

Visual outcomes and late complications in ROP

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ROP is one of the major causes of blindness among children

Cataracts from rubella.

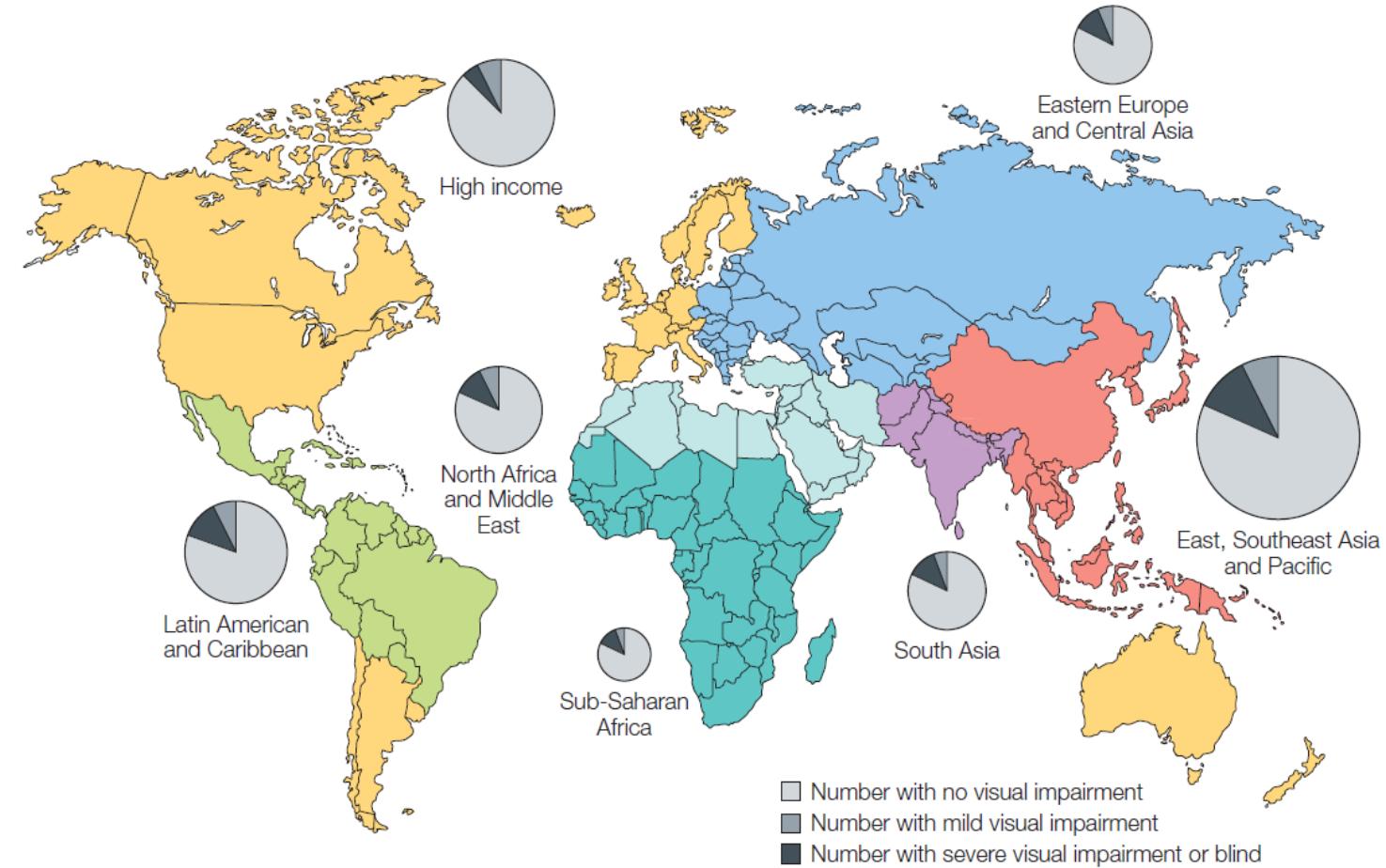
Corneal scarring from measles, Vitamin-A deficiencies.

