Asymptomatic Peripheral Ischemic Retinopathies in Pediatric Routine Ophthalmologic Examination

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ABSTRACT

Purpose: In this study our aim is to evaluate asymptomatic peripheral retinal ischemia cases detected in pediatric routine ophthalmologic examination.

Material-Methods: 6 patients in between 6 to 12 years who underwent routine ophthalmological examination were included. Peripheral retinal ischemia and retinal neovascularization were observed in dilated fundus examination of all patients. All patients underwent fundus fluorescein angiograpy (FFA) and spectral domain optical coherence tomography (SD-OCT). Argon laser photocoagulation or intravitreal anti-vascular endothelial growth factor (anti-VEGF) injection was performed in required cases.

Results: Mean age was 8.8±2.3 (6-12) years. Two of six patients were siblings. Three patients were diagnosed with incontinenta pigmenti. Detailed history revealed preterm birth in two patients and retinopathy of prematurity examination has not been performed. One patient was diagnosed with sickle cell anemia. Argon laser photocoagulation was performed in 4 patients, intravitreal anti-VEGF treatment was performed in 1 patient and 1 patient was followed-up without any treatment. No complications such as vitreous hemorrhage due to neovascularization were observed in any of the patients in 1 year follow-up period.

Conclusion: Detailed retinal examination is an important component of pediatric ophthalmological examination. If a retinal pathology is detected, appropriate diagnostic tests and treatment should be performed to diagnose the primary disease and prevent possible complications. Since retinal findings may be the first sign of many systemic diseases, detailed systemic evaluation is very important in these patients.

Keywords: peripheral retinal examination, peripheral retinal neovascularization, pediatric retinal examination.

INTRODUCTION

Routine ophthalmological examination should be performed for every child periodically starting from the newborn stage.[1] First examination is generally performed by pediatricians or general practitioners using the red reflex test and patients with potential ocular abnormalities require urgent referral to an ophthalmologist. However newborns with a history of preterm birth or hereditary eye disease should be referred to an ophthalmologist promptly. According to the American Academy of Pediatrics, a comprehensive ophthalmological examination including a detailed fundus examination should be performed until the age of three.[2,3] Fundus examination aims the evaluation of the optic nerve, macula and the peripheral retina in details. This examination is specifically crucial for differential diagnoses of diseases like retinoblastoma, retinopathy of prematurity, ischemic retinopathies, retinal detachment which affect the peripheral retina however do not cause an acute visual loss. However if these pathologies are not diagnosed and treated properly they may threaten vision and life. A thorough retinal examination is required in cases when there is history of low birth weight, preterm birth, prenatal infections, parenteral alcohol and drug use, family history of enucleation, impaired vision or progressive visual loss. However, a retinal exam could occasionally be omitted in asymptomatic children without a compelling story like these.

Pediatric ischemic retinopathy is characterised with ischemia secondary to insufficient vascularisation.[4] Many

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different disease like retinopathy of prematurity, familial exudative retinopathy, Norrie disease, incontinentia pigmenti may cause peripheral retinal ischemia.[5] If ischemia is not diagnosed and treated, visual loss due to complications like vitreous hemorrhage or tractional retinal detachment may be seen secondary to angiogenesis.

Our aim in this study is to address the importance of detailed retinal examination in patients who apply for routine ophthalmologic examination with our cases in pediatric population.

MATERIAL AND METHODS

Asymptomatic patients who presented to our pediatric ophthalmology department for routine eye examination between 2017 and 2021 with peripheral retinal ischemia and/our neovascularization were involved in our study. All patients underwent fundus fluorescein angiograpy (FFA) and spectral domain optical coherence tomography (SD-OCT). Required patients underwent retinal argon laser photocoagulation or intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections. Patients were screened for systemic diseases which may cause peripheral retinal ischemia and referred to related departments.

RESULTS

Of six patients included 4 were female and 2 were male. The mean age was 8.8±2.3 (6-12) years. One patient was diagnosed with incontinentia pigmenti (IP) and 2 were finally diagnosed with IP. Two of them were siblings whom were under the investigation of dermatology department. Two cases had a history of preterm birth under 35 weeks of gestational age without any history of ROP examination. One case was diagnosed with sickle cell anemia after being referred to the department of pediatric haematology.

