Retinopathy of prematurity: it is time to take swift action

In the 21st century, South Asia faces an additional new challenge of childhood blindness from retinopathy of prematurity (ROP). The epidemic of ROP blindness is here and is rapidly spreading across all countries in South Asia.

Advances in science and technology, coupled with human compassion, focused goals and enhanced global collaboration, have greatly improved our ability to eliminate some of the most dangerous diseases around the world. Even without the power of the internet, fast transport and communication systems available today, health workers and governments worked together in successfully wiping away the scourge of small pox from the world in the early seventies. The more recent success like prevention of polio and maternal tetanus from large parts of the world encourage many health workers and policy makers to believe that “yes, we can!”

Blindness and vision loss in babies and infants is often not perceived by parents and public as being preventable. Although most health workers are aware of preventable conditions like ophthalmia neonatorum or treatable conditions like congenital cataract, the general public perception remains that babies are born blind, and very little can be done in terms of public health preventive measures. Blindness and eye diseases in young children are considered difficult to diagnose and treat and lack of public awareness of these eye diseases including the absence of formal curriculum in medical or nursing schools, are few of the key challenges in the region. In many places in South Asia, health workers including doctors are not...
This issue of the Community Eye Health Journal South Asia brings together the knowledge and experiences of ophthalmologists, neonatologists, paediatricians, care givers, nurses and health workers in an accessible style. Since the region has diverse cultures and terrains, different health systems and financing mechanisms, with huge gaps in human resources, local ROP leaders have modified the models of care to align with local needs for effective implementation. We hope that the experiences documented in this journal will provide an impetus to implement ROP programmes in all communities that have an SNCU/UNC so that no baby goes needlessly blind. Premature babies can take heart that ROP service providers are all very enthusiastic and working towards their Right to Sight!

A preterm infant admitted to an SNCU in India.

References


About this issue

More neonatal services worldwide means more that babies are surviving, including those born prematurity. Sadly, many of these babies will go blind from retinopathy of prematurity. But there is hope ROP can be prevented and treated. In this issue, we offer up-to-date information and guidance for each member of the clinical team involved in the care of preterm babies, including neonatologists, nurses, and ophthalmologists, and emphasise the importance of involving patients in every aspect of their child’s care. We hope that you will be inspired to share this knowledge within your team and with others in the neonatal unit and thereby help to save the sight of many young children.

Contents

1. Retinopathy of prematurity: it is time to take action
2. Development of retinopathy of prematurity
3. Screening for retinopathy of prematurity
4. Treatment of retinopathy of prematurity
5. Role of neonatal team including nurses in prevention of ROP
6. Innovations in technology and service delivery to improve ROP care
7. Classification of retinopathy of prematurity: from then till now
8. Role of many young children.
9. Classification of retinopathy of prematurity: from then till now
10. Role of neonatal team including nurses in prevention of ROP
11. Innovations in technology and service delivery to improve ROP care
12. Classification of retinopathy of prematurity: from then till now
13. Role of many young children.

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Development of retinopathy of prematurity

Retinopathy of prematurity (ROP) is an ocular disorder which affects infants born before 34 weeks of gestation and/or with birth weight of less than 2000 grams. If not detected on time and appropriately managed, it can lead to irreversible blindness.

How does ROP develop?

The retinal blood vessels first appear between 15-18 weeks of gestation. These vessels grow outwards from the central part of the retina and extend towards the retinal periphery. The nasal part of the retina is fully vascularised by 36 weeks of gestation followed by the temporal retina which is completely vascularised between 36-40 weeks of gestation age (Figure 1). Following a premature birth, the growth of retinal blood vessels is halted and does not reach the periphery of retina (Figure 2).

Phase I (vaso-cessation): from birth to 30-32 weeks of gestational age

With increasing age of the preterm infant the retina matures. There is an increase in metabolic demand and oxygen consumption by the retina, creating a relative decrease in oxygen level. This promotes increase in the level of vascular endothelial growth factor (VEGF), triggering the formation of new blood vessels along the inner retinal surface. A demarcation ridge develops along the retina that separates the central vascularised retina from the peripheral avascular retina (Figure 4).