Strabismus.

Retinopathy of prematurity

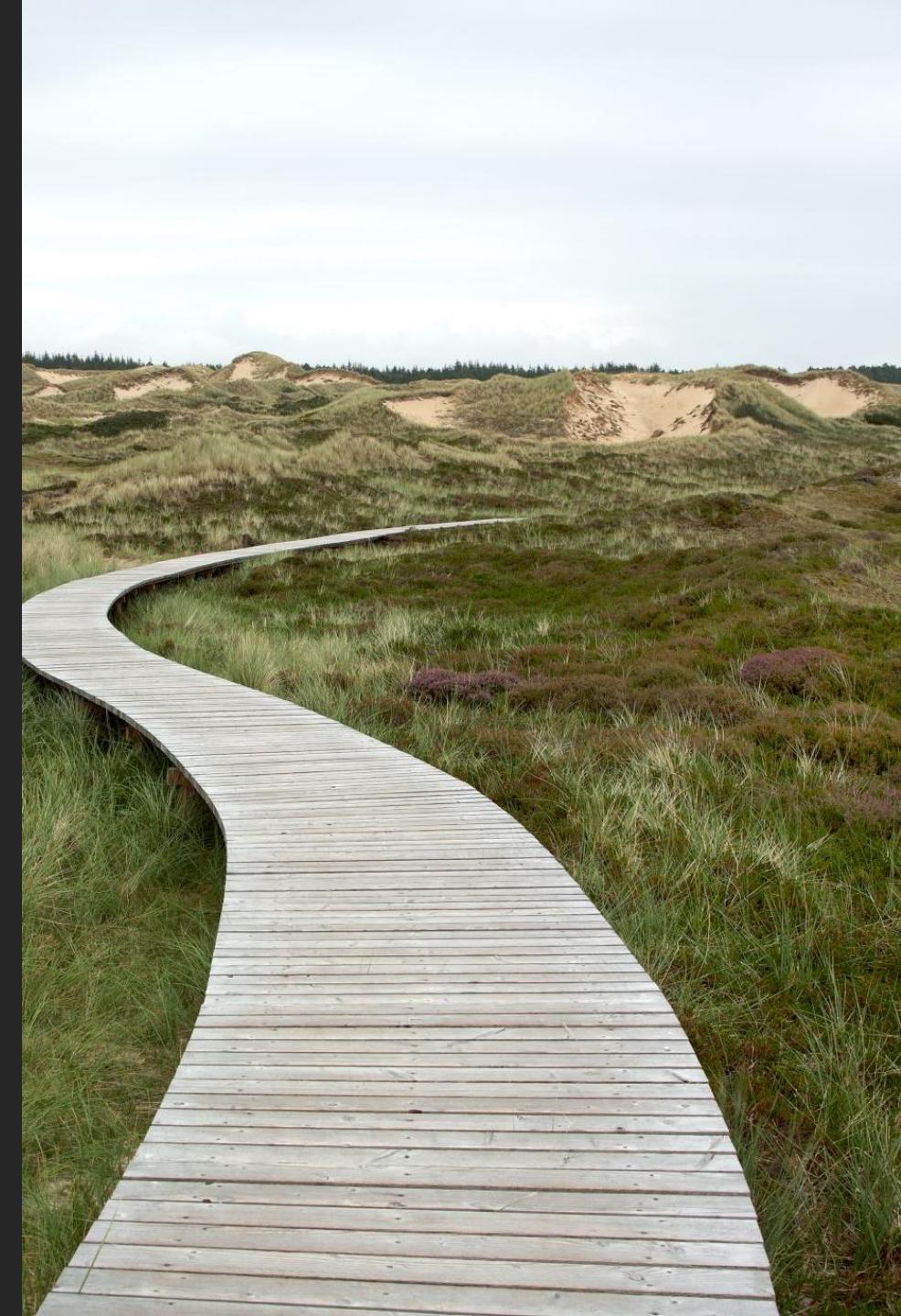
Retinopathy of prematurity (ROP) is responsible for up to 15% of all causes of blindness in developed countries and up to 60% in middle income countries

In Iran?



