MODERN MEDICINE AND PRACTICE
https://inovatus.es/index.php/ejmmp
EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE
Vol. 4 No. 10 (Oct - 2024) EJMMP ISSN: 2795-921X

# CLINICAL AND FUNCTIONAL VARIANTS OF CICATRICIAL RETINOPATHY OF PREMATURITY, PROGNOSIS, TACTICS OF DISPENSARY OBSERVATION

***Sabirova Dilrabo Baxodirovna***
*Samarkand State Medical University, Department of Ophthalmology*

**Annotation:** The work is based on the results of a dynamic examination of 58 children (82 eyes, 767 studies) with grades 3 and 4 of the cicatricial phase of ROP aged from 6 months to 16 years (children under 1 year - 12%, 1-3 years - 36%, 3-10 years - 28%, 10-16 years - 24%). 36 children (62.1%) were observed for a long time (at least 5 years). In accordance with the used classification, eyes with the following clinical manifestations were classified as grade 3: traction deformation of the optic disc, ectopia of the macular, displacement of the vascular bundle and changes in the course of the vessels, dystrophic changes in the retina, pre- and intraretinal fibrosis, residual avascular zones (47 eyes). The 4th degree, in addition to the above changes, is manifested by the presence of folds or local retinal detachment (35 eyes). All examined children were born prematurely at a gestational age of 26-36 weeks (average 29 weeks) and with a body weight of 830-2920 g. (average 1377 g). Active phase treatment was performed on 46 eyes (56.1%). Of these, transpupillary laser coagulation of avascular zones of the retina was performed on 31 eyes (68%), in the remaining cases - cryocoagulation or combined interventions. Surgical interventions for late complications of ROP (retinal detachments and ruptures, traction retinoschisis) were required on 32 eyes (39%) at the age of 8.75±3.61 years. As a comparison group, 18 healthy full-term children (23 eyes) of similar age groups were examined. All patients were examined in the Department of Ofthalmology SamMY.

**Key words:** retinopathy of prematurity, diagnostics and prognosis, structural and functional changes in the eyes, particular retinal detachment, of proliferative processes in the retina.

**Introduction:** Retinopathy of prematurity (ROP) is a vasoproliferative disease of the retina of premature infants. Despite great achievements in the detection and treatment of ROP, it currently remains one of the main causes of blindness and low vision from early childhood in developed countries [Gogate P., Gilbert C., Zin A., 2011; Patel D.K. et al.; 2011; Quinn G. et al., 2010; Stepanova E.A., 2010; Katargina L.A., 2010]. Moreover, visual disability can develop not only in the terminal stages, but also in children with relatively favorable outcomes of ROP. The most difficult is to predict the development of vision and the occurrence of late complications at stages 3-4. This is due to the variability of the clinical picture and functional prognosis of stage 3-4 ROP, as indicated by a number of authors [Repka M. et al., 2011; Katargina L.A., Kogoleva L.V., 2010; Saydasheva E.I., 2010], but this issue has not been studied in detail or in a targeted manner. It should be emphasized that the standard diagnostic methods of ROP currently used do not allow for a full identification of the diversity of clinical manifestations of cicatricial and regressive stages of the disease due to insufficient accuracy, subjectivity, and controversial interpretation of research results. In this regard, the search for and introduction into clinical practice of new diagnostic technologies and methods that allow for a qualitatively new level of assessment of the condition of the eyes at various stages of ROP and an

