

# India to gear up to the challenge of “third epidemic” of retinopathy of prematurity in the world

*P Sai Kiranmayee, Viswanath Kalluri*

Many of the causes of childhood blindness are avoidable, being either preventable or treatable. Retinopathy of prematurity (ROP) remains one of the most preventable causes of childhood blindness worldwide. Currently, India is facing the third epidemic of ROP. In India, the health system involving the mother and child health services needs to be strengthened with a policy to cover the existing inadequacies in neonatal care and implementation of program covering newborn, especially premature. The access, availability, and affordability of services related to the care of premature babies need strengthening in India. ROP-trained ophthalmologists and neonatal care pediatricians and a professional togetherness is a big issue. Inadequacies in awareness of ROP among the parents, health care workers, counsellors add up to the problem. Community-based health workers such as Accredited Social Health Activist are a good dependable force in India and are needed to be trained in awareness and establishing a proper identification for prompt referral. ROP prevention needs a multidisciplinary team approach. ROP management stands as a good example of all the strategies for prevention, which includes primary prevention (improving obstetric and neonatal care), secondary prevention (screening and treatment programs), and tertiary prevention (treating complications and rehabilitation to reduce disability). Given its demographic and cultural diversity, India faces numerous challenges, with significant rural–urban, poor–rich, gender, socioeconomic, and regional differences. So, we need to gear up to face the present challenge of the third epidemic of ROP and prevent ROP-related childhood blindness as it is the need of the hour.

**Key words:** Childhood blindness, prevention, retinopathy of prematurity, ROP awareness

The prevention of blindness in children is considered a high priority within the World Health Organization’s Vision 2020.<sup>[1]</sup> Many of the causes of childhood blindness are avoidable, being either preventable or treatable. Recent estimates show that there are 1.26 million children who are blind, globally. Out of these, 280,000 children are from India.<sup>[2]</sup> Economic development and specific interventions are changing the pattern of blindness in children all over the world including India.<sup>[3]</sup> The world is currently witnessing the third epidemic of retinopathy of prematurity (ROP)<sup>[4,5]</sup> and it is emerging as a major public health concern in low- and middle-income countries, including India.<sup>[5]</sup>

## Third Epidemic of ROP: Multifactorial Challenge

The first epidemic of ROP occurred due to unrestricted oxygen use and second epidemic due to increased survival of very preterm babies in high-income countries. India and other middle-income countries are facing the third epidemic of ROP due to various factors, such as increased survival of preterm babies, inadequate quality of neonatal care, and low coverage of screening and treatment services for ROP.

### Increased survival of preterm babies

Approximately 15 million babies are born preterm worldwide each year and India has the highest number of preterm births.<sup>[6]</sup>

Department of Vitreo-Retinal Services, Pushpagiri Vitreo-Retinal Institute, West Marredpally, Secunderabad, Telangana, India

**Correspondence to:** Dr. P Sai Kiranmayee, Pusphagiri Vitreo-Retinal Institute, Uma Plaza, West Marredpally, Secunderabad, Telangana - 500 026, India. E-mail: drsaiikiranmayee@gmail.com

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In 2010, there was an estimate of 3,519,100 preterm births in India.<sup>[7]</sup> If 30% of these babies have access to neonatal care, about one lakh babies are found to survive each year who are at risk of developing ROP requiring screening.<sup>[8]</sup> To address this vast disparity, newborn health had captured the attention of policymakers in India. This resulted in strong political commitment to end preventable newborn stillbirths and deaths and also to recognize newborn health as a national development necessity.<sup>[9]</sup>

As a result, a nationwide network of facility-based newborn care was established at various levels: 14,135 Newborn Care Corners at the point of child birth; 1810 Newborn Stabilization Units; 548 Special Newborn Care Units (SNCUs) for sick and small newborns, with care to more than 6 lakhs newborns being provided in SNCUs each year.<sup>[9]</sup> The number of these units has increased over a period of time. This led to increased survival of babies who are at risk to develop blindness due to ROP.

### Inadequate quality of neonatal care

The scale-up of neonatal care in India improved the survival of preterm babies but the quality of care needs attention. In

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middle-income countries the neonatal care expanded without attention to quality of care provided, infrastructure availability, and training to the care providers.<sup>[8]</sup> Owing to wide variation in the neonatal care, it is found that more mature and heavier babies develop ROP.<sup>[10-12]</sup> This further escalates the number of babies to be screened and increases development of vision-threatening ROP.

