UOT: 617.735-053.32

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# COMPLICATIONS OF RETINOPATHY OF PREMATURITY

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## SUMMARY

**Purpose** – to study the prevalence and treatment of complications of retinopathy of prematurity.

**Materials and methods**

The study included 636 babies with retinopathy of prematurity (ROP) who received treatment at the Perinatal Center, Scientific Research Institute of Pediatrics named after prof. K.Farajova, Scientific Research Institute of Obstetrics and Gynecology, and applied to the National Centre of Ophthalmology named after acad. Zarifa Aliyeva in 2015-2020. The average weight of these children was 1521,5±15,0 grams, and the average gestational age was 30,9±0,1 weeks.

**Results**

In this study, the listed complications were found in children with ROP: Strabismus 5,97%, glaucoma 0,47%, high myopia 5,35%, astigmatism 12,42%, other refractive errors 4,56%, retinal detachment 7,55%, other retinal disorders 6,29%, cerebral vision impairment 3,46%.

**Conclusion**

Detection of ROP in premature children and the organization of correct and timely examination and treatment prevent such complications that may arise in the future.

**Key words:** *retinopathy of prematurity*

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# VAXTINDAN ƏVVƏL DOĞULMUŞLARIN RETİNOPATİYASININ FƏSADLARI

## XÜLASƏ

**Məqsəd** – vaxtından əvvəl doğulmuşların retinopatiyasının ağırlaşmalarının yayılması və müalicəsini öyrənmək.

**Material və metodlar**

Tədqiqata 2015-2020-ci illərdə Perinatal Mərkəz, Elmi-Tədqiqat Mamalıq və Ginekologiya İnstitutu, prof. K.Fərəcova adına Elmi-Tədqiqat Pediatriya İnstitutunda müalicə alan, eləcə də Akademik Z.Əliyeva adına Milli Oftalmologiya Mərkəzinə müraciət edən 636 vaxtından əvvəl doğulmuşların retinopatiyasının (VDR) olan uşaq daxil edilmişdir. Bu uşaqların orta çəkisi 1521,5±15,0 qram, orta hamiləlik müddəti isə 30,9±0,1 həftə olub.

**Nəticə**

Bu tədqiqatda VDR olan uşaqlarda aşağıdakı fəsadlar aşkar edilmişdir: çəpgözlük 5,97%, qlaukoma 0,47%, yüksək miopiya 5,35%, astiqmatizm 12,42%, digər refraktiv qüsurlar 4,56%, tor qişanın qopması 7,55%, digər retinal patologiyalar 6,29%, serebral görmə pozğunluqları 3,46%.

**Yekun**

Vaxtından əvvəl doğulmuş körpələrdə VDR-in müəyyən edilməsi, düzgün və vaxtında müayinə, müalicənin təşkili gələcəkdə yarana biləcək belə fəsadların qarşısını alır.

**Açar sözlər:** *vaxtından əvvəl doğulmuşların retinopatiyası*

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# ОСЛОЖНЕНИЯ РЕТИНОПАТИИ НЕДОНОШЕННЫХ

РЕЗЮМЕ

**Цель** – изучить распространенность и лечение осложнений ретинопатии недоношенных.

**Материалы и методы**

В исследование были включены 636 детей с ретинопатией недоношенных (РН), проходивших лечение в Перинатальном центре, НИИ педиатрии имени проф. К.Фараджовой, НИИ акушерства и гинекологии, а также обратившихся в Национальный Центр Офтальмологии имени акад. Зарифы Алиевой в 2015-2020 годах. Средний вес этих детей составил 1521,5±15,0 грамм, а средний срок беременности – 30,9±0,1 недели.

**Результаты**

В данном исследовании у детей с РН выявлены перечисленные осложнения: косоглазие 5,97%, глаукома 0,47%, миопия высокой степени 5,35%, астигматизм 12,42%, другие аномалии рефракции 4,56%, отслойка сетчатки 7,55% и другие патологии сетчатки 6,29%, нарушения церебрального зрения 3,46%.