objective prognosis of the disease remains relevant. Such modern highly informative methods include spectral optical coherence tomog raphy (OCT), which makes it possible to non-invasively and with high reliability examine not only the central sections, but also the periphery of the retina. Works devoted to the use of OCT in children with ROP are isolated and descriptive in nature, and the main object of study is the macular region of the retina. At the same time, all authors point to a pronounced polymorphism of structural changes in the posterior pole of the eye at grades 3 and 4 ROP [Muni R. H. et al., 2010; Vinekar A. et al., 2010; Chavala S. H. et al., 2009]. It should also be noted that at present there is no unified approach and algorithm for the use of OCT in the diagnosis of ROP in children. The main method that allows an objective assessment of the functional state of the visual analyzer in young children with cicatricial ROP is electrophysiological studies (EPS). Deviations in the general electroretinogram (GERG) parameters have been revealed, in particular a decrease in the amplitude of a- and b-waves and oscillatory potentials even after a mild form of ROP, without visible residual changes in the fundus [Fulton A., Hansen R., 2005]. Dysfunction of the retina can develop and persist for a long time even with a favorable course of ROP. A significant decrease in GERG waves in stages 2-3 of the disease and a practical absence of GERG at stages 4-5 of the process have been described [Katarhina L.A., Kogoleva L.V., 2013]. To assess the function of glial cells, which according to modern data play a major role in the development of ROP [Fletcher E.L. et al., 2010], there is an EFI indicator - the glial index (GI). It has been established that an increase in the glial index will reflect retinal proliferation, and degenerative processes (retinal atrophy and dystrophy) will be accompanied by a decrease in the index [Neroev V.V., Zueva M.V. et al., 2005]. In this case, the glial index was calculated as the ratio of the amplitude of the b-wave of the OERG and the rhythmic electroretinogram (REG) at 12 Hz [Fletcher E.L. et al., 2010, Neroev V.V., Zueva M.V. et al., 2010]. However, GI in ROP has not been studied. There have been virtually no studies of the relationship between structural and electrophysiological changes in the retina of the cicatricial phase of ROP. Thus, the diversity of clinical and functional manifestations of grades 3-4 cicatricial ROP, as well as the steady increase in the number of patients (adolescents and adults) who have had ROP, requires clarification of the functional prognosis and justification of the tactics of dispensary observation, which forms the basis of this work and determines its purpose.

**Purpose of the study.**

Improving the diagnostics and prognosis of clinical and functional outcomes of grade 3-4 cicatricial retinopathy of prematurity based on the study of structural and functional changes in the eyes.

**Material and methods.** The work is based on the results of a dynamic examination of 58 children (82 eyes, 767 studies) with grades 3 and 4 of the cicatricial phase of ROP aged from 6 months to 16 years (children under 1 year - 12%, 1-3 years - 36%, 3-10 years - 28%, 10-16 years - 24%). 36 children (62.1%) were observed for a long time (at least 5 years). In accordance with the used classification, eyes with the following clinical manifestations were classified as grade 3: traction deformation of the optic disc, ectopia of the macular, displacement of the vascular bundle and changes in the course of the vessels, dystrophic changes in the retina, pre- and intraretinal fibrosis, residual avascular zones (47 eyes). The 4th degree, in addition to the above changes, is manifested by the presence of folds or local retinal detachment (35 eyes). All examined children were born prematurely at a gestational age of 26-36 weeks (average 29 weeks) and with a body weight of 830-2920 g. (average 1377 g). Active phase treatment was performed on 46 eyes (56.1%). Of these, transpupillary laser coagulation of avascular zones of the retina was performed on 31 eyes (68%), in the remaining cases - cryocoagulation or combined interventions. Surgical interventions for late complications of ROP (retinal detachments and ruptures, traction retinoschisis) were required on 32 eyes (39%) at the age of 8.75±3.61 years. As a comparison group, 18 healthy full-term children (23 eyes) of similar age groups were examined. All patients were examined in the Department of Ofthalmology SamMY. All children underwent a comprehensive eye examination, including visometry, refractometry (if optical

media allowed), biomicroscopy, ophthalmoscopy, tonometry, keratometry, electrophysiological studies and spectral OCT. The author performed the entire range of studies independently. Children under 3 years of age and restless older children were examined under conditions of deep physiological or narcotic sleep.