#### Low coverage of ROP screening and treatment services

India accounts for nearly 10% of the worldwide estimate of blindness and visual impairment due to ROP. It has been reported that majority of babies present with stage 5 disease due to lack of screening.<sup>[11,13]</sup> The 11-City 9-State study done to assess the services for ROP in India recommended that eye care services for ROP need to expand.<sup>[14]</sup> Low screening rates are also due to lack of awareness among neonatologist/pediatricians and nonavailability of trained ophthalmologists.<sup>[15-17]</sup>

#### *Burden for a lifetime*

Although the number of blind children is relatively low, they have a lifetime of blindness ahead, with an estimated 75 million blind-years (number blind × length of life).<sup>[18]</sup> It is estimated that at least 2–3 lakhs children in India have severe visual impairment or blindness<sup>[19]</sup> and more than 3000 infants become blind or visually impaired each year due to lack of screening and treatment for ROP.<sup>[7]</sup> A study by Vinekar *et al.* showed that the fiscal quantum of blind person-years saved is 108.4 million USD annually by expansion of telemedicine screening for ROP to 10 states in India.<sup>[20]</sup> The formula: number of babies requiring treatment × life expectancy × per capita income was used to calculate the “burden of blindness.”

### Multidisciplinary Approach and Prevention

ROP-related blindness can be prevented by a multidisciplinary team approach, which includes obstetricians, neonatologists/pediatricians, nurses, ophthalmologists, health care workers, and parents.

ROP stands a good example of all the strategies for prevention which includes:

- i. Primary prevention: prevention of the disease by improving obstetric and neonatal care.
- ii. Secondary prevention: screening and treatment programs for ROP.
- iii. Tertiary prevention: treating complications and rehabilitation to reduce disability.

#### Primary prevention

Primary prevention of ROP includes reducing rates of prematurity by improving antenatal and perinatal care.

#### *Reducing preterm births*

Preterm birth is defined as >20 and <37 completed weeks of gestation of the fetus at birth. Although many children born preterm lead a normal and healthy life, a significant proportion experience lifelong disability and health issues.<sup>[21]</sup> The socioeconomic impact on individuals, families, and society is considerable as are the health care costs associated with perinatal care and lifelong disability.<sup>[22,23]</sup>

Preterm birth has multiple causes; therefore, solutions will not come through a single discovery but rather from an array of discoveries addressing multiple biological, clinical,

and social-behavioral risk factors. Better understanding of the causes and mechanisms will advance the development of prevention solutions.<sup>[6]</sup> Adolescent pregnancy, short time gap between births, unhealthy prepregnancy weight (underweight or obesity), chronic disease (e.g. diabetes), infectious diseases (e.g. HIV), substance abuse (e.g. tobacco use and heavy alcohol use), and poor psychological health are risk factors for preterm birth.<sup>[6]</sup> Interventions before and during pregnancy can help in reducing preterm births.

#### Before pregnancy

Preconception care emphasizes maternal and child health. Health education and other programs delivered to all women during adolescence, before conception, and between pregnancies improve a woman's own health during pregnancy as well as that of her babies.

Control of intrauterine infection, nutritional supplementation (periconceptual folate<sup>[24]</sup> and iron), cessation of smoking, improving high or low body mass index, reducing adolescent pregnancies, and increasing birth interval can help in prevention of preterm births.<sup>[6]</sup>

Judicious use of fertility treatments help, as children born due to assisted reproductive technology have an excess risk of birth defects when compared to spontaneously conceived children, further increasing the chance of obstetric intervention and preterm birth.<sup>[25]</sup>

Assisted fertility treatment increases the risk of multiple pregnancy which is more likely to be born preterm.<sup>[6]</sup> Vaginal progesterone and cerclage can be effective in preventing preterm birth and improving perinatal outcomes in pregnancies with history of previous preterm birth and in those where ultrasound imaging demonstrates short cervix.<sup>[26]</sup>

#### During pregnancy

Increasing access to care during pregnancy is an essential step toward addressing the growing problem of preterm birth. Good antenatal care should be ensured for all pregnant women.<sup>[6]</sup> Proper screening and management of pregnant women who are at high risk of preterm birth, e.g. multiple pregnancy, diabetes, high blood pressure is essential. Additional interventions such as behavioral, social, nutritional, and financial support are also needed.

