Current Medicine Research and Practice 9 (2019) 211–212

Contents lists available at ScienceDirect

Current Medicine Research and Practice

journal homepage: www.elsevier.com/locate/cmrp

Editorial

Retinopathy of prematurity: Challenges of a growing epidemic in India

Retinopathy of prematurity (ROP) is rapidly emerging as an important cause of childhood blindness worldwide, and India is particularly susceptible as it is having the highest number of preterm births in the world.[1] The world is experiencing the third epidemic of ROP.[2] High-income developed nations have been able to counter this challenge effectively by high-quality neonatal care, effective screening and treatment protocols. However, low-/middle-income developing nations such as India are facing a growing epidemic of ROP-related blindness that has to be urgently addressed if this epidemic has to be contained effectively.

ROP is a unique disease that can be prevented by good neonatal practices and possibly the only pediatric eye disease which requires screening/telescreening programs to detect disease in time and has multiple effective treatments available. Yet a large number of preterm babies in India continue to go blind because of lack of screening/treatment with a huge socioeconomic burden on the community.[3]

1. ROP screening programs essential for timely detection

As a large number of newborn care units continue to mushroom across the country, more ROP is occurring because of improved survival of sick preterm babies. On the other hand, poor neonatal care practices (due to poorly trained pediatric teams/inadequate equipment) is leading to severe ROP in bigger babies as well.[4] Thus, unlike American ROP screening guidelines[5] which recommend screening smaller babies aged <30 weeks gestational age (GA)/<1500 g birth weight (BW), developing countries such as India need to screen smaller as well as bigger babies, thereby increasing the screening burden significantly. The need for repeated follow-up every few weeks to monitor disease regression/progression also requires proper counseling and demands prolonged compliance from parents/caregivers.

The Ministry of Health, Government of India, has realized the rising importance of ROP in the community. Rashtriya Bal Suraksha Karyakram (RBSK), with support of the National Program for Control of Blindness, released the national ROP screening guidelines[6] which provided better insights for treating physicians about proper screening, management, and referral practices. It advised screening all babies <2000 g BW and <34 weeks GA; while bigger babies 34–36 wks GA can also be screened if they have risk factors for developing ROP. First screening is advised at 30 days of birth or as early as 2–3 in very small babies (<28 weeks GA and <1200 g BW). The government also supports free screening and treatment for ROP babies younger than 1 year under the Janani Shishu Suraksha Karyakram (JSSK) program in participating hospitals.

Notably, there is a gross lack of awareness about ROP and poor collaboration among ophthalmologists and neonatologists.[7] The country has a large rural population and does not have enough screening/treatment centers, with very few trained personnel even in larger cities to cater to this increased burden. Therefore, a large number of babies are ending up with irreversible blinding end-stage disease, and these will eventually lead to more medico-legal cases in the future. The Indian Retinopathy of Prematurity Society is a notable effort to bring together ROP specialists across India to develop expertise and share knowledge to overcome challenges.[8]

2. Changing profile of ROP and rise of pharmacotherapy

Laser treatment of the avascular retina has been the time-tested treatment for ROP.[9] However, over the last decade, the profile of ROP has changed with occurrence of severe disease variants such as aggressive posterior ROP (APROP)[10] and posterior zone 1 disease,[11] where even the macula is not vascularized. In these cases, the retina development is severely restricted, and the disease progresses rapidly to blindness and is difficult to treat with laser alone.

Over the last few years, intravitreal anti-VEGF (vascular endothelial growth factor) drugs such as bevacizumab and ranibizumab have rapidly emerged as the first-line treatment in the management of zone 1 disease and APROP.[12] They not only help in rapid disease regression but also lead to vascular regrowth with improved visual fields and lesser myopia. These drugs are technically easier to administer, without the prolonged pain experienced by preterm babies under topical anesthesia due to the lack of effective pain protocols. However, there are still concerns regarding frequent recurrences, unknown long-term side effects, what actual dose to use, and the number of injections that can be safely given.[13] There is now a need for longer follow-up to detect recurrences, and proper training in injection technique is essential to avoid rising complications such as cataracts and endophthalmitis.[14]

The recent RAINBOW trial results gave useful insights about the superiority of ranibizumab over laser and led to its approval as the first pharmacological treatment for ROP in the European Union.[15] Just like laser therapy replaced cryotherapy, pharmacological treatment for ROP is expected to significantly increase in the future as more data is available regarding its safety and efficacy.