CASE 1

Eight-year-old girl presented to our clinic for routine eye examination. She was diagnosed with incontinentia pigmenti since 6-months of age. On examination best corrected visual acuities (BCVA) were 0.8 in the right eye and counting fingers at 30 cms in the left eye. Decreased visual acuity of the left eye was not recognised by her family prior to our examination. The full cycloplegic refraction was -0.50 -0.50x20° in the right eye and -5.0 -1.0x15° in the left eye. But the best corrected visual acuity (BCVA) did not increase in the left eye in spite of full refractive correction. In orthoptic examination, the patient had 18 prism diopter (PD) exotropia (XT) and 3 PD dissociated vertical deviation (DVD) at the distance, and 12 PD XT at the near. The distance fusion was suppressed in the left eye, and the random dot stereopsis did not exist. Biomicroscopic examination was unremarkable on both eyes however fundus examination showed peripheral retinal pigment alterations in the right eye (Figure 1A) Left eye fundoscopy showed temporal optic disc pallor, sheathing of the vessels, ghost vessels, arterial attenuation, pigment alterations and lattice degeneration on the temporal peripheral retina and decreased foveal reflex accompanied by foveal atrophy. (Figure 1B-C) Fundus fluorescein angiography did not show a significant change in the right eye (Figure 1D) however left eye showed 360 degrees of retinal ischemia and secondary neovascularization. (Figure 1E-F) Avascular areas were treated with argon laser photocoagulation (Figure 1G). Optical coherence tomography of the optic disc showed retinal nerve fibre layer loss and macula OCT showed foveal atrophy in the left eye. (Figure 1H) No complications were recorded during the follow-up period. The refractive prescription and occlusion therapy were given, and the final BCVA was 0.05 on Snellen chart in the left eye. The manifest deviation was 10-12 PD XT and 3 PD DVD in the far and near. Stereopsis and fusion did not develop during the follow-up period.

CASE 2

Six-year-old girl who was the sister of case 1 was examined in our department upon the request of her family because of her sister's clinical course. Best corrected visual acuities were 1.0 and biomicroscopic examination was unremarkable in both eyes. Dilated fundus examination showed peripheral retinal ischemia, oral FFA also revealed avascular retinal areas, however no neovascularization was seen. Argon laser photocoagulation was performed to avascular retinal areas and patient started to be followed-up. Concurrently she was refferred to dermatology department because of her skin findings and she was also diagnosed with incontinentia pigmenti. No complications were observed during the follow-up period.

CASE 3

Eleven-year-old girl presented to our department for routine ophthalmological examination. Concurrently she was under investigation of dermatology department. Best corrected visual acuities were 1.0 in each eye with cycloplegic refraction +1.00x50 in the right eye +1.25 x145 in the left eye with normal orthoptic examination. Retinal examination showed cluster pigmentation and bilateral peripheral avascular areas which were confirmed by FFA. Argon laser photocoagulation was offered however her family declined because of the potential complications of general anesthetics. No neovascularization was observed during one year follow-up.

CASE 4

Twelve-year-old boy presented for a routine examination, his BCVAs were 0.9 in the right eye and 1.0 in the left