The Spectralis HRA+OCT device (Heidelberg Engineering, Germany) was used for OCT. The research technique is contactless. The measurement error is up to 1 μm. The required pupil diameter is ≥2.5 mm. To assess the morphometric parameters of the neuroepithelium and localize the retinal vessels, a study protocol was used that included scanning the fundus area of 20° x 20° (25 linear scans/512 A-scans) in all 3 zones. The scanning area was located in the ophthalmoscopically intact fundus zones and included 3-20 retinal vessels. To assess the internal structure and features of changes in the reflectivity of the fundus structures, the fundus area was scanned, capturing zones with pathological changes (retinal folds, schisis zones, atrophic foci, and preretinal fibrosis zones). For the purpose of topographic orientation of the OCT scans, the selection of different retinal areas was carried out in accordance with the international classification of the active phase of RN [An International Classification of Retinopathy of Prematurity, 1984, 1985, 1987, 2005]. Electrophysiological studies included recording of OERG and RERG at 30 Hz, visual evoked potentials to a flash stimulus in accordance with the ISCEV 2008-2009 standards. For the electroretinogram, a loop electrode (HK-Loop) was used as an active electrode, placed behind the lower eyelid. Initially, OERG was recorded with an interval between stimuli of 10 s. Then, RERG was recorded after preliminary light adaptation for 5 min. After RERG, visual evoked potentials (VEP) were recorded. To assess the state of glial cell function (Müller cells) and the activity of the proliferative process, the author calculated the glial index (OERG/RERG b-wave amplitude, norm - 6-8). An increase in GI was assessed as the activity of proliferative processes in the retina, a decrease - degenerative ones. For the functional assessment of retinal blood flow, the b/a ratio (b-wave OERG amplitude/a-wave OERG amplitude, norm 6-10) was calculated.

Considering the presence of fairly extensive avascular zones or coagulates on the periphery of the retina, significantly affecting the results of the study, the use of 12 Hz RERG for calculating the glial index in patients with cicatricial ROP was considered inappropriate, since 12 Hz RERG can be reduced due to the interaction of ON and OFF retinal pathways [Kondo M. et al., 2001], which can be significantly changed in eyes with ROP [Luu C. et al., 2005]. We have developed a method for calculating the glial index using 30 Hz RERG, which, in this case, on the contrary, is more stable, and also convenient to use, since it does not require changes to the standard examination protocol.

**Results of research**

Analysis of clinical manifestations showed that grade 3 ROP was in 47 eyes (57.3%), grade 4 – in 35 eyes (42.7%). Asymmetric outcomes of ROP were detected in 34 patients (58%), and in 18 cases (31%) there was a combination of grades 3-4 with grade 5 in the fellow eye.

The spectrum and severity of ophthalmoscopic changes in grades 3-4 ROP were characterized by pronounced polymorphism. Considering that in some cases it was not possible to reliably differentiate grades 3 and 4 regressive ROP using standard research methods, and also that in grades 3-4 regressive ROP late complications, in particular retinal detachment, most often have a similar development mechanism, grades 3 and 4 cicatricial ROP were analyzed together to identify prognostic criteria.

Residual avascular zones were detected in all eyes, which were most often (73 eyes, 89%) located in zone 2. In patients who underwent prophylactic treatment in the active phase of ROP, coagulates were visualized in the avascular zone, which were atrophic chorioretinal foci with clear boundaries. Shift of the vascular bundle of varying severity (from 0 to 140 degrees between vascular arcades, on average - 74 ± 36) was observed in 81 eyes (98.8%). In 6 eyes, the shift was to the nasal side, in the remaining cases - to the temporal side. Ectopia of the maculae was detected in 80 eyes (98%). Of these, in 11% of cases, the macular

shift was to the nasal side with a decrease in the optic disc - macula distance to 1.5 mm. In other cases, a temporal shift was noted with an increase in the optic nerve head – macula distance to 9.3 mm (on average – 5.8±1.5 mm). At the same time, it was possible to differentiate the macular zone ophthalmoscopically only in 26 eyes (32%), in the remaining cases, the macula was localized using OCT. Extraretinal tissue of varying severity was ophthalmoscopically visualized in 52 eyes (63%), and was distinguished by pronounced polymorphism (from “delicate” translucent preretinal membranes fixed to the retina both in the central sections and on the periphery, to coarse fibrous changes in the vitreous body, fused with a retinal fold or fixed at the border with an avascular zone).