The delayed screening/treatment leads to many babies with advanced ROP (with retinal detachment) being referred to tertiary eye care facilities for surgical management. But again, there are only a few eye centers in the country with trained personnel and advanced vitreoretinal surgical setups which can cater to this rising need to operate advanced cases being referred across the country. It is very important that the treatment services also develop rapidly,

https://doi.org/10.1016/j.cmrp.2019.11.004

in tandem with screening programs, as more babies are getting referred for treatment.

3. Digital screening, telescreening models, and artificial intelligence

With the advent of wide-field digital retinal imaging cameras, telescreening programs are helping to overcome the limitations of trained experts and resources needed for ROP screening. Several successful telescreening programs such as the Karnataka Internet Assisted Diagnosis of Retinopathy of Prematurity (KIDROP) model[16] have enhanced the reach of screening programs like never before and are reducing ROP-related blindness in the community. Experts situated in remote cities can opine and guide on images being taken across the target population via mobile screening units powered by retinal cameras. With the availability of cheaper indigenously developed retinal cameras, the scope of telescreening programs will grow even further.[17,18] Neonatology-led screening with digital cameras in neonatal units may change the way babies may be screened in the future.[19]

New technologies such as artificial intelligence and deep learning are rapidly integrating with these models and will further enhance the predictability of the development of severe ROP and treatment outcomes in an automated manner.[20] Prediction algorithmic models such as WINROP are helping to predict the occurrence of severe ROP even before it develops.[21] The amount of research going into these technology-driven models is astounding and will help in prioritizing babies in more need for ROP care in resource-limited settings.

4. Prevention is better than cure

It is well known that best-quality neonatal practices can help lower the incidence of ROP.[22] Every case of aggressive posterior ROP and advanced end-stage blinding ROP is an indicator of poor neonatal care and lack of effective ROP services, respectively. There is a need for policy/legislation necessitating minimum basic quality of neonatal care and the mandatory implementation of ROP screening programs in every newborn care unit.

Obstetricians must be made aware of their essential role in counseling mothers undergoing preterm labor, regarding the need and importance of eye screening after birth to detect ROP. Their long-trusted association with these parents will ensure their better compliance for subsequent ROP screening, follow-up, and treatment.

We need to realize that there will never be enough ROP specialists to deal with this rising epidemic. Prevention is the best way to deal with these rising numbers and prevent blindness in these preterm babies. Uniform preferred practice patterns, knowledge sharing, focused training, multidisciplinary collaboration, and infrastructure development are urgently needed to tackle this growing epidemic of ROP in India.

Declaration of competing interest

Author has no conflict of interest.