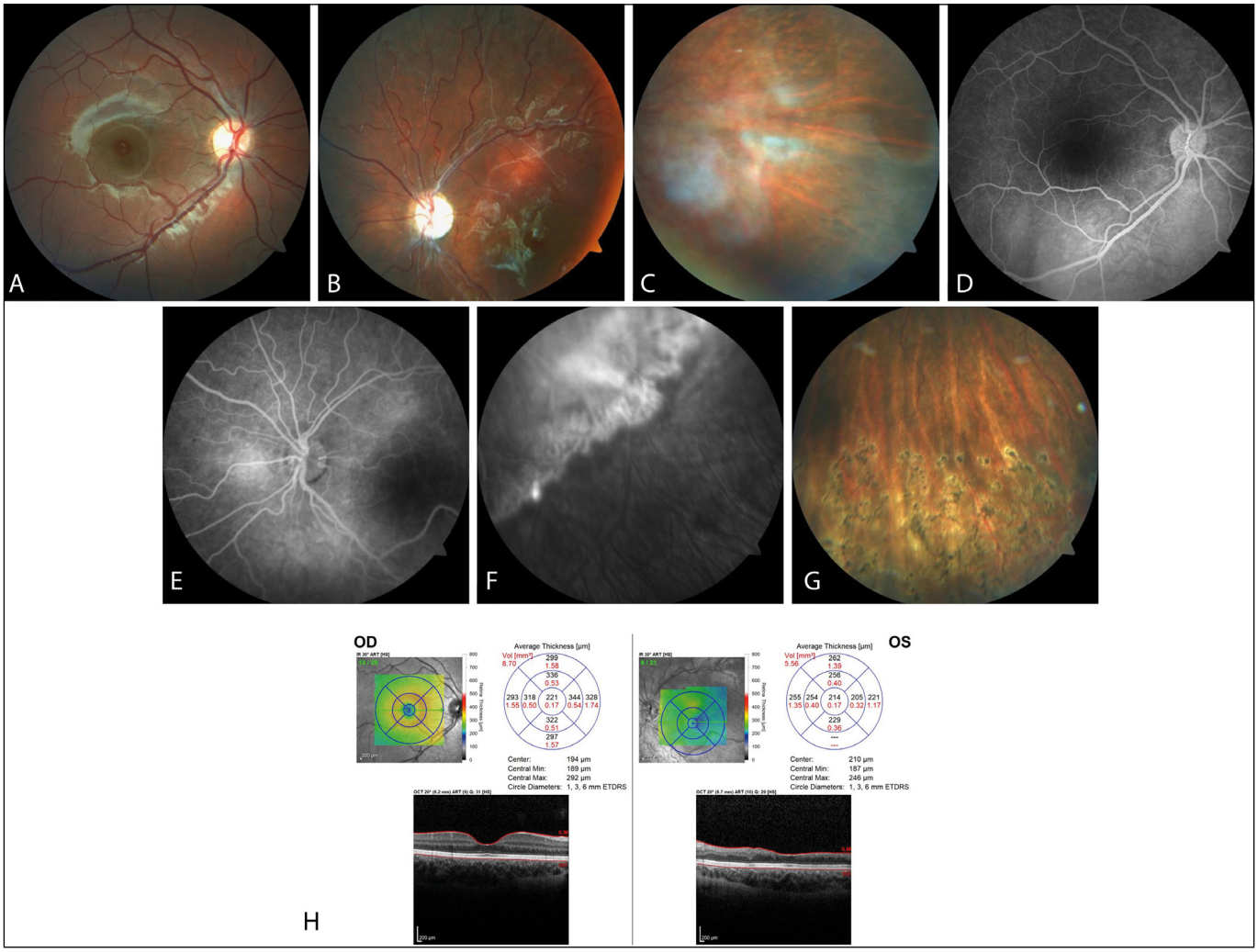

Figure 1A: *Normal FFA of the right eye.* **B:** *Color fundus photograph of the left eye shows temporal optic disc pallor and sheathing of the vessels.* **C:** *Color fundus photograph shows avascular areas in the periphery of the left eye.* **D:** *On FFA no serious pathology is observed in the right eye.* **E-F:** *FFA shows peripheral avascular area and neovascularization.* **G:** *Color fundus photograph shows the argon laser treatment which is applied to peripheral retinal avascular areas and Lattice degeneration in the left eye.* **H:** Macula OCT showed foveal atrophy in the left eye.

eye. Anterior segment examination was unremarkable in both eyes. Dilated fundus examination showed peripheral retinal vascularisation in the left eye. (Figure 2 A,B) On FFA peripheral retinal ischemia and neovascularization was observed. (Figure 2 C,D) Since he had a history of anemia he was referred to Pediatric Hematology Department and was diagnosed with Sickle Cell Anemia (SCA). Peripheral retinal avascular areas were treated with argon laser photocoagulation and no complications were observed during follow-up. (Figure 2 E,F)

CASE 5

Ten-year-old boy presented for a routine examination, his BCVAs were 1.0 in both eyes. Since dilated fundus examination showed avascular areas FFA was performed and confirmed the peripheral retinal ischemia. Later on, detailed history revealed preterm birth at 35 weeks with a birth weight of 2800 grams without any examination for ROP. Since the neovascularization was small intravitreal anti-VEGF injection was performed. Neovascularization regressed completely during follow-up no additional treatment was needed.