#### *Prevention of ROP in a preterm infant*

Although it is proved that early gestational age ≤30 weeks and low birth weight ≤1500 g are the important risk factors in the development of ROP, there are also other factors such as poor weight gain, reduced insulin-like growth factors increase, percentage of oxygen in the inhaled air, hypoxia, respiratory distress syndrome, anemia, blood transfusion, sepsis, etc., which have a significant impact.<sup>[27-29]</sup> Improved quality of neonatal care is needed not only for improved survival but also to reduce morbidity.<sup>[29,30]</sup> In middle-income countries, although survival is improving, morbidities are higher (probably due to varying standards and suboptimal care) and more mature and heavier babies develop ROP.<sup>[10-12]</sup>

A safe and standard perinatal and neonatal care can prevent ROP in a preterm baby.

### *Care of the preterm delivery: Role of obstetricians*

A significant reduction in the risks of mortality, respiratory distress syndrome, and intraventricular hemorrhage has been confirmed after antenatal administration of steroids in women threatening premature delivery before 34 weeks gestation.<sup>[31]</sup> Therefore, it is recommended that women in preterm labor before 34 weeks and those with preterm rupture of membranes under 32 weeks should receive either betamethasone or dexamethasone.<sup>[32,33]</sup> In India, dexamethasone is used as it is inexpensive and widely available. Recommended dose is intramuscular injections of 6 mg for four doses to be given 12 h apart.<sup>[34]</sup> Delivery room care also needs to be improved, which includes prevention of hypothermia,<sup>[35]</sup> consideration of delayed cord clamping,<sup>[36]</sup> minimizing lung damage by avoiding initial 100% oxygen,<sup>[37]</sup> and the early use of nasal continuous positive air pressure (CPAP), if required, rather than mechanical or manual ventilation.<sup>[38]</sup>

### *Improving neonatal care: role of neonatologist/pediatricians*

Standard practices in neonatal care can prevent ROP. In a prospective meta-analysis by Askie *et al.*, it was found that lower SpO<sub>2</sub> target range (85–89%) was associated with lower risk of ROP treatment than the high saturation (91–95%).<sup>[39]</sup> Proper oxygen saturation targets and reduction of large fluctuations of oxygen saturations help in reducing ROP. Other important practices include early breast feeding to promote weight gain, use of kangaroo mother care, and measures to reduce the rates of sepsis.<sup>[40,41]</sup> As it has been reported that many newborn units do not have enough functioning pulse oximeters,<sup>[42]</sup> air oxygen blenders, and CPAP units, availability of proper infrastructure also needs attention.

To follow all the above-mentioned safe and standard practices, regular training and retraining programs and workshops should be conducted for obstetricians, neonatologists, pediatricians, and nurses. All the infrastructure required for standardized neonatal care should be present in all the neonatal units all over the country.

### *Role of community-based health workers*

In India, where majority of people live in rural areas with less access and availability of health care facilities, community-based health workers are a dependable force. Although reducing preterm births is a difficult task, some cost-effective interventions such as family planning, nutritional supplementation can help. Community health workers play an important role in this aspect. Health care workers should ensure facility-based deliveries of women in preterm labor. Auxiliary nurse midwives (ANMs) can help by administering intramuscular injection dexamethasone as a prereferral dose to a pregnant woman in preterm labor (between 24 and 34 weeks of gestation) and appropriate referral to health facility utilizing the free referral transport.<sup>[34]</sup> In case the referral is delayed, refused, or referral is not possible, ANM may complete the full course of treatment (four doses 12 h apart). Health workers should educate the mothers in safe practices in bringing up their child. They can also improve compliance for ROP screening and follow-up.

### **Secondary prevention**

Secondary prevention includes screening and treatment programs. There are many challenges in screening and treatment programs for ROP.

#### *Infrastructure and facilities*

The escalation and standardization of the neonatal care have led to better survival of preterm babies. But, availability of ROP screening and treatment programs is not in pace with this increased rate of survival, leading to increased ROP blindness. Nonavailability of trained personnel, infrastructure such as indirect ophthalmoscope for screening, and laser machine for treatment contributes to the present situation.

#### *Facility for ROP screening and treatment*

For scaling up ROP screening and treatment programs to every neonatal unit in India the National Neonatology Forum (NNF) accreditation must only be given to units which provide ROP services, as it should be standard of care.<sup>[42]</sup> Availability of infrastructure and standard facilities should be given attention. The United Kingdom's Queen Elizabeth Diamond Jubilee Trust has started a model program to reduce the incidence due to ROP by providing infrastructure (indirect ophthalmoscopes and laser machines) and capacity building which needs to be scaled up nationwide.