Folds and local retinal detachments were diagnosed in 35 eyes (43%), classified as grade 4 ROP. They were fibrously altered, tractionally deformed retina with included retinal vessels, differing in different localization, structure and profile. In 9 eyes (29%), the above changes affected the macular zone, i.e., most retinal detachments did not affect the macular zone of the retina ophthalmoscopically. Visual acuity was extremely variable and ranged from 0.005 to 1.0 (at grade 3 - 0.3 ± 0.3, at grade 4 - 0.08 ± 0.15, on average - 0.26 ± 0.25). In 9 cases (29%), when retinal detachment affected the macular zone, visual acuity did not exceed 0.1 (0.03 ± 0.01). However, a decrease in visual acuity was caused not only by changes in the fundus, but also by concomitant pathology. From the side of the central nervous system, pathology of the conducting pathways and higher parts of the visual analyzer was detected in 22% of cases. Ametropia and concomitant high-degree amblyopia - 78% of cases. Among refractive anomalies, myopia was determined in most cases (61%).

By analyzing the localization, degree and nature of residual cicatricial changes, it is possible to estimate the probability and timing of the development of late complications of regressive ROP. To identify the appropriate prognostic criteria, it is necessary to conduct an in-depth anatomical and functional study.Considering that generally accepted ophthalmoscopic methods do not allow a full assessment of the variety of clinical manifestations of regressive ROP grades 3-4 due to insufficient accuracy, subjectivity and controversial interpretation of research results, we used OCT for a more accurate diagnosis of retinal changes and their subsequent systematization. Thus, the type of extraretinal changes serves as important criteria for the severity of the process, allowing us to predict the development of late complications in cicatricial ROP at grades 3-4. In all eyes with grade 4 regressive ROP, local retinal detachments or folds were detected ophthalmoscopically. They were fibrously altered, tractionally deformed retina with included retinal vessels, differing in different localization, structure and profile. When analyzing tomograms, we identified 4 most characteristic types of detachments:

1. Deformation of the retinal profile, local thickening of the neuroepithelium with a significant increase in reflectivity and loss of structural organization (12 eyes) - characterized by different localization.
2. Deformation of the macula (2 eyes), having a "double-humped" profile, with a sharp increase in the reflectivity of the inner layers of the retina - is noted in the case of pronounced traction of the temporal arcades from the avascular zone and a decrease in the angle between the outer vascular arcades to 30 ° or less.
3. Fold with schisis (3 eyes) - a fold of various localizations, characterized by multiple or single optically empty cavities (retinoschisis) in the layers of the retina.
4. Detachment of the neuroepithelium (20 eyes) of various localizations - is characterized by an optically empty cavity under a structurally altered neuroepithelium.

Detection of retinal detachments of types 1 and 2 in eyes with zones of pre-, epi- and intraretinal fibrosis of varying area and intensity in the absence of extraretinal tissue indicates the importance of horizontal traction in their formation. Detachments of types 3 and 4 were detected in eyes with extraretinal tissue attached to the retina, which emphasizes the role of vertical traction in their genesis (a "ridge" is often visible on OCT

along the upper interface of retinal detachment). The direction of traction can be used as a prognostic criterion for the development of late retinal detachments in grades 3-4 regressive ROP. Of great interest is the fact that in all eyes with grade 3-4 cicatricial ROP in the avascular zone unaffected by coagulates, a diffuse increase in optical density (hyperreflectivity) of the neurosensory retina and loss of the layered structure were detected. For objective assessment of tissue optical density, a method of optical densitometry was developed (patent No. 2488344 dated 27.07.2013, Katargina L.A., Ryabtsev D.I.). In accordance with the developed method of differential diagnostics of pathological changes in the posterior segment of the eye (patent No. 2482785 dated 27.05.2013, Katargina L.A., Ryabtsev D.I.), these changes in the neuroepithelium were assessed by us as a manifestation of intraretinal fibrosis. It is noteworthy that in the overwhelming majority of cases (66 eyes – 80.5%) similar focal changes in the neuroepithelium were also present in zone 1 of the fundus. On OCT, atrophic foci and coagulates were zones of increased optical density (hyperreflectivity) of the neurosensory retina with loss of layered structure, but, unlike foci of intraretinal fibrosis, were characterized by sharp thinning of the neuroepithelium and pronounced changes in the choroid.