CASE 6

Ten-year-old girl presented to our department for a routine examination and her BCVAs were 1.0 in the right eye and 0.9 in the left eye. Anterior segment examination was unremarkable. Fundus examination showed peripheral retinal neovascularization in both eyes. (Figure 3 A-D) Detailed medical history revealed preterm birth at 34 weeks of gestational age with 2400 grams birth weight. FFA confirmed the peripheral retinal ischemia and neovascularization (Figure 3 E-H). Argon laser photocoagulation was performed to peripheral ischemic

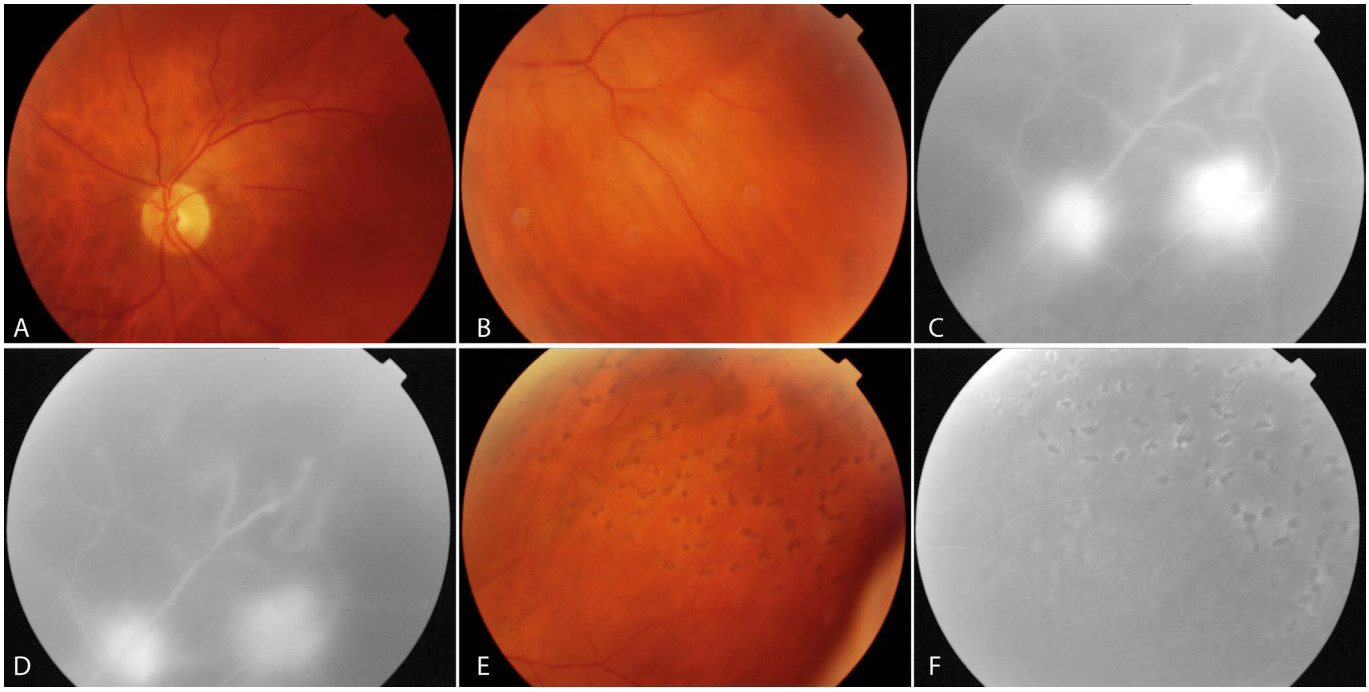

Figure 2A: *Color fundus photograph revealed normal central retina and optic disc in the left eye.* **B:** *Color fundus photograph revealed the peripheral retinal neovascularization.* **C-D:** *FFA confirmed the peripheral retinal neovascularization.* **E-F:** *Color fundus photograph and FFA of the left eye after argon laser photocoagulation.*

areas (Figure 3.I-J). No complication was observed during follow-up.

DISCUSSION

Pediatric retinal diseases which may have various hereditary or environmental origins generally affect the peripheral retina such as familial exudative vitreoretinopathy, ROP, Coats disease. Hemoglobinopathies and incontinentia pigmenti should also be kept in mind in differential diagnosis of the peripheral retinal ischemia.[4,5]