Natural course of ROP?

ROP is a transient disease in most infants, and spontaneous regression occurs in 85% of eyes.



Regression of ROP

Most common outcome

Involutorial sequalae

- peripheral avascularity

- abnormal branching and arcades

- pigmentary change

- vitreo-retinal interface changes

Threshold ROP

- Threshold ROP eventually develops in approximately 7%-10% of infants with a birth weight of 1250 g or less.
- Eyes that demonstrate progression undergo a gradual transition from the active to the cicatricial stage of ROP:
variable degrees of fibrosis,
contracture of the proliferative tissue,
vitreous and retinal traction,
macular distortion,
vitreous and retinal hemorrhages,
retinal detachment.

Importance of treatment

CRYO- ROP Study in 1988

4099 infants with BW <1250 gr
enrolled at 23 centers

Results reported at 3-month, 1 year
, 3-year, 5-year , 10 and 15 years

50% decrease in unfavorable
outcomes!

After 10 years, blindness in treated
infants was lower than control group

Complications

Associated with severe ROP

High myopia

Amblyopia

Strabismus

Hydrocephalus and IVH

Retinal detachment

Complications

Associated with ablative treatment

Cataract

Corneal haze

Visual field constriction

Macular pigmentary lesions

High myopia and astigmatism

Myopia

Children who were preterm had an increased prevalence of all refractive errors, especially myopia.

Myopia is a consequence of low birth weight even in the absence of ROP.

Myopia is a well-known complication of severe ROP.



Prematurity myopia vs. severe ROP myopia

myopia of prematurity= Pre-school years

myopia associated with severe ROP= onset in infancy + progression during the first year after birth.

Myopia of ROP

The exact mechanism is **unknown**.

Increased lens thickness

Shallower anterior chamber depth

Anterior shift of lens iris and ciliary complex

A mechanism of altered anterior segment development in ROP leading to high myopia.

Epidemiology

CRYO-ROP trial:

- * Overall prevalence of myopia (< -0.25 D) among all subjects at 1 year= **21%**,
prevalence of myopia among the severe ROP subgroup= **80%**
- * Overall prevalence of high myopia (< -5.0 D)= **3.9%**
prevalence of high myopia among the severe ROP subgroup= **~43%**
- * Each *100g decrease* in birth weight: *10% increase* in the prevalence of myopia.

ET-ROP study:

enrolled participants with pre-threshold ROP:

prevalence of myopia and high myopia: **~65%** and **~35%** respectively.

Myopia :Laser vs. cryotherapy

cryotherapy for threshold ROP is associated with a greater degree of myopia than laser therapy in the first year of life. The myopia increased at a greater rate in the cryotherapy treated infants over the 9-month study period.

Laws, F., D. Laws, and D. Clark, *Cryotherapy and laser treatment for acute retinopathy of prematurity: refractive outcomes, a longitudinal study*. British Journal of Ophthalmology, 1997. 81(1): p. 12-15.



Is there a correlation between refractive error and extent of retinal laser ablation ?

- The extent of myopia after retinal laser ablation for ROP is higher if a greater number of laser burns or a larger proportion of the retina is treated.
- A positive correlation between the degree of myopia (in diopters) and the number of laser shots used: $-0.14D/100$ laser shots.



Young-Zvandasara, T., et al., *Is the severity of refractive error dependent on the quantity and extent of retinal laser ablation for retinopathy of prematurity?* Eye, 2020. 34(4): p. 740-745.

Geloneck, M.M., et al., *Refractive Outcomes Following Bevacizumab Monotherapy Compared With Conventional Laser Treatment.* JAMA Ophthalmology, 2014. 132(11): p. 1327.

Myopia: Laser Photocoagulation vs. Bevacizumab

The myopic status between laser and IVB treatment did not differ statistically.