The growth of retinal blood vessels at this stage may restart normally or may progress to significant ROP as seen by an abnormal growth of retinal vessels into the vitreous and over the surface of the retina. These new vessels are weak and underdeveloped failing to fulfill the oxygen demand of retinal tissue resulting in continuous growth of abnormal vessels. There is leakage of fluid or blood from these weak blood vessels. If not treated on time this can result in scarring or traction of the retina leading to retinal detachment and blindness (Figure 5).

Phase II (vaso-proliferation): after 30-32 weeks of gestational age

Relative hyperoxia and oxygen toxicity, inhibiting the production of VEGF. This is followed by temporary stopping or stoppage of normal retinal growth, and construction of new immature vessels. As a result, there is a reduction of blood supply to retinal tissue and shortage of oxygen needed for metabolism.

The disease is staged according to severity, in four stages. It was also realised that the disease can exist in more than one stage in the eye at a time. For staging, the worse stage was noted, however, for proper documentation, it was recommended that the extent of each stage should be defined in clock hours.4

Stage 1, demarcation line

A thin delicate line-like white structure separating the vascular and avascular retina is visible. There is abnormal branching and arcading leading to it. It is relatively flat and lies in the plane of the retina.

Stage 2, ridge

It is a line which has grown and has a volume of thickness and height. It extends above the plane of the retina. Small tufts of new vessels may be found.

Stage 3, extraretinal fibrovascular proliferation

This stage is reached when the component of extraretinal fibrovascular proliferation which is continuous with the posterior border of the ridge appears. It grows into the vitreous perpendicular to the ridge.

Stage 4, retinal detachment

When the fibrovascular proliferation leads to a retinal detachment, it is classified as stage 4. It is often tractional and sometimes exudative.

Plus disease

Progressive vascular incompetence presenting as dilatation and tortuosity of vessels in four quadrants at posterior pole, iris vascular engorgement leading to pupillary rigidity and vitreous haze comprises the

Location

The retina is divided into three zones centered on the optic disc (Figure 2). More posterior the disease, more severe and likely the progression is seen. Zone 1 is defined as the circle, the radius of which is twice the distance between the center of optic disc and center of macula. Zone 2 is defined as the area from the edge of the zone 1 peripherally to a point tangential to the nasal ora serrata. Zone 3 is the residual temporal crescent of retina anterior to zone 2.2
active and progressive status of ROP and is termed as the plus disease.²

**Prethreshold and threshold ROP**

Threshold ROP was defined as a condition with 50% risk of retinal detachment if left untreated. This includes ROP of more than 5 contiguous or 8 cumulative clock hours of stage 3 plus ROP in zone 1 or zone 2. All eyes with threshold disease were recommended to be treated.

Prethreshold ROP was defined as any zone 1 ROP less than threshold, zone 2 stage 2 with plus, zone 2 stage 3 without plus or zone 2 stage 3 with plus but less than 5 contiguous or less than 8 cumulative clock hours of ROP. Initial recommendations advised follow-up of these eyes.

Three major problems were encountered while using the ICROP classification of 1984. The first one was the anatomical delineation of zone 1. Anatomical landmarks are ill-defined in premature eyes and hence the divisions of the zones were arbitrary. Secondly, it was also recognised that there was a need to further classify stage 3 due to its prognostic importance. Tractional detachments were classified as stage 4. However, the cicatricial (fibrous scar) forms of the ROP continuum were not classified in the ICROP classification. A revised ICROP classification was put forward in 2005 by a committee of 15 ophthalmologists. This new classification tried to cover the gaps of the previous one with the new insights provided by the upgraded imaging technologies for prematures.⁴

The revised classification was recommended to use a 25 or 28D lens with the original classification. The zones were defined as in the earlier classification. For better understanding during practical use, it was recommended to use a 25 or 28D lens with the optic disc at the nasal edge. The image formed was described as zone 1.

Extent

Degree of the disease was described in clock hours as per the original classification.

Severity

The revised classification² divided ROP into five stages.

**Stage 1, demarcation line**

Same as ICROP 1984.