#### *Expertise for ROP screening and management*

Nonavailability of trained ophthalmologists and absence of ophthalmologists affiliated to hospitals with inpatient neonatal care are major hindrances in ROP screening and treatment programs.<sup>[16,17]</sup> As ROP has not been included in the curriculum, there are inadequate trained ophthalmologists skilled in ROP screening. As per the Indian ROP society, there are <200 ROP specialists nationwide.

#### *Capacity building*

Although there is increased awareness among the neonatologists/pediatricians in the recent past, ROP screening and treatment programs are not in place in many neonatal care units. Continuous medical education programs and workshops on ROP should be conducted. Training and awareness programs may be conducted for pediatricians/neonatologists and ophthalmologists together, to improve rapport among them. An effort was made by WHO and the Ministry of Health and Family Welfare, by conducting ROP workshops initiated by R.P. Center, All India Institute of Medical Sciences, Delhi, India across the country. They were the first to bring neonatologists and ophthalmologists onto one platform.<sup>[43]</sup> Training programs have also been carried out in partnership with NGOs such as Sight savers, Orbis International, and the Queen Elizabeth Diamond Jubilee Trust.

As isolated, time-bound efforts will not generate the workforce required to deliver ROP screening and treatment, ROP has to be included in all levels of training for pediatricians and ophthalmologists. Exposure to neonatal care and ROP screening and treatment should be given in residency programs. Even in undergraduate training, awareness about ROP should be created so that each and every graduated doctor will be aware of this preventable cause of childhood blindness.

In case of nonavailability of ophthalmologist or other facilities, the unit may take the help of other institutes/



organizations who can provide these services. Public-private partnerships may be encouraged. With lack of ROP specialists nationwide, telescreening may be an option such as the KIDROP program.<sup>[44]</sup> Newer, low-cost, wide field imaging cameras for ROP screening are also being developed.<sup>[42]</sup>

#### *Guidelines for screening*

ROP programs in India have reported sight-threatening ROP in babies >1500 g.<sup>[44,45]</sup> The guidelines followed in countries such as United States of America,<sup>[46]</sup> Canada,<sup>[47]</sup> United Kingdom,<sup>[48]</sup> etc., recommend screening babies  $\leq 30/32$  weeks or  $\leq 1500$  g. However, these guidelines cannot be followed in a country such as India, as larger and more mature babies are at risk of developing sight-threatening ROP, due to the variation in the standard of neonatal care.<sup>[4]</sup>

In a pilot survey of clinical practices regarding screening for ROP among pediatricians in India, only 14.5% followed standard guidelines.<sup>[16]</sup> The neonatologist/pediatrician and nurses in neonatal units should be well versed in the national guidelines on when to screen and whom to screen, and in their role in screening, e.g. identifying and preparing babies to be screened or treatment and care using these procedures.

As many studies in India found that more mature and heavier babies developed ROP, the revised guidelines recommend to screen all babies with birth weight <2000 g or gestational age <34 weeks or infants with unstable clinical course who are at risk (as determined by neonatologist or pediatrician).<sup>[49]</sup> To avoid inconsistencies, ambiguity, and confusion about the timing of first screening, Jalali *et al.*<sup>[50]</sup> recommended to undertake the first ROP screening session definitely before "day 30" of life and by "day 20" of life in smaller babies (possibly <30 weeks and/or birth weight <1200 g). This day 30 and day 20 strategy helps in the compliance of timing of screening as date of birth is well known to all and easy to follow by all the care providers.

#### *Treatment*

As it is a time-bound disease, laser treatment for sight threatening ROP should not be delayed [especially in aggressive posterior ROP (APROP)]. The treatment is warranted within 48 h of diagnosis in classic form of disease and as soon as possible in APROP. The rationale is that the disease can advance rapidly and any delay in treatment will reduce the chance of success.<sup>[49]</sup> Antivascular endothelial growth factor injections are also given in the management of ROP for zone 1 disease. However, owing to lack of evidence about safe dose, timing, ocular and systemic effects, they need to be used with discretion.

#### **Awareness of ROP among parents**

##### *Parents awareness and apprehensions on ROP screening and treatment*

The most common challenge faced in the ROP screening program is compliance and follow-up, mostly due to lack of awareness. ROP screening may require multiple screening episodes, including after discharge from the neonatal unit and lack of knowledge about the disease and importance of frequent follow-up and lack of proper communication with parents leads to reduced compliance.