The BEAT-ROP study: a lower prevalence of myopia in those treated with IVB. The prevalence of myopia at 2.5 years in individuals with zone 1 ROP was 79% in the laser group and 43% in the IVB group

Kuo, H.K., et al., *Refractive Error in Patients with Retinopathy of Prematurity after Laser Photocoagulation or Bevacizumab Monotherapy*. Ophthalmologica, 2015. 234(4): p. 211-217.

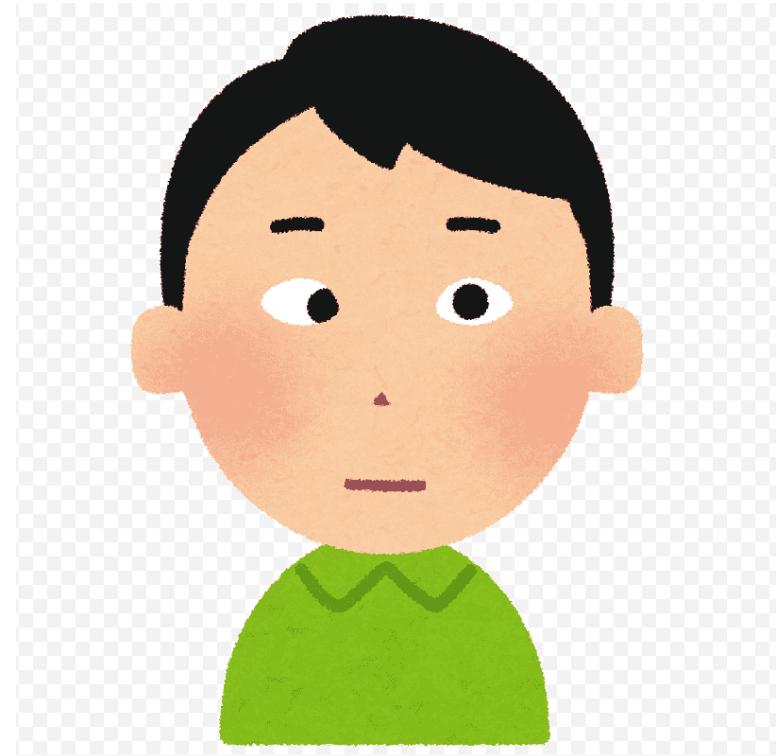
Mintz-Hittner HA, Kennedy KA, Chuang AZ;BEAT-ROP Cooperative Group. Efficacy of intravitreal bevacizumab for stage 3+ retinopathy of prematurity. N Engl J Med. 2011;364(7):603-615.



strabismus

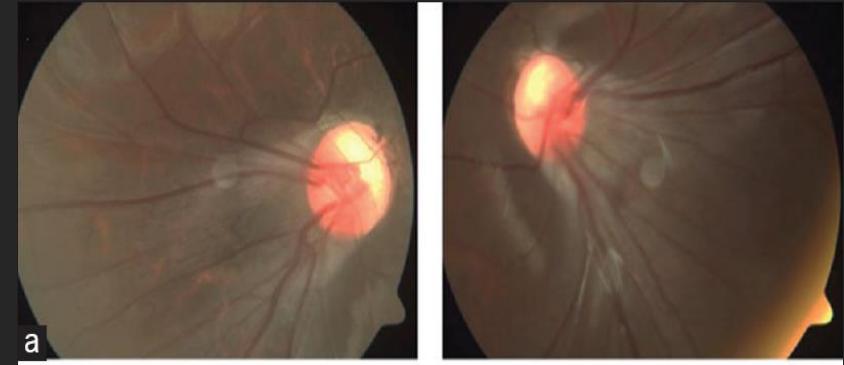
The prevalence of strabismus is increased by preterm birth and by ROP stage (even mild ROP).

The incidence of strabismus is raised from around 6% to over 60%, and this increases as acute phase ROP increases.