**Stage 2, ridge**

Same as ICROP 1984.

**Stage 3, extraretinal fibrovascular proliferation**

Same as ICROP 1984. In addition proliferation was further divided into mild, moderate and severe.

**Stage 4, partial retinal detachment**

The 2015 revision classifies the tractional retinal detachments into extrafoveal (Stage 4A, Figure 3d) and foveal (Stage 4B, Figure 3e). They are usually circumferentially oriented and described according to the clock hours involved.

**Stage 5, total retinal detachment**

They are funnel shaped and mostly tractional in nature (Figure 3c).

**The concept of “pre-plus disease”**

The revised ICROP classification recognised and defined the state of active ROP where the features were insufficient for the diagnosis of plus disease but the vascular changes were more marked than normal. This entity was called “pre-plus disease” (Figure 4). This signified the pre stage which could in further course of time develop into plus disease.

**Plus disease**

Increased venous dilatation and arteriolar tortuosity of posterior vasculature, with increasing iris engorgement, pupillary rigidity and vitreous haze were defined under the more active ROP, “plus disease”⁵. A standard clinical photograph (Figure 5) was used to define the disease. At least two quadrant involvements of the signs were required to define the disease as plus disease. This was a change from the original four quadrants.

**Aggressive posterior ROP**

A rapidly progressive, ill-defined form of ROP had been previously described as type II ROP or “Rush disease”⁶ or “Fulminate ROP”. It was not specifically included in the original ICROP classification. The revised classification defines it as the “aggressive posterior ROP” (Figure 6a). It is characterised by severe dilatation and tortuosity of the vessels which is out of proportion to the peripheral retinopathy. The disease is limited to the posterior pole in zone 1 or posterior zone 2 and usually does not progress through the classic stages 1-3 of ROP.
Newer disease presentations have been described such as ‘hybrid ROP’ that has components of both staged ROP and APROP (Figure 6b). Other gaps in ROP classification include absence of classifying regressing new vessels in ROP, regression of plus stages to post plus stages, classifying the rare exudative or rhegmatogenous presentations, classifying progressive stage 5 ROP, identifying various severities of evolving APROP, and classifying the disease based on possible differences in the pathogenesis of staged ROP and APROP.

**Table 1** Staged ROP versus APROP

<table>
<thead>
<tr>
<th>Pattern of vessels</th>
<th>Dichotomously branching</th>
<th>Looping and shunting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plus and preplus</td>
<td>Clearly made out</td>
<td>Very subtle and appears suddenly</td>
</tr>
<tr>
<td>Location of new vessels</td>
<td>Appear at junction of vascular and avascular retina, often temporally</td>
<td>Appear at any place, especially can start nasally as well</td>
</tr>
<tr>
<td>Type of new vessels</td>
<td>As individual nips growing vertically into vitreous</td>
<td>Flat new vessels with each vessel ill defined and almost like a globe of vessels</td>
</tr>
<tr>
<td>Junction</td>
<td>Avascular and vascular junction are very well defined and often ‘wavy’ and continuous</td>
<td>No definitive junction as multiple pockets of avascular retinal tissue are enclosed within vascularised boundary. Pockets are discontinuous.</td>
</tr>
<tr>
<td>Location</td>
<td>In any zone</td>
<td>In zone I or posterior zone II</td>
</tr>
<tr>
<td>Progression timeline</td>
<td>Progresses to detachment over 3-6 weeks or more going through each stage for variable time periods</td>
<td>Progresses to detachment within few days and may not show each stage clearly</td>
</tr>
<tr>
<td>Progression pattern</td>
<td>Progresses through each stage with each stage lasting at least for 1-2 weeks</td>
<td>Early phases of APROP are not classified as well yet. Each phase may be lasting for only short time</td>
</tr>
<tr>
<td>Response to timely treatment</td>
<td>Excellent response in most cases</td>
<td>May respond poorly and treatment failures can occur</td>
</tr>
<tr>
<td>Detection of disease</td>
<td>Not difficult as findings are clear</td>
<td>Often missed as findings are unclear</td>
</tr>
</tbody>
</table>

References:

**Screening for ROP**

A low-cost, portable camera developed in India, 3Nethra Neo has made transport, imaging and scaling-up of the KIDROP programme easier.

