only 18% of hyperopia. In our study, none of laser treated eyes have presented hiperopia, all of them were myopic. Instead, Pozzi et al. [20] found an incidence of hyperopia of 33.3% in laser treated group. There is a statistical significant difference between the incidences of hyperopia in the group without ROP compared with the regressed ROP group ($p < 0.001$), hence the occurrence of retinopathy predisposes to a less hyperopic eye.

Overall incidence of astigmatism at the age of 3 years was 8.8%. These results are lower compared to other studies [2,6,12], which recorded astigmatism incidence between 11–42%. The presence of ROP and laser treatment are significantly correlated with the appearance of astigmatism ($p < 0.001$). This aspect can be explained by the changes in the axial eye which occur due to structural changes caused by laser scars. In a study from 2009, Davitt et al. [23] reported that the incidence of astigmatism has increased from 32% at 6 months to approximately 42% at 3 years. Nearly 43% of eyes treated at high-risk prethreshold ROP developed astigmatism ≥1.00 D and nearly 20% had astigmatism ≥2.00 D.

## Conclusions

There is an increased incidence of refractive errors and strabismus in premature infants at risk for retinopathy of prematurity.

A thorough follow-up of these children, especially in the first year of life and in early childhood is mandatory.

The main purpose of screening and adequate therapy is that of obtaining a visual function closer to normality.

## References


1. Mills MD. The Eye in Childhood. Am. Fam. Physician. 1999;60(3), 907-916.
2. Holmström G, Rydberg A, Larsson E. Prevalence and development of strabismus in 10-year-old premature children: a population-based study. J Pediatr Ophthalmol Strabismus. 2006;43(6):346-352.
3. O'Connor AR, Stephenson TJ, Johnson A, Tobin MJ, Ratib S, Fielder AR. Strabismus in children of birth weight less than 1701g. Arch Ophthalmol. 2002;120(6):767–773.
4. Pennefather PM, Clarke MP, Strong NP, Cottrell DG, Dutton J, Tin W. Risk factors for strabismus in children born before 32 weeks' gestation. Br J Ophthalmol. 1999;83:514-518.
5. Bremer DL, Palmer EA, Fellows RR, Baker JD, Hardy RJ, Tung B et al. Strabismus in premature infants in the first year of life. Arch Ophthalmol. 1998;116:329-333.
6. Darlow BA, Clemett RS, Horwood J, Mogridge N. Prospective study of New Zealand infants with birth weight less than 1500g and screened for ROP: visual outcome at age 7-8 years. Br J Ophthalmol. 1997;81(11):935-940.
7. Kushner BJ. Strabismus and amblyopia associated with regressed ROP. Arch. Ophthalmol. 1982;100:256-261.
8. Holmström G, Azzazi M, Kugelberg U. Ophthalmological follow up of preterm infants: a population based, prospective study of visual acuity and strabismus. Br J Ophthalmol. 1999;83(2):143-145.
9. Schaffer DB, Quinn GE, Johnson L. Sequelae of arrested mild retinopathy of prematurity. Arch Ophthalmol. 1984;102(3):373-6.
10. Robinson R, O'Keefe M. Follow-up study on premature infants with and without retinopathy of prematurity BritishJournal of Ophthalmology. 1993;77:91-94.
11. Ricci B. Refractive Errors and Ocular Motility Disorders in Preterm Babies with and without Retinopathy of Prematurity. Ophthalmologica. 1999;213 (5):25-26.
12. Tuppurainen K, Herrgård E, Martikainen A, Mäntyjärvi M. Ocular findings in prematurely born children at 5 years of age. Graefe's Archive for Clinical and Experimental Ophthalmology. 1993;231(5):261-266.
13. Pennefather PM, Clarke MP, Strong NP, Cottrell DG, Fritz S, Tin W. Ocular outcome in children born before 32 weeks gestation. Eye (Lond). 1995;9:26-30.
14. Jenny M, Dana Robaei, Annette Kifley, Jie Jin Wang, Kathryn A. Rose, Paul Mitchell. Prevalence of Hyperopia and Associations with Eye Findings in 6- and 12-Year-Olds. Ophthalmology. 2008;115(4):678-685.
15. Larsson EK, Rydberg AC, Holmstrom GE. A population-based study of the refractive outcome in 10-year-old preterm and full-term children. Arch Ophthalmol. 2003;121(10):1430-1436.
16. Fielder AR, Quinn GE. Myopia of prematurity: nature, nurture, or disease? Br J Ophthalmol. 1997;81:2-3. doi:10.1136/bjo.81.1.2
17. Burgess P, Johnson A. Ocular defects in infants of extremely low birth weight and low gestational age. British Journal of Ophthalmol. 1991;75(2):84-87.
18. Cats B, Tan K. Prematures with and without regressed retinopathy of prematurity comparison of long-term (6-10 years) ophthalmological morbidity. Pediatr Ophthalmol Strabismus. 1989;26:271-5.
19. Choi MY, Park IK, Yu YS. Long term refractive outcome in eyes of preterm infants with and without retinopathy of prematurity: comparison of keratometric value, axial length, anterior chamber depth, and lens thickness. Br J Ophthalmol. 2000;84:138-143.
20. Pozzi S, Provenzano L, Boni D, Branco AC, Moraes N, Farah M. Retinopathy of prematurity: refractive errors in patients treated with cryotherapy or laser. Arq Bras Oftalmol. 2000;63(5):403-6.
21. Hsieh Cj, Liu Jw, Huang Js, Lin Kc. Refractive outcome of premature infants with or without retinopathy of prematurity at 2 years of age: A prospective controlled cohort study. Kaohsiung Journal of Medical Sciences. 2012;28(4):204-211.
22. Gunton KB, Nelson LB, Olitsky SE. Ocular Development in Childhood. Harley's Pediatric Ophthalmology. 2005:57-58.
23. Davitt BV, Quinn GE, Wallace DK, Dobson V, Hardy RJ, Tung B, Lai D, Good WV. Early Treatment for Retinopathy of Prematurity Cooperative Group. Astigmatism progression in the early treatment for retinopathy of prematurity study to 6 years of age. Ophthalmology. 2011;118(12):2326-9.