**Заключение**

Выявление РН у недоношенных детей, организация правильного своевременного обследования и лечения предупреждают возможные будущие осложнения заболевания.

**Ключевые слова:** *ретинопатия недоношенных*

Retinopathy of prematurity (ROP) is a vasoproliferative disorder that affects normal retinal vascularization. ROP is a rapidly progressive disease characterized by abnormal retinal vascularization and fibrosis that can result in blindness. This disease is one of the main causes of childhood blindness in developed countries [1, 2].

The most important factor in preventing the complications of ROP is a proper screening program. Although spontaneous regression occurs in the acute period or regression is achieved with on time treatment, it is a lifelong disease with its complications. These complications are anatomical and functional.

In order to detect the disease early, premature babies should be examined at scheduled times depending on their gestational age. The time of the first examination children of which born between 22-27 weeks is when they reach the 31st week and 4 weeks after birth in those born 28-32 weeks [3, 4]. Neovascularization, vitreous hemorrhages, and vitreoretinal tractions, eventually resulting in irreversible blindness, occur in eyes with ROP that are not treated on time. Also, anatomical and functional disorders of the eye – poor visual acuity, color blindness, contrast sensitivity disorders, defects of the visual field, myopia, strabismus, anterior segment anomalies, peripheral degenerations and tears of the retina are found in premature children [5]. All over the world, among the causes of disability at an early age, diseases of the visual analyzer occupy one of the first places. The CNS (cerebral palsy, 60%) and vision analyzer (poor vision, retinopathy of prematurity – ROP, 30%) are the most damaged organs and systems as a consequence of premature births. Even if ROP is not found in children born prematurely, visual acuity and contrast vision are poorer than those born at normal time. This condition also applies to children with stage 1 and 2 ROP detected, spontaneously regressing, and lasts up to 12 years. In a study comparing the visual function of preterm and full-term children at 10 years of age, visual acuity was poorer in both ROP and preterm children due to neurological reasons. It is caused by the fovea not developing normally [6, 7].

**Purpose** – to study the prevalence and treatment of complications of retinopathy of prematurity.

**Materials and methods**

The study included 636 babies with ROP – who received treatment at the Perinatal Center, Scientific Research Institute of Pediatrics named after prof. K.Farajova, Scientific Research Institute of Obstetrics and Gynecology, and applied to the National Centre of Ophthalmology named after acad. Zarifa Aliyeva

in 2015-2020. The average weight of these children was 1521.5±15.0 gr, the average gestational age was 30.9±0.1 weeks. During the years of our research, blind children who applied to the National Ophthalmology Center named after Academician Z. Aliyeva on the 5th stage of the ROP were registered. The first stage of examinations was carried out while those children were treated in the intensive care unit or the pathology department of premature babies. Examinations were performed on dilated pupil and under local anesthesia (oxybuprocaine or proparacaine hydrochloride 0.5% instillation) using a pediatric lid speculum. Peripheral parts of the retina were examined with the opposite forehead ophthalmoscope and 20 D, 28 D lenses, optic disc and macula, and then scleral indentation (depression). To determine the stage of the disease, the all avascular parts of the retina were examined. Babies underwent their next examination at the National Ophthalmology Center in the second stage. Refractometry, biomicroscopy, fundus contrast ophthalmoscopy, ERQ examinations were performed on all children. All children included in the study (children without retinopathy until complete revascularization, and those with retinopathy until complete regression) were observed. Patients diagnosed with ROP were observed for 1-3 weeks until the disease regressed, depending on the stage of the disease and localization in the retina. In cases where treatment was indicated, treatment was carried out within 3 days.

**Results and discussion**

We have presented the 5 stages of the typical ROP and the prevalence of the A-ROP form among children in table 1.