Screening is an essential first step in management of retinopathy of prematurity (ROP). This requires training, skill, patience and appropriate equipment. Identification of a child requiring treatment for ROP has a short window period, and a high-risk of poor outcome if the diagnosis is missed.

Although indirect ophthalmoscopic retinal examination is the standard for examining the retina of infants, imaging based examination and screening is gaining popularity. This article focuses on the use of wide-field imaging as the primary method in ROP screening. This is especially relevant in countries that lack ROP specialists. Wide-field in the context of ROP would be 120-degree field of view (or greater), as the disease affects the peripheral retina first. Photographic documentation is a powerful tool in recording medical findings. This also serves as strong medical and legal evidence.

Can wide-field imaging based ROP screening be used in countries with few ROP specialists?

India with a population of 1.3 billion people, has less than 1,000 trained retinal surgeons, of which less than 150 are currently practicing management of ROP programmes. A majority of rural areas devoid of such experts, wide-field imaging performed within the neonatal intensive care unit (NICU) by trained and accredited non-physicians could help to bridge the gap.

Who can take images of infants?

Practically anyone with aptitude can be trained to take ROP-related images of infants. In the Karnataka Internet Assisted Diagnosis of Retinopathy of Prematurity (KIDROP) programme (www.kidrop.org) in India, doctors, ophthalmic imagers, optometrists, nurses and para-medics have been trained to capture retinal images as well as review, record and report them within minutes. They can help them act as the ‘first triage’ in the community, enabling ‘on-the-go’ diagnosis for mothers living in rural areas, even before the ROP-specialist reviews these via a tele-medicine platform.1,2

How are images reported?

To aid reporting by non-physicians a ‘decision-aiding algorithm’ was developed with three-way triaging code of red (requiring treatment or urgent review by the MD), orange (disease or immature retina that can be followed) and green (mature retina in both eyes). The algorithm is based on the International Classification of ROP (ICROP). The remote specialist views and reports these images on his or her smartphone. Over 97% sensitivity is possible while reporting on the smartphone. Owing to low internet speeds in some rural areas, the upload time for a single infant's images using a four-wheeler and can be moved between several NICUs. The camera is rugged and can withstand the rigors of a tropical climate and rural roads. In the KIDROP programme, 110 NICUs are covered by five cameras, each managed by a separate team. On average, 7,000 kilometres of travel are undertaken to reach these centres wherein 1500-2000 imaging sessions are performed every month.1,2 More recently, a low-cost, portable camera that was developed in India, 3Nethra Neo has made transport, imaging and scaling-up of the programme easier.

**What kind of on-site imaging and documentation can be expected?**

Once the device reaches the scheduled centre, it is wheeled into the NICU where the identified infants have their eyes dilated by the nurses. Images can be taken inside the incubator or in an adjoining ‘step-down’ room. A special infant wide speculum keeps the eyes open. The camera comes into contact with the cornea with a coupling agent between the two surfaces. Images are captured in the video mode, to reduce movement. Artefacts and the required quadrants are saved as still images. A ROP card is filled out for the mother with the diagnosis and date for next follow-up. Images are used to educate the mother and the treating neonatologist. This reduces follow-up attrition. Findings are recorded and maintained in an onsite register and online. All images are backed up on to a secure online database and are read by the remote expert.1,2

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**What equipment may be useful in South Asia?**

The most commonly used camera worldwide is the RetCam. The ‘shutter version’ of this device is portable...
images can range from two to over 15 minutes. The reporting time on an average after upload is four minutes. The time taken to report all ‘severe cases’ of any session that need urgent attention is less than 30 minutes.6 How are imagers trained and accredited? A KIDROP STAT (Score for Training and Accreditation of Technicians) score has been developed to train and certify imagers. This comprises of three levels (I, II and III) and has a 20 point score, which tests the knowledge, skill, and practice of the imager in their native setting. On an average, training a new imager can take between 30 and 90 working days. This period has been considerably shortened after the introduction of online training.