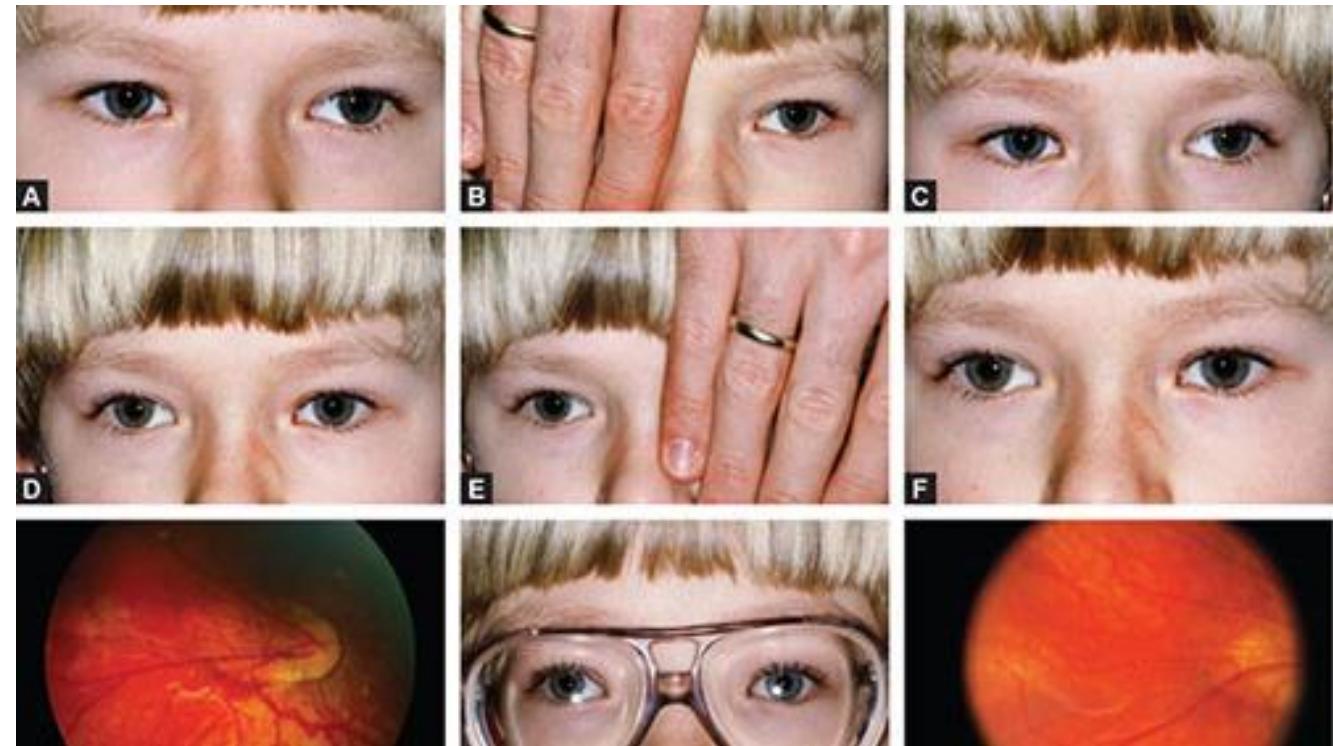
Macular dragging

in addition to retinal detachment, other sequelae of ROP include macular heterotopia, unless it is very mild, it usually results in poor central vision.



Pseudo strabismus

When present in the fixing eye, it also causes pseudoexotropia due to positive angle kappa as the eye is directed temporally to allow images to focus on the displaced macula.



Glaucoma

Patients with retinopathy of prematurity (ROP) are known to be at risk for neovascular glaucoma that typically occurs during infancy due to retinal ischemia.



late onset angle-closure glaucoma should be considered as a possible complication of ROP. Most cases had axial hyperopia, but some eyes had complex biometry with axial myopia combined with relative anterior microphthalmos.



Glaucoma

Although earlier treatment of significant ROP has resulted in better retinal structure and visual acuity outcomes, nearly 2% of the eyes with high-risk prethreshold ROP developed glaucoma at some point during the first 6 years of life.