The complications of ROP that we found during the years of the study are shown in the diagram below (fig.1).

Table 1

**Prevalence of ROP**

| ROP | Number | % |
|---|---|---|
| A-ROP | 31 | 4,9% |
| Stage 1 | 406 | 63,8% |
| Stage 2 | 99 | 15,6% |
| Stage 3 | 50 | 7,9% |
| Stage 4 | 2 | 0,3% |
| Stage 5 | 48 | 7,5% |

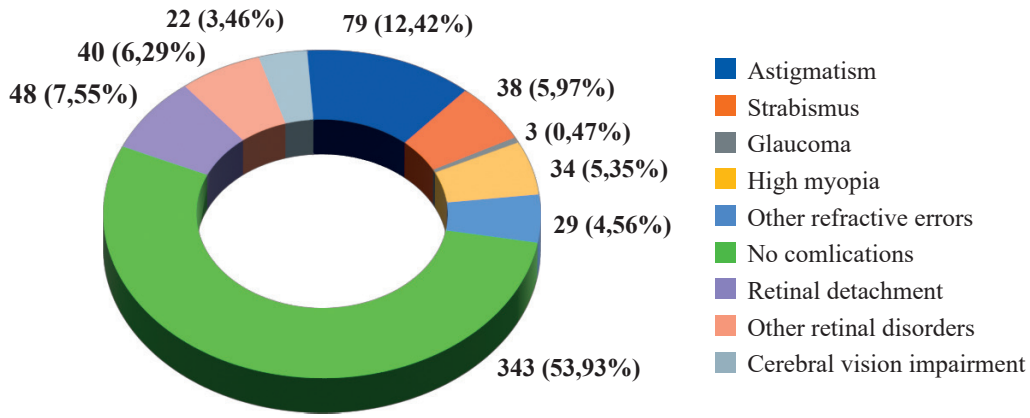


**Fig.1**. Complications of ROP

In the years of our research, the number of blind children born in 2015-2020 was 48. These children made up 7.5% of the 636 children identified during the research years. We compared children diagnosed with blindness with children with ROP according to geographical area, year of birth, sex, number of fetuses, gestational age and birth weight. The results are shown in table 2. Looking at the table, it can be seen that the distribution of children blind due to ROP according to geographical zones was more in Baku-Absheron 42 (53.3%). 9 (11.8%) children were found in the Greater Caucasus region, 18 (23.7%) in the Kura intermountain region, 3 (3.9%) in the Lesser Caucasus region, and 4 (5.3%) in the Lankaran region. The result of the division was as follows. 9 (11.8%) of children diagnosed with blindness were born between 23-27 weeks, 34 (44.7%) were born between 28-29 weeks, 15 (19.7%) were born between 30-31 weeks, and 18 (23.7%) were born between 32-34 weeks.

The distribution of blind children according to their birth weight is 7 (9.2%), those born between 600-999 grams, 21 (27.6%), those born between 1000-1249 grams, and 10 (13.2%), those born between 1250-1499 grams. 22 (28.9%) were born between 1500-1749 grams, 10 (13.2%) were born between 1750-1999 grams, and 6 (7.9%) were born between 2000-3200 grams. Here too, depending on the body weight at birth and gestational week, the smaller the babies are, the greater the risk of blindness.

Among children diagnosed with blindness, boys predominated over girls. Thus, 48 (63.2%) boys and 16 (36.8%) girls. 73 of these children (96.1%) were born from a singleton pregnancy, and 3 (3.9%) were twin foals. During comparison between groups, it can be seen that blindness was more common in children with low gestational age ($p<0.001$), low birth weight ($P\chi2=0.029$, PU=0.047). When collecting anamnestic information from the parents of these children, it was found that most of the children were blind at the first examination, and this examination was carried out on average 4 months after birth, and the children were not included in the screening during the progressive stages of ROP. This shows that there are problems with screening and early diagnosis of ROP and confirms the necessity of taking serious complex measures in this regard.