What is the impact of tele-screening? An impact assessment of scaling up the image based tele-ROP programme in India showed that in the 10 high-risk ROP states, with a population of roughly 680 million, over 35,000 infants would be detected with ROP and over 1,200 need treatment annually. The financial saving in ‘blind-person-years’ (BPY) is estimated at USD 108 million.7 Over 650 government owned special newborn care units (SNCUs) are already functional in most of the district headquarters in India and many private NICUs also exist. Most of these centres are currently not providing in-house ROP screening. This gap must be met. The United Nations Development Programme (UNDP) report on the tele-imaging programme and the National Health and Medical Research Council (NHMRC, Australia) report based on the Center for Disease Control (CDC) guidelines on the KIDROP programme both strongly suggest that wide-field imaging is likely to become the new gold standard in ROP screening, and similar models would allow rapid replicability and scalability in countries like India and others with similar ROP demographics.

References

Finding in the other eye

Rural Government owned neonatal intensive care unit which are overburdened with admissions and limited resources. INDIA.

TREATMENT

Treatment of retinopathy of prematurity (ROP)

Although laser is the mainstay of ROP treatment, antibodies against vascular endothelial growth factor (VEGF) are being increasingly used. In either case long term follow up is essential.

Which babies require treatment? Treatment indications are primarily governed by the findings of two clinical trials: Cryo-ROP trial and Early treatment ROP (ETROP) trial.8 The Cryo-ROP trial identified treatment indications are:

- Stage 3 ROP involving a threshold number of at least five contiguous or eight total clock hour sectors of zone 1 or 2, and plus disease.9

Although this trial used cryotherapy as the treatment modality its findings have been applied to laser therapy as well. The subsequent ETROP study found benefit in laser treatment of some babies who did not meet the criteria in the Cryo-ROP trial. These indications have been identified in the ETROP study, defined as high risk threshold ROP:1

- Zone I, any stage ROP with plus disease
- Zone I, stage 3 ROP without plus disease
- Zone II, stage 2 or 3 with plus disease
- Zone III, stage 3 plus disease is not recognised as an indication for treatment in either study, although these babies are sometimes treated. In addition another indication for treatment called Aggressive Posterior ROP (APROP) is increasingly being recognised. This condition is characterised by dilated and tortuous vessels in the posterior pole, although clear definitions and treatment indications are lacking.

What treatment modalities are available? Cryotherapy has mainly been superseded by laser therapy. Intra-vitreal injections of VEGF antibodies (bevacizumab and ranibizumab) are also used.

Detached retinas that have occurred due to failure of treatment or late presentation require vitreoretinal surgery.

Laser treatment

Laser therapy is applied to the area of avascular retina that is anterior to the ridge or demarcation line. Both diode and green (argon or double frequency) Nd:YAG laser ( yttrium aluminium garnet) can be used and delivered via a laser indolent ophthalmoscope. General anaesthesia is ideal for the procedure although sedation and/or topical anaesthesia is extensively used in the South Asian region. The baby has to be monitored during the procedure.

Anti VEGF therapy

Intra-vitreal injection of bevacizumab or ranibizumab is used in the management of very severe ROP, when laser treatment fails or when the baby is unstable for laser treatment. Bevacizumab eliminates the angiogenic threat of ROP (BEAT-ROP) and other studies have shown the efficiency of this procedure in causing regression of ROP. However the long term risk to the retina and the baby as a whole have not been studied extensively.

Follow up after treatment

Babies need to be followed up after treatment to ensure that ROP is completely regressed and does not recur. Babies treated with anti-VEGF agents need a longer period of follow-up until the retina is completely vascularised. In addition long term follow-up with regard to the possibility of refractive errors and corneal visual impairment has to be instituted.

References
Role of neonatal team including nurses in prevention of ROP

Neonatal nurses are pillars of the neonatal intensive care units (NICU). Their knowledge and clinical skills are essential in providing best practices in quality care in preventing ROP in preterm babies.