Bremer, D.L., et al., *Glaucoma in the Early Treatment for Retinopathy of Prematurity (ETROP) study*. Journal of AAPOS : the official publication of the American Association for Pediatric Ophthalmology and Strabismus, 2012. **16**(5): p. 449-452.

Retinal detachment

* Retinal detachment will occur in some cases of ROP even when the neovascular phase of the disease is managed with the best available treatment:

ETROP study:

- *unfavorable outcomes in almost 1/10 of infants despite timely and thorough laser*
- *Some eyes with retinal detachment were treated with vitreoretinal surgery, but outcomes were generally poor (attached macula present at 6 years in only 31% of stage 4A (5 of 16), 60% of stage 4B (6 of 10), and 0% of stage 5 (0 of 10) eyes)*

Late-Onset Retinal Findings

Eyes with ROP not meeting the treatment threshold during infancy showed various late retinal findings and complications, of which RDs were the most concerning.

Complications were seen in all age groups, including patients born after the Early Treatment for Retinopathy of Prematurity Study.

Late-Onset Retinal Findings

Multicenter case series of premature patients with no prior ROP treatment at infancy and no RD at infancy who demonstrated late retinal findings, manifestations, or complications.

Table 3. Findings and Complications for the Entire Patient Cohort

Findings and Complications	No. (%)
Total eyes	363
Lattice-like changes	196 (54.0)
Retinal hole	126 (34.7)
Retinal tear	111 (30.6)
Retinal detachment	140 (38.6)
Retinoschisis	44 (12.1)
Vitreous condensation ridge-like interface	112 (30.9)
Macular dragging	44 (12.1)

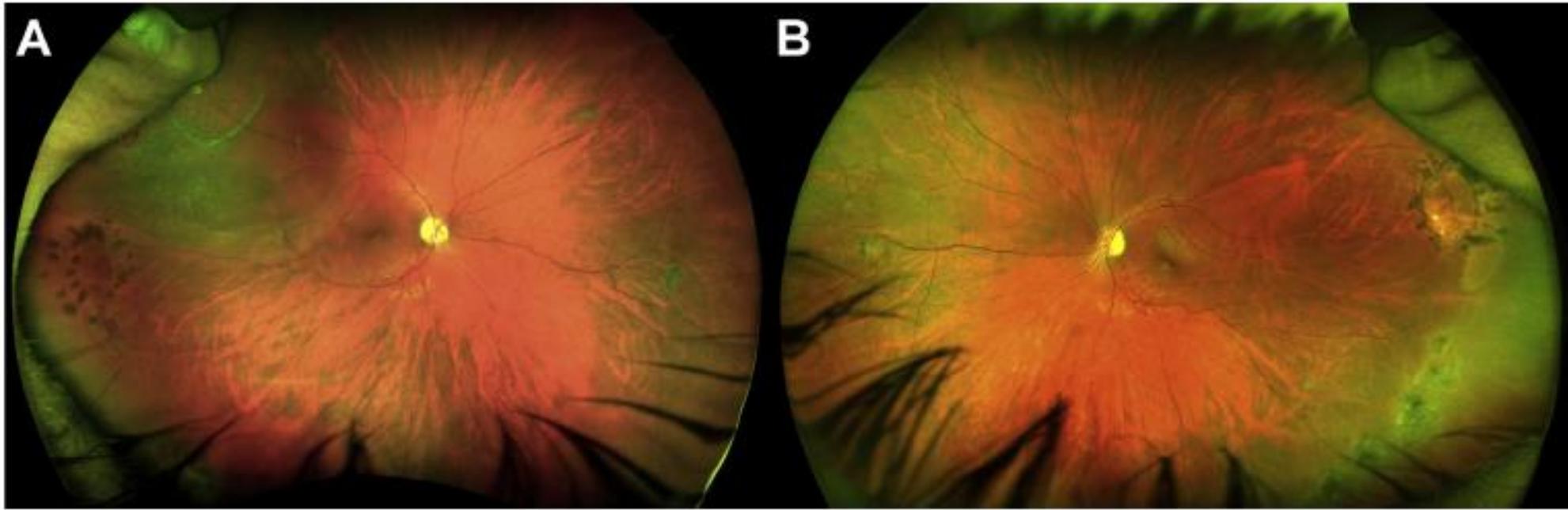
Hamad, A.E., et al., *Late-Onset Retinal Findings and Complications in Untreated Retinopathy of Prematurity*. Ophthalmology Retina, 2020. 4(6): p. 602-612.