Analysis of the localization of retinal vessels in patients with grades 3-4 regressive ROP revealed a more superficial location compared to the physiological one. In the ganglion cell layer, the retinal vessels were located only in 12 eyes out of 82 (15%). In 29 eyes (35%), they were located in the nerve fiber layer, and in 41 eyes (50%), they were extraretinal (on the surface of the retina). Thus, the "physiological" location of vessels in the ganglion cell layer occurred only in 15% of cases. We did not find any changes in the localization of vessels as they grew older. It is well known that the blood supply to the outer third of the retina is provided by the choroid. The choroid has an absolute priority in feeding the photoreceptor layer. However, when it comes to the outer nuclear and outer retinal layers, the participation of the retinal vessels in their nutrition cannot be ruled out. Thus, it can be assumed that the displacement of the retinal vascular network can be one of the reasons for the development of atrophic processes in the retina.

The factors that cause the dislocation of retinal vessels are unknown, however, in our opinion, the theoretical justification for the causes of vessel displacement can be: thinning of the retina, leading to the "pushing out" of vessels, due to the discrepancy between the biomechanical characteristics of these tissues.

pathological growth of vessels and vitreoretinal proliferation, causing the newly formed vessels to “pull” the retinal vascular bed itself to the retinal surface. We studied the position of the retinal vessels in various clinical situations (It was found that significant thinning of the retina corresponds to the extraretinal position of the vessels. With other variants of the location of the vessels, there was no significant deviation of the retinal thickness from the physiological one. The study of the depth of the vascular bed and the presence of extraretinal tissue showed a high level of interrelation between these parameters. It was found that significant thinning of the retina corresponds to the extraretinal position of the vessels (p<0.01). With other variants of the location of the vessels, there was no significant deviation of the retinal thickness from the physiological one. The study of the depth of the vascular bed and the presence of extraretinal tissue showed a high level of interrelation between these parameters.

**Conclusion.** Dynamic observation, performed jointly with PhD Kogoleva L.V. and Belova M.V., revealed the appearance of atrophic foci in the fundus of various localizations, as well as in some cases the development of traction retinoschisis and / or an increase in the area of retinal detachment. When analyzing the dynamics of these changes as the child grows older, a tendency was revealed for an increase in the incidence of late complications of ROP from 67% - in children under 1 year, to 100% - in children over 10 years old. Thus, the possibility of increasing traction not only in the active, but also in the cicatricial phase is confirmed. The possibility of increasing retinal traction in patients with ROP as they grow older, regardless of its stage, indicates the importance of monitoring this category of patients in dynamics.

We have analyzed the dependence of the frequency of development of late complications of cicatricial RP, such as atrophic changes.