Retinopathy of Prematurity (ROP) is a preventable cause of blindness in children. As smaller and sicker neonates are surviving in the neonatal intensive care unit (NICU), the incidence and severity of ROP is also on the rise. We are now facing the third epidemic in India: ROP; the first being in 1950s with liberal oxygen use, the second one in the developed world where smaller and smaller babies survived and the third epidemic in India: developing world, where ROP is additionally seen in bigger babies, for lack of optimal care and oxygen administration. It is time to identify the preventable causes of ROP and implement solutions that would result in reduction of incidence and severity of ROP. In this article we aim to identify the role of nurses and health staff in preventing ROP and in identifying at-risk babies in the NICU for effective screening of ROP.

Prevention of ROP

Prevention of ROP includes improved care in the NICU. Improved care results in reduced morbidity and reduced risk factors that put a neonate at-risk for developing ROP. Improved neonatal care is the domain of healthcare professionals, medical officers, resident doctors and neonatal nurses who are involved in the care of these babies. Any intervention to improve quality care of a neonate can contribute to reducing the incidence of ROP in developing countries.

Judicious oxygen therapy

Oxygen is a drug and should be administered in a quantity that is appropriate to the need. Each neonatal unit should have a written policy outlining appropriate use of oxygen therapy. Oxygen level in the blood should be continuously monitored using a pulse oximeter. A target of 90-95% SpO2 in all newborns on any respiratory support, including oxygen therapy, should be maintained. One should avoid 100% oxygen in the labour room and use a blender to target SpO2. The most important tool at hand today is control of oxygen saturation. It is also important to avoid fluctuations in SpO2 especially at high levels.

Judicious use of blood transfusions

Transfusion of packed RBCs is another ROP risk factor. Adult haemoglobin has α2β2 chains which have low affinity for oxygen as compared to the haemoglobin of preterm babies, hence more tissue delivery of oxygen results in hyperoxia. Adult RBCs are rich in 2, 3 Diphosphoglyceric acid (DPG) and this binds with deoxygenated haemoglobin and stabilises the low oxygen carrier state making it difficult for oxygen to bind, resulting in more release of oxygen to the retinal tissue. Significantly low haemoglobin or platelets on the other hand can also worsen ROP. Hence written guidelines for transfusion in the NICU will help in restricting adult blood transfusions.

Prenatal steroids

Use of prenatal steroids is a well-known approach to prevent respiratory distress and intraventricular hemorrhage, two important risk factors of ROP. All women expected to deliver between 24 to 34 weeks of gestation should be given a course of either betamethasone or dexamethasone intramuscularly at-least 24 hours before the delivery of the baby.4,5

Nutrition

Postnatal weight gain predicts risk of retinopathy of prematurity. Poor weight gain in postnatal period increases the risk of severe ROP.6,7 Insulin-like growth factor 1 (IGF-1) controls VEGF-mediated vascular growth, which is important for retinal vasculature. Hence both increased nutrition and adequate IGF-1 concentrations seem to be necessary for postnatal growth and reduction in risk of ROP.8 Ensuring early administration of colostrum, exclusive and aggressive use of mothers own milk or donor milk, human milk fortification, kangaroo mother care, mothers involvement in baby care are some of the interventions in improving the nutritional status of preterm infant.

Infections

Neonatal infections, particularly fungal infections, are also risk factors for ROP. A systematic review and meta-analysis of eight studies found that systemic fungal infection in very low birth weight infants was significantly associated with ROP and severe ROP.9 Neonatal bacteremia is associated with severe retinopathy of prematurity in extremely low gestational age neonates. The increased risk associated with infection might be partly due to systemic inflammation, which could act synergistically with hyperoxia. Chorioamnionitis is often associated with higher levels of circulating proinflammatory cytokines which could act with postnatal infections resulting in higher cytokines and later development of ROP. Some of the Dos and Don’ts in prevention of neonatal infections are described in Table 1.