Myopia of premature children is called "Myopia of prematurity (MOP)". This is directly related to ROP. However, it also occurs in premature babies without ROP. For every 100 g less weight, there is a 10% more risk of developing myopia. In the ETROP study, myopia was found in 65% and high myopia in 35%. In the BEATROP study, in children with ROP in Zona, myopia was found in 79% of those who received laser treatment, and in 43% of those who received intravitreal anti-VEGF treatment. The most common complication of ROP is myopia. Myopia occurred in 6-9% of eyes without ROP, and in 16-90% of eyes with ROP. 90% can be found in serious anatomical complications of ROP. 40-62% risk of myopia in eyes with stage 3 pretresthold ROP laser treatment further increases myopia. A positive correlation was found with the number of laser spots and the occurrence of myopia (-0.14D/100). There are also reports that scleral depression causes myopia [8,9].

In our study, high myopia was found in 5% cases, and complex myopic astigmatism was found in 12% cases. Refractive examination was performed using Plus optix and Retinoscope (after cycloplegia), glasses correction was prescribed according to international protocols, children were monitored at least 3 times a year. Anti-VEGF intravitreal injection is more appropriate as a primary treatment method for prevention.

According to literature data, strabismus is detected in 14% of children with ROP, it is found even in mild stages of ROP, and increases as the severity of ROP increases. In our study, it was found in 6% of cases. The main reason for this is visual impairment, anisometropia, as well as CNS damage. Children with macular traction have a positive kappa angle, resulting in pseudo exotropia. Treatment is correction of refractive errors, treatment of amblyopia, surgical correction [10,11].

It should be noted that the number of blind infants born in 2015-2020 was 48. They made up 7.5% of the 636 infants identified during the research years. However, among those born blind before the research years, who applied to the Medical Expertise Commission of the National Centre of Ophthalmology named after acad. Zarifa Aliyeva, 76 infants were diagnosed with ROP stage 5. A blindness morbidity analysis of patients with ROP by year of birth shows that since 2014, the blindness rate has been decreasing among patients with ROP over the years. This is due to the rapid development of neonatology, the neonatal care provided to infants in the critical care units, as well as timely identification, monitoring, and proper treatment of the early ROP stages.

Table 2

**Comparison of blind children with ROP children according to geographical area, year of birth, gender, number of fetuses, gestational age, birth weight**

| | | Blindness | | | | | | Pχ2 | PU |
|---|---|---|---|---|---|---|---|---|---|
| | | No | | Yes | | Total | | | |
| | | Number | % | Number | % | Number | % | | |
| Geographical zone | Baku-Absheron | 299 | 50,8% | 42 | 55,3% | 341 | 51,3% | 0,866 | 0,557 |
| | Greater Caucasus | 82 | 13,9% | 9 | 11,8% | 91 | 13,7% | | |
| | Kura Intermountain | 157 | 26,7% | 18 | 23,7% | 175 | 26,3% | | |
| | Lesser Caucasus | 15 | 2,5% | 3 | 3,9% | 18 | 2,7% | | |
| | Lankaran | 36 | 6,1% | 4 | 5,3% | 40 | 6,0% | | |
| Gestational age | 23-27 weeks | 24 | 4,1% | 9 | 11,8% | 33 | 5,0% | <0,001 | <0,001 |
| | 28-29 weeks | 123 | 20,9% | 34 | 44,7% | 157 | 23,6% | | |
| | 30-31 weeks | 185 | 31,4% | 15 | 19,7% | 200 | 30,1% | | |
| | 32-34 weeks | 215 | 36,5% | 18 | 23,7% | 233 | 35,0% | | |
| | 34-36 weeks | 42 | 7,1% | 0 | 0,0% | 42 | 6,3% | | |
| Weight | 600-999 gr | 38 | 6,5% | 7 | 9,2% | 45 | 6,8% | 0,029 | 0,047 |
| | 1000-1249 gr | 89 | 15,1% | 21 | 27,6% | 110 | 16,5% | | |
| | 1250-1499 gr | 137 | 23,3% | 10 | 13,2% | 147 | 22,1% | | |
| | 1500-1749 gr | 161 | 27,3% | 22 | 28,9% | 183 | 27,5% | | |
| | 1750-1999 gr | 78 | 13,2% | 10 | 13,2% | 88 | 13,2% | | |
| | 2000-3200 gr | 86 | 14,6% | 6 | 7,9% | 92 | 13,8% | | |
| Number of fetuses in pregnancy | 1 | 446 | 75,7% | 73 | 96,1% | 519 | 78,0% | <0,001 | <0,001 |
| | 2 | 121 | 20,5% | 3 | 3,9% | 124 | 18,6% | | |
| | 3 | 22 | 3,7% | 0 | 0,0% | 22 | 3,3% | | |
| Gender | Boy | 313 | 53,1% | 48 | 63,2% | 361 | 54,3% | 0,099 | 0,099 |
| | Girl | 276 | 46,9% | 28 | 36,8% | 304 | 45,7% | | |