Table 10. Percent Detachment by Gestational Age

Gestational Age (wks)	No. of Eyes	Average Age (yrs)	No. of Retinal Detachments	Eyes with Retinal Detachment (%)	P Value Compared with 30 to 34 Weeks
25 or less	98	23.7	32	32.7	0.0060
26–27	48	22.9	21	43.8	0.0004
28–29	44	34.0	21	47.7	0.0002
30–34	40	45.3	4	10.0	

Table 11. Percent Detachment by Zone of Furthest Vascularization

Zone of Furthest Vascularization	No. of Eyes	Average Age (yrs)	No. Retinal Detachments	Eyes with Retinal Detachment (%)	P Value Compared with Zone 3
Posterior zone 2	22	37.5	12	54.5	0.009
Mid zone 2	32	42.8	11	34.4	0.273
Anterior zone 2	75	25.6	24	32.0	0.270
Zone 3	41	22.5	9	22.0	



Case

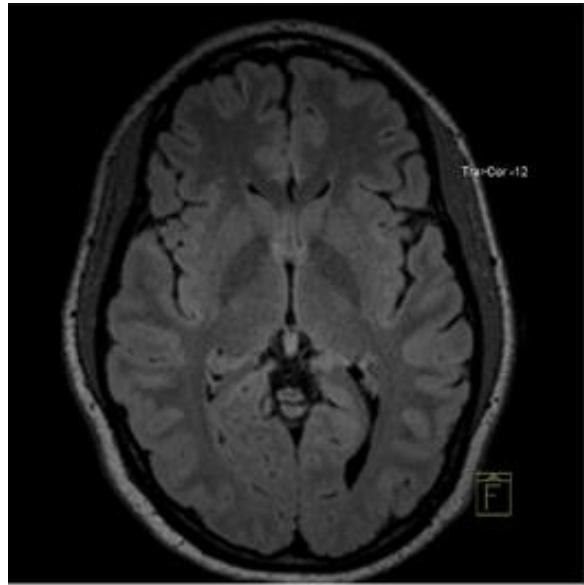
Neuro -ophthalmologic considerations



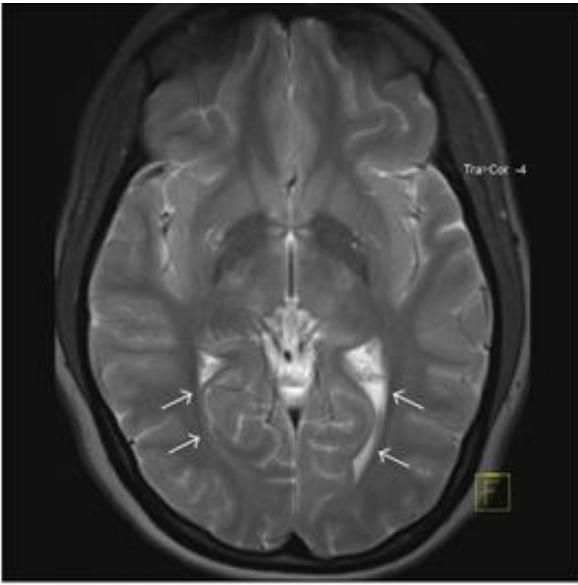
Optic radiation damage

Periventricular/intraventricular hemorrhage (PVH/IVH)