To summarise, prevention of ROP by reducing risk factors that disrupt normal retinal vascularisation is likely to be more effective than late treatment of neovascularisation. This is not only with respect to vision, but also with other co-morbidities of a premature birth. Careful control of oxygen saturation, normalisation of serum IGF-1 concentrations, provision of adequate nutrition, curbing the negative effects of infection and inflammation, judicious use of oxygen in delivery room and the NICU, and a reduction in blood transfusion in the NICU could promote adequate postnatal growth and improve neural and vascular development of the retina. Nurses in the NICU are the backbone of all NICUs across the world. All the nurses should promote quality care and developmentally supportive care in the NICU.

Secondary prevention of ROP: early case detection and treatment

The unit should have protocols that cover all steps of screening and management of ROP.

• The simplest method to ensure that all eligible infants are examined at an appropriate time is to identify them when they are first admitted to the NICU. A nurse can help by entering details into a book or electronic database, noting the date of the first examination and subsequent examinations. This helps in ensuring no baby is missed for ROP screening.

• Deciding when examinations are complete and organising timely treatment and long-term follow-up also remains a challenge. Nurses can help in establishing clear communication between neonatologists, resident doctors and ophthalmologist in the NICUs and, importantly, with parents.

• ROP prevention is a team responsibility, and parents must be seen as equal partners in that team. Good communication is at the heart of the relationship between the baby’s present medical caregivers and the parents, the future caregivers. Nursing staff inevitably spend the maximum time talking to parents. They are often the most trusted members of the team, so their input into written material and how it is presented is vital.

• Good awareness of communication problems, clear-cut organisational responsibilities and most importantly, working closely with parents as equal partners should prevent most of the difficulties in ROP screening.

Nurses role in prevention can be summarised in the following manner

Specialist knowledge in clinical management

Nurses should be aware of all the risk factors known to be associated with ROP. They should form the core team in implementing good practices such as target oxygen saturation, encouraging breastfeeding, hand hygiene and asepsis to reduce infections, and support for nutrition to achieve good weight gain. These would help in reducing ROP in the unit.

Clinical advocacy

Nurses are primary care givers in a neonatal ICU. They can also advocate for providing best practices in the NICU. Some of these include kangaroo care, thermal care, infection prevention and breastfeeding. Advocating for the adjustment of environmental factors (minimal handling, noise and light) and developmental care are core components of nursing. That will maximise the chances of healthier developmental outcomes in extremely preterm newborns, including vision, hearing and cognitive function.

Leadership and mentoring

For sustainable change, leadership from within the nursing profession for policies on educational opportunities and competency-based training programmes is needed. Experienced nurses can coach the young nurses to improve quality care in the NICU.

Counseling

Nurses are key personnel who counsel parents regarding breast milk and kangaroo care. They provide emotional support and motivate parents in developmental care, adherence to ROP screening and follow-up. Using innovative strategies such as ROP appointment and follow up cards for parents or using mobile applications can ensure timely management of ROP.

Continues overleaf

A nurse optimising oxygen for a preterm infant by adjusting the IO2 with a blender at Fernandina Hospital, INDIA

A nurse helping a new mother providing kangaroo mother care. INDIA

Srinivas Murki
Chief Neonatologist
Fernandez Hospital, Hyderabad, India.

Sandeep Kadam
Neonatologist
KEM Hospital, Pune, India.

FERNANDEZ HOSPITAL

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529

Continues overleaf

A nurse optimising oxygen for a preterm infant by adjusting the IO2 with a blender at Fernandina Hospital, INDIA

A nurse helping a new mother providing kangaroo mother care. INDIA

Srinivas Murki
Chief Neonatologist
Fernandez Hospital, Hyderabad, India.

Sandeep Kadam
Neonatologist
KEM Hospital, Pune, India.

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ROP in images: before and after screening

No Retinopathy of Prematurity

- Immature blood vessels in the retina
- No ROP. Blood vessels grow normally

Retinopathy of Prematurity

- ROP starts to develop, stage 1 (left) & 2 (right)
- ROP progresses to stage 3
- Sight threatening ROP develops
- Treatment by an experienced ophthalmologist

Blindness

- Without treatment, ROP can progress to blindness
- Post Laser ROP gets better. Sight is saved.

- No Retinopathy of Prematurity
- Blood vessels grow normally
- ROP gets better on its own and blood vessels grow normally

Sucheta Kulkarni
Medical