*Note: P- statistical significance of the difference in indicators between the corresponding groups (according to the x-square and Mann-Whitney U test)*

The distribution of blind infants by birth weight shows that the smaller the newborn, the higher the risk of blindness, depending on both birth weight and gestational week. Among infants diagnosed with blindness, boys predominated over girls: 48 boys (63.2%) and 16 girls (36.8%). 73 (96.1%) of these infants were born from a singleton, and 3 (3.9%) - twin pregnancy.

Blindness is more common in infants with small gestational age ($p<0.001$) and low birth weight ($P\chi2=0,029$, PU=0,047). According to anamnestic data, in the majority of infants, blindness was identified during the first examination performed, on average, 4 months after birth, and infants were not screened at the progressive ROP stages. This confirms the need for serious complex measures to solve the problems related to screening and early ROP diagnosis.

Most of those treated for ROP were born between 23 and 31 weeks. Infants with and without ROP were distributed by birth weight. Birth weight between 1,250-1,499 g predominated (35.7%), and most patients (66.7%) were in stage 1. 42 (22.6%) of the infants diagnosed with ROP were treated.

A habilitation program has been developed for early recovery of visual functions in treated infants. To study the program efficiency, visual functions were studied in 32 infants with regressed ROP. The average gestational age weight, and regression period were, respectively, 26.5 weeks, 900 g, and 5.7 weeks.

Patients were divided into two groups. Spontaneous regression was 62% (16 infants, 32 eyes) in group 1 and 59% (16 infants, 32 eyes) in group 2. An early rehabilitation program was designed for group 1. Patients were treated according to this program, which covered three quarters, three basic phases. Infants were treated according to this program for 9 months. Group 2 was not treated according to this program.

After the treatment, general ophthalmological examinations were performed. Best-corrected visual acuity was achieved at the age of 3 years. Best-corrected visual acuity was compared between the two groups. The average visual acuity in groups 1 and 2 was, respectively, 6/12 and 6/3. After early intervention and treatment according to the habilitation program, the best corrected visual acuity in group 1 was higher than in group 2. The early visual habilitation program will help infants with regressive ROP achieve higher levels of vision.

Another dangerous complication of ROP is glaucoma. It is classified as secondary angle-closure glaucoma. Occurs in 30% of eyes with advanced ROP and ROP in the scarring period. The main reason is the anterior coming of the iridolental diaphragm and narrowing of the anterior chamber angle due to fibrovascular proliferation. Secondary closed angle, lens size, inflammation, rubeosis have also been mentioned in the literature as other causes. In the CRYO-ROP study, glaucoma was 2.9% in the treatment group and 6.1% in the control group in the 5.5-year-old examinations of children with bilateral threshold ROP. In the ETROP study, glaucoma occurred in 2% of children with pre-threshold ROP before the age of 6 years [12,13]. In 0,47% of the patients included in our study, a full examination (GDT, corneal diameter, thickness, A-B scan, fundus) was performed under general anesthesia, hypotensive drops and surgical treatment were prescribed.