**References**.

1. Хватова А.В., Катаргина Л.А., Дементьева Г.М., Коголева Л.В., Фролова М.И., Скринец П.П. Эффективность выявления и профилактического лечения ретинопатии недоношенных. Вестн. офтальмол. 2000; 5: 34–36.
2. Антонов А.Г., Байбарина Е.Н. Профилактика развития ретинопатии недоношенных при лечении детей, находящихся в критическом состоянии. Мат-лы симпозиума «Профилактика и лечение ретинопатии недоношенных». М. 2000. С. 17–19.
3. Сайдашева Э.И. Факторы риска ретинопатии недоношенных в неонатальном периоде. Тез. I Междунар. науч.-практ. Конф. по пролиферативному синдрому. М. 2000. С. 29–30.
4. Seiberth V., Linderkamp O. Risk factors in retinopathy of Prematurity. A multivariate statistical analysis. Ophthalmologica. 2010; 214 (2): 131–135.
5. Juan E. Retinopathy of Prematurity. Practical Atlas of Retinal Disease and Therapy. NewYork. 2003. P. 299–318.
6. Сайдашева Э.И., Сомов Е.Е., Фомина Н.В. Избранные лекции по неонатальной офтальмологии. СПб. 2006. С. 127–187.
7. Хватова А.В., Катаргина Л.А. Состояние и перспективы исследований по проблеме ретинопатии недоношенных. Материалы симпозиума «Профилактика и лечение ретинопатии недоношенных». М. 2000. С. 3–16.
8. Marek E. Prost. Problems of the pathogenesis of ROP. New York. 2009. P. 5.
9. Катаргина Л.А., Слепова О.С. Скринец П.П., Дементьева Г.М., Черноног И.Н., Каламкаров Г.Р. Гуморальный иммунный ответ на S-антиген сетчатки у недоношенных детей и его роль в развитии и течении ретинопатии недоношенных. Вестн. офтальмол. 2003; (1): 20–22.
10. Дементьева Г.М., Коголева Л.В., Фролова М.И. Недоношенность: факторы риска ретинопатии. Мат-лы симпозиума «Профилактика и лечение ретинопатии недоношенных». М. 2000. С. 19–24.
11. Retinopathy of prematurity in Asian Indian babies weighing greater than 1250 grams at birth: Ten year data from a tertiary care center in a developing country. Indian J. Ophthalmol. 2007; 55: 331.
12. Сабирова, Д. Б., Юсупов, А. А., Искандаров, Ш. Х., Кадырова, А. М., & Тулакова, Г. Э. Клиническая оценка озонотерапии и криопексии у пациентов с герпетическим кератитом // Точка зрения. Восток–Запад, (2016). (1), 147-149.
13. Сабирова, Д. Б., Тулакова, Г. Э., & Эргашева, Д. С. Комплексное лечение диабетической макулопатии путем применения пептидного биорегулятора" Ретиналамин" и лазеркоагуляции сетчатки // Точка зрения. Восток-Запад, (2017). (2), 114-116.
14. Сабирова, Д. Б., Искандаров, Ш. Х., Косимов, Р. Э., Эргашева, Д. С., & Юсупов, А. А. Совершенствование лечения герпетических кератитов с использованием озона в виде газа через очки аппарата" Орион-си" // Российский общенациональный офтальмологический форум, (2015). 1, 159-163. EUROPEAN JOURNAL OF MODERNMEDICINE AND PRACTICE Vol. 4 No. 8 (Aug - 2024) ISSN: 2795-921X 174

15. Сабирова, Д. Б., Облоёров, И. Х., & Хазратова, Д. Ф. КЛИНИКОЭПИДЕМИОЛОГИЧЕСКИЕ ОСОБЕННОСТИ ВЕСЕННЕГО КАТАРА И ЛЕЧЕНИЕ ИММУНОКОРРЕГИРУЮЩИМИ СРЕДСТВАМИ // НАУЧНЫЕ ИССЛЕДОВАНИЯ, (2019).52.
16. Тулакова, Г. Э., Сабирова, Д. Б., Хамракулов, С. Б., & Эргашева, Д. С. Отдалённые результаты ксеносклеропластики при миопии высокой степени // Научный форум. Сибирь, (2018). 4(1), 80-80. International Journal of Integrative and Modern Medicine Copyright © 2024 The Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium 9 provided the original work is properly cited.
17. Юсупов, А. А., Бобоев, С. А., Хамракулов, С. Б., Сабирова, Д. Б., & Косимов, Р. Э. Взаимосвязь функциональных и анатомо-оптических параметров глаза при врожденной близорукости // Вопросы науки и образования, (2020). (22 (106)), 44-53.