Even after identifying a baby requiring laser photocoagulation, treatment can be delayed, leading to stage

5 ROP. Sometimes, babies are brought only after noticing a "white reflex" in the eye at about 6 months of age or so. The delay in treatment could be due to lack of awareness about the rapid progression of the disease and the need for early intervention. The parents think they can delay laser and are apprehensive about it, thinking it is harmful and painful to the child.

#### *Counseling*

A proper counseling and reminder by the neonatologist will have a better impact as the parents are confident in them because they are the ones due to whose efforts, their babies survive. ROP nurses also play a major role as they have more frequent interaction with the babies and parents. Parents should be counseled and reassured by the ophthalmologists that screening and laser treatment will not cause any harm to their child. In rural areas, Accredited Social Health Activist (ASHA) workers may be educated about ROP screening and need for follow-up, so that they can counsel the parents in the daily home visits and play a pivotal role by improving the compliance and follow-up.

#### *Raising public awareness*

Increasing awareness about ROP through print and electronic media and other advocacy activities helps in improving the compliance and preventing blindness due to ROP. ROP walks and runs should be conducted. Hoardings about ROP with celebrities can attract attention and increase awareness. As every individual in the country has some knowledge about vaccinations in a newborn, measures may be taken to create similar awareness about ROP.

#### **Tertiary prevention**

Tertiary prevention includes treating complications to prevent vision impairment or improve visual function, such as correction of refractive errors and rehabilitation to reduce disability.

#### *Treating complications*

Lack of screening has been the common reason for majority of babies presenting with stage 5 ROP, in India.<sup>[11,13]</sup> Sometimes, despite adequate treatment with LASER the disease progresses to stage 4 or 5. Even after resolution of treated sight-threatening ROP, vision-impairing ocular morbidities can develop.<sup>[51,52]</sup> In children treated for ROP the reasons for visual impairment are structural abnormalities (e.g. retinal detachment, macular dragging, optic atrophy), refractive errors (especially high myopia), strabismus, amblyopia, cataract, glaucoma, and cortical visual impairment.<sup>[52]</sup>

Surgical modalities such as scleral buckling, lens sparing vitrectomy, lensectomy with vitrectomy, or open sky vitrectomy are needed to treat four and five stages of ROP.<sup>[53]</sup> These surgeries need a lot of medical expertise which can be done only by pediatric retinal surgeons whose number is very low. A high financial investment is also required for providing the infrastructure and facilities. A pediatric anesthetist and a full-time neonatal care unit are also required which are available only in very few ophthalmic centers in India.

#### *Prevention of disability*

By creating awareness about screening for ROP and escalating the screening programs to all the neonatal units in the country,

we can prevent stage 4 or stage 5 ROP from occurring. If all these babies are screened and treated in time, the burden for treating these complications is immensely reduced.

The preterm infants treated for ROP should be followed long term to prevent visual disability. These children need the attention of pediatric ophthalmologist or/and pediatric vitreo-retinal surgeons who are available in tertiary care centers. Parents also must be counseled about the long-term morbidities and the need for long-term follow-up.

#### *Visual rehabilitation*

Low vision interferes with the ability to perform everyday activities. Blind children are often discouraged and experience social and economic isolation. It is estimated that more than 3000 infants become blind or visually impaired each year in India. It is a difficult task for the child and the family to cope up with the situation and start early intervention.

#### *Rehabilitation*

Rehabilitation (literally, the act of making able again) helps to achieve physical, social, emotional, spiritual independence, and quality of life. Rehabilitation does not undo or reverse the cause of damage; it seeks to promote function and independence through adaptation.

Children who are blind should receive special education about how to function without sight from the beginning. Early intervention always has better results. More vision rehabilitation centers and blind schools are to be established for training and educating them. If given proper support the blind children can live more fully, improving both their own lives and their family and community.

#### *Parent education on visual rehabilitation*

Parents play the most important role in the success of their blind child. There will be lot of misconceptions about the abilities of a blind child. The parents and other family members should be made aware that blindness does not lessen their child's value and usefulness in life. Mothers should be counseled, educated, trained, and encouraged to support their child to perform as equal as a normal child.

## Conclusion

India needs to gear up to face the challenge of the third epidemic and prevent ROP-related blindness, which is the need of the hour. ROP remains one of the preventable causes of childhood blindness. ROP stands a good example of all the strategies of prevention, which include primary, secondary, and tertiary prevention. Emphasis should be laid on improving the quality of neonatal care and expansion of screening and treatment programs. A multidisciplinary team approach is essential. Improving awareness among community-based health workers and parents, along with training of medical professionals (paediatricians, ophthalmologists, nurses) can help in effective and prompt care in India.

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