Incontinentia pigmenti which is also known as Bloch-Sulzberger Syndrome is a multi system disease affecting ectodermal tissues. The disease has a X-linked dominant inheritance pattern and since it is usually lethal to male fetuses, it is only seen in females.[6] 36.5% of children with IP has ocular abnormalities and half of the affected cases may results in blindness.[7] Although two different screening scheme is recommended for children with IP there is still no consensus.[8,9] Holmstrom et al recommends the first examination as soon as possible after birth, followed by monthly examination for 3-4 months, 3 monthly until the age of four, and annual examination after the age of four. However O'Doherty et al recommends a more flexible approach in children with normal retinal findings at the first examination.[8,9] In a series of 464 patients Carney et al showed serious ocular findings in 20% of the cases and minimal ocular findings in 15% of the cases.[10] Nystagmus, strabismus, microphthalmia, ptosis, blue sclera, conjunctival pigmentation, corneal findings, cataract, optic atrophy, vitreous hemorrhage and myopia are the most frequent ophthalmological complications. These complications tend to be unilateral however if bilateral asymmetric involvement is observed.[9] The most important ocular complication of the IP is retinal detachment secondary to ischemic retinopathy and is seen in 11.5% of the patients.[9,10] That's why it is critical to apply cryotheraphy or laser photocoagulation to these ischemic areas to prevent retinal detachment.[11,12] Intravitreal anti-VEGF injections are also an effective method to treat retinal neovascularization.[13] As a result patients with IP should be followed up closely starting from the birth for retinal avascular areas, vasculopathy and sight threatening complications such as secondary neovascularization, rhegmatogenous retinal detachment, retinal hemorrhage and optic nerve atrophy. Incontinentia pigmenti is a disease which should be kept in mind in the presence of skin findings and patients should be referred to ophthalmologists.[14]

Retinopathy of prematurity is a potentially sight threatening vasoproliferative disease of the premature infants. According to the American Academy of Pediatrics (AAP) and American Academy of Ophthalmology (AAO) guidelines published in 2018 infants with a birth weight (BW)≤1500 g or gestational age (GA)≤30 weeks or less and selected infants with a BW between 1500 and 2000 g or GA of >30 weeks with an unstable clinical course should be screened for ROP.[15] In Türkiye ROP Neonatal Study Group