References

1. Blencowe H, Moxon S, Gilbert C. Update on blindness due to retinopathy of prematurity globally and in India. *Indian Pediatr*. 2016;53(2):S89–S92.
2. Gilbert C. Retinopathy of prematurity: a global perspective of the epidemics, population of babies at risk and implications for control. *Early Hum Dev*. 2008;84:77–82.
3. Azad R, Chandra P, Gangwe A, Kumar V. Lack of screening underlies most stage-5 retinopathy of prematurity among cases presenting to a tertiary eye center in India. *Indian Pediatr*. 2016;53(2):S103–S106.
4. Gilbert C, Fielder A, Gordillo L, et al. Characteristics of infants with severe retinopathy of prematurity in countries with low, moderate, and high levels of development: implications for screening programs. *Pediatrics*. 2005;115:e518–e525.
5. Fierson WM. American academy of pediatrics section on ophthalmology, American academy of ophthalmology, American association for pediatric ophthalmology and strabismus, American association of certified orthoptists. Screening examination of premature infants for retinopathy of prematurity. *Pediatrics*. 2018;142, e20183061. pii.
6. *Guidelines for Universal Eye Screening in Newborns Including Retinopathy of Prematurity*. Rashtriya bal swasthya karyakram; 2017 [cited 2019 Sep 25]. Available from: https://www.nhm.gov.in/images/pdf/programmes/RBSK/Resource_Documents/Revised_ROP_Guidelines-Web_Optimized.pdf.
7. Patwardhan SD, Azad R, Gogia V, Chandra P, Gupta S. Prevailing clinical practices regarding screening for retinopathy of prematurity among pediatricians in India: a pilot survey. *Indian J Ophthalmol*. 2011;59:427–430.
8. Vinekar A, Azad RV. The Indian Retinopathy of Prematurity (iROP) society: challenges ahead. *Indian J Ophthalmol*. 2019;67:722.
9. Good WV. Early treatment for retinopathy of prematurity cooperative group. Final results of the early treatment for retinopathy of prematurity (ETROP) randomized trial. *Trans Am Ophthalmol Soc*. 2004;102:233–248. discussion 248-250.
10. Chandra P, Tewari R, Jain S. The restless retina in aggressive posterior retinopathy of prematurity: prevention is better than cure. *Community Eye Health*. 2018;31:S27–S28.
11. Katoch D, Dogra MR, Aggarwal K, et al. Posterior zone I retinopathy of prematurity: spectrum of disease and outcome after laser treatment. *Can J Ophthalmol*. 2019;54:87–93.
12. 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;364:603–615.
13. Sankar MJ, Sankar J, Chandra P. Anti-vascular endothelial growth factor (VEGF) drugs for treatment of retinopathy of prematurity. *Cochrane Database Syst Rev*. 2018 08;1, CD009734.
14. Vanathi M, Kumawat D, Singh R, Chandra P. Iatrogenic crystalline lens injury in pediatric eyes following intravitreal injection for retinopathy of prematurity. *J Pediatr Ophthalmol Strabismus*. 2019;56:162–167.
15. Stahl A, Lepore D, Fielder A, et al. Ranibizumab versus laser therapy for the treatment of very low birthweight infants with retinopathy of prematurity (RAINBOW): an open-label randomised controlled trial. *Lancet Lond Engl*. 2019 Sep 12. https://doi.org/10.1016/S0140-6736(19)31344-3.
16. Vinekar A, Jayadev C, Mangalesh S, Shetty B, Vidyasagar D. Role of telemedicine in retinopathy of prematurity screening in rural outreach centers in India - a report of 20,214 imaging sessions in the KIDROP program. *Semin Fetal Neonatal Med*. 2015;20:335–345.
17. Sharma A, Goyal A, Bilong Y, et al. Comparison of a smartphone-based photography method with indirect ophthalmoscopic assessment in referable retinopathy of prematurity: a smart retinopathy of prematurity model pilot study. pii: S2468-6530 *Ophthalmol Retina*. 2019;(19):30313–30316. https://doi.org/10.1016/j.oret.2019.06.006 [Epub ahead of print].
18. Vinekar A, Rao SV, Murthy S, et al. A novel, low-cost, wide-field, infant retinal camera, "neo": technical and safety report for the use on premature infants. *Transl Vis Sci Technol*. 2019;8:2.
19. Gilbert C, Wormald R, Fielder A, et al. Potential for a paradigm change in the detection of retinopathy of prematurity requiring treatment. *Arch Dis Child Fetal Neonatal Ed*. 2016;101:6–9.
20. Gupta K, Campbell JP, Taylor S, et al. A quantitative severity scale for retinopathy of prematurity using deep learning to monitor disease regression after treatment. *JAMA Ophthalmol*. 2019 Jul 3. https://doi.org/10.1001/jamaophthalmol.2019.2442 [Epub ahead of print].
21. Sanghi G, Narang A, Narula S, Dogra MR. WINROP algorithm for prediction of sight threatening retinopathy of prematurity: initial experience in Indian preterm infants. *Indian J Ophthalmol*. 2018;66:110–113.
22. Sivanandan S, Chandra P, Deorari AK, Agarwal R. Retinopathy of prematurity: AIIMS, New Delhi experience. *Indian Pediatr*. 2016;53(2):S123–S128.

Parijat Chandra, MD DNB, Professor of Ophthalmology
Dr Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, India
E-mail address: parijatchandra@gmail.com.

1 October 2019
Available online 13 November 2019