**Conclusion**

Detection of ROP in premature children, organization of correct and timely examination and treatment prevents such complications that may arise in the future. Due to the scientific and technical progress in the field of neonatology in Azerbaijan, the probability of survival of premature children is increasing, so the risk of ROP in such children is also increasing. For this, ophthalmologists, neonatologists, and pediatricians should work together. Neonatologists should inform ophthalmologists about premature children and take part in timely eye examination of these children, informative conversations should be held with the patient's parents. In terms of the possibility of complications, dynamic dispensary observation of children who are included in the risk group remains an urgent issue today.

REFERENCE:

1. Qasımov, E.M. Yarımçıq doğulmuşların retinopatiyası / E.M.Qasımov, M.İ.Kərimov // Göz xəstəlikləri, Oftalmoloqlar üçün vəsait, – 2014. – s.301-306.
2. Azad, R. Retinopathy of prematurity / R. Azad, M.T.Trese // – 2013.
3. Early Treatment for Retinopathy of Prematurity Cooperative Group. The Incidence and Course of Retinopathy of Prematurity: Findings From the Early Treatment for Retinopathy of Prematurity Study // Pediatrics, – 2005. 116, – p.15-23.

4. Hartnet, M.E. Advances in understanding and management of retinopathy of prematurity // Surv. Ophthalmol., – 2017. 62, №3, – p.257-276.
5. Palmer, E.A. Chapter 85-Retinopathy of Prematurity. Ed: Ryan S.J. / E.A.Palmer, A.Patz, D.L.Phelps [et al.] // Mosby, St. Louis. Retina, – 2001. – p.1472-1499.
6. Park, K. Retinal nerve fiber layer thickness in prematurity is correlated with stage of retinopathy of prematurity / K.Park, S.Oh // Eye (Lond), – 2015. 29, №12, – p.1594 1602.
7. Пальчик, А.Б. Неврология недоношенных детей / А.Б.Пальчик, Л.А.Федорова, А.Е.Понятишин // МЕДпресс информ, – Москва: – 2010. – с.31-45.
8. Попова, Н.В. Ретинопатия недоношенных. Обзор / Н.В.Попова, А.П.Гойдин, О.Л.Фабрикантов // Офтальмология, – 2021. 18, №3, – с.399-407.
9. Quinn, G.E. Progression of myopia and high myopia in the Early Treatment for Retinopathy of Prematurity Study: Findings at 4 to 6 years of age / G.E.Quinn, V.Dobson, B.V.Davitt [et al.] // Journal of American Association for Pediatric Ophthalmology and Strabismus, – 2013. 17, – p.124-128.
10. Vander Veen, D.K. Prevalence and course of strabismus in the first year of life for infants with prethreshold retinopathy of prematurity / D.K.Vander Veen, D.K.Coats, V.Dobson [et al.] // – 2006.
11. Alfieri, M.C. The Annete von. Droste-Hulshoff Pseudo-strabismus secondary to macular heterotropia: A / Alfieri, M.C. Magli A., Chiosi E. [et al.] //.
12. Kwitko, M.L. Secondary glaucoma in infancy and childhood. A review // Can. J. Ophthalmol., – 1969. 4, – p.231.
13. Kushner, B.J. Medical Treatment of Glaucoma Associated With Cicatricial Retinopathy of Prematurity / B.J. Kushner, S.Sondheimer // Case Reports Am. J. Ophthalmol.

**Müəllif münaqişələrin (maliyyə, şəxsi, peşəkar və digər maraqları) olmamasını təsdiqləyir.**

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