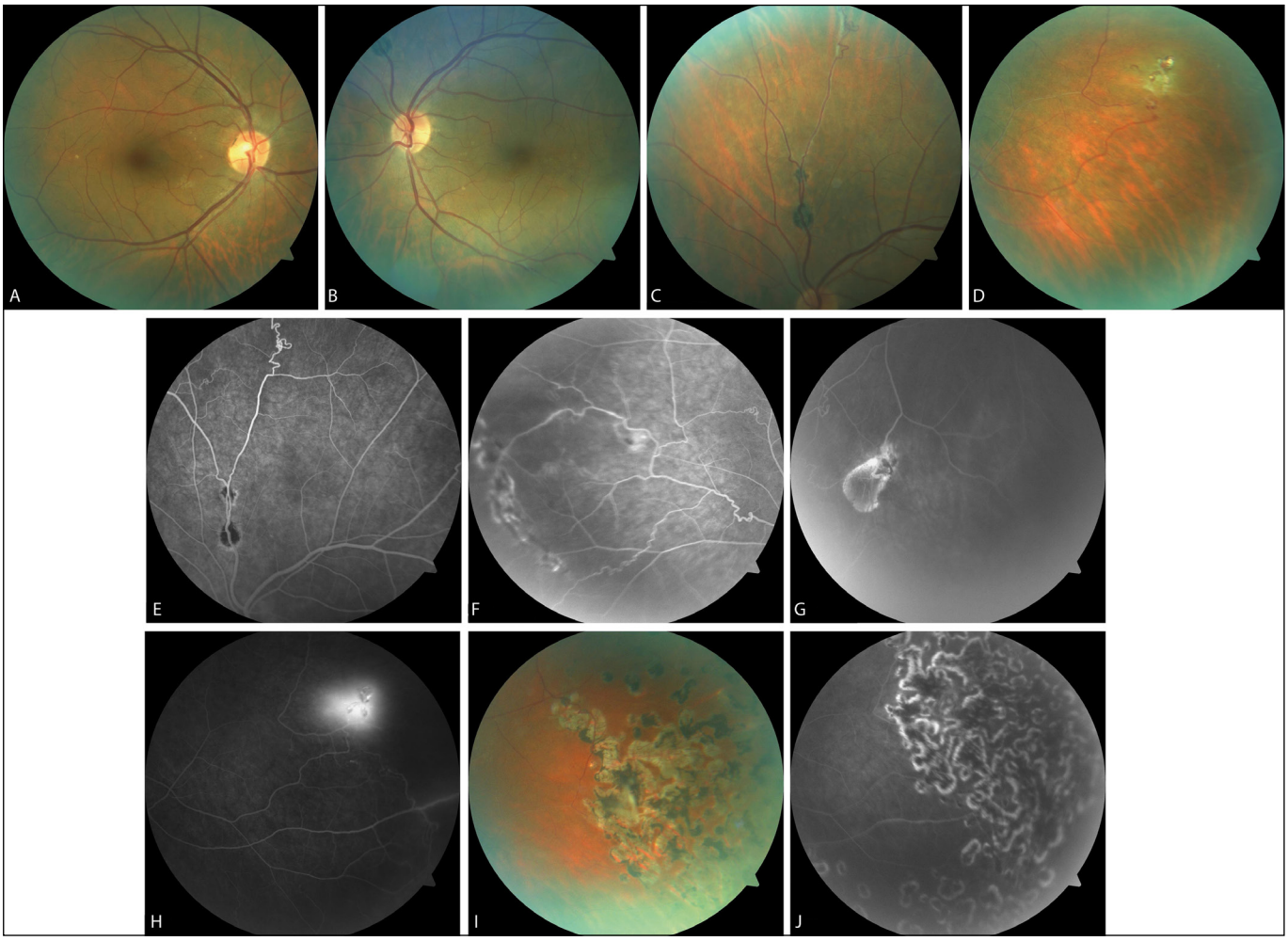

Figure 3A-B: *Color fundus photograph revealed normal macula and optic disc in both eyes.* **C-D:** *Peripheral retinal avascular areas and neovascularization is observed in both eyes.* **E-H:** *FFA confirmed the peripheral retinal neovascularization on the border of the vascular and avascular retina.* **I:***Color fundus photograph shows the retinal scars after argon laser photocoagulation.* **J:** *FFA following argon laser photocoagulation does not show any new neovascularization.*

recommends ROP screening for infants with GA≤32 weeks and BW≤1500 grams.[16] First screening should be planned at 31 weeks for infants with GA≤27 weeks and at postnatal 4th week for infants with GA>27 weeks.[17] Because of the variability of care in pediatric intensive care units among our country and according to the TR-ROP Study Group data, it seems reasonable to screen newborns with GA≤34 weeks or a BW<1700 gr or GA>35 weeks or BW>1700 gr with an unstable clinical course, history of intensive care unit or incubator.[18] Although retinal examination is crucially important to prevent serious morbidity in preterm babies, detailed fundoscopy including the periheral retina as a part of the routine examination must be performed for term infants as well.[19]

For ROP the clinical course may change in between spontaneous regression and blindness.[15,20] Ju et al revealed the spontaneous regression rates as 86.7 % for stage 1, 57.1 % for stage 2 and 5.9% for stage 3.[21] After the regression of acute phase ROP some retinal findings may be seen like peripheral vascular abnormalities, pigmentary changes, scatricial vitreoretinal interface problems, peripheral retinal folds, lattice degeneration, retinal tears, tractional and rhegmatogenous retinal detachment. In a series of Kaiser et al adulthood regressed ROP cases revealed 14-26% retinal detachment, 8-11% retinal tear, 9-11% Lattice degeneration and 34% retinal dragging.[22] It is important to remember that undiagnosed and untreated ROP cases may present with different retinal pathologies in pediatric or adult ophthalmology clinics as seen in our study.[23]

Hemoglobinopathies occur as a result of genetic mutations which causes structural changes in the hemoglobin. These changes result in decreased oxygen transportation capacity, precipitation and vascular occlusion.[24] The most frequent hereditary haematologic disease is Sickle Cell

Disease (SCD) and it may affect the eye as many different organs.[25] Proliferative retinopathy is the most serious and sight threatening complication of SCD.[26] Typical findings are salmon patch hemorrhage due to peripheral arterial occlusions, black sun-burst lesions and refractile deposits.[25,26] Local ischemia may result in peripheral neovascularization may cause vitreous hemorrhage and tractional retinal detachment. [27,28]

Since SCD lesions may regress spontaneously by auto infarction, all lesions do not need to be treated.[26] In the presence of large neovascularization areas and vitreous hemorrhage argon laser photocoagulation should be applied.[29] With the recent developments of retinal imaging the macular atrophy seen in SCD patients is on OCT-Angiography is thought to occur secondary to deep capillary plexus ischemia [30] According to the AAP children with HbSS ve HbSC trait has to be followed annually after the age of 10.[31]

As a result in every patient presenting for a routine examination in pediatric age group detailed fundus examination should be performed. In this study our aim is to demonstrate the retinal findings, their relation to systemic diseases and treatment methods in asymptomatic patients with peripheral ischemic retinopathy and point out the importance of detailed fundus examination in pediatric patient group.

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