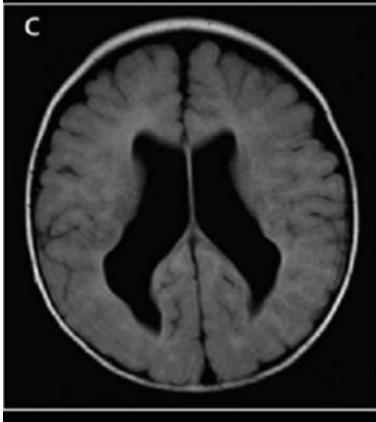
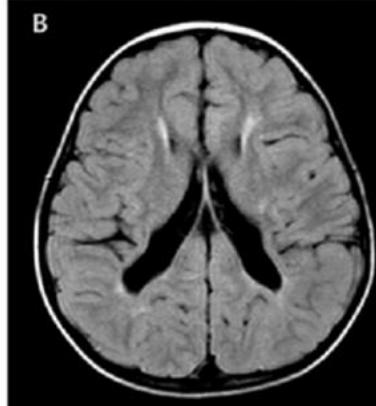
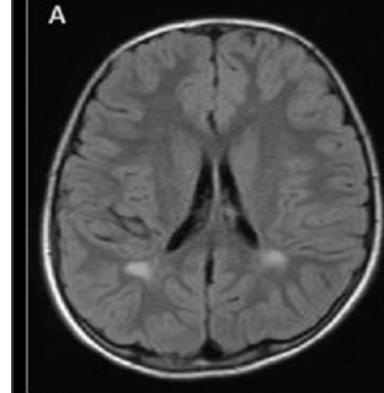
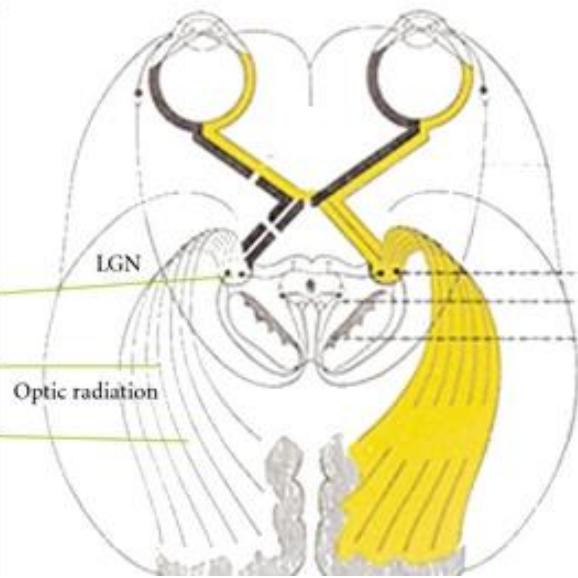
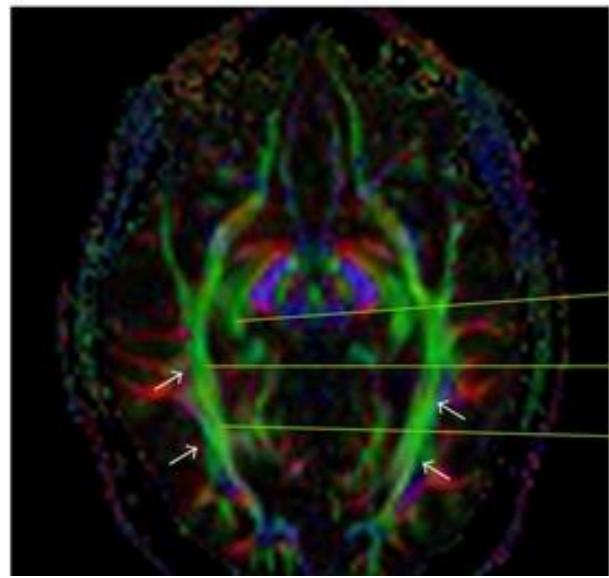
periventricular leukomalacia



(c)



(d)



Take home message



Prevention is the key



Long term follows up for late complications is necessary



Cerebral visual impairment (CVI) also may accompany ROP patients

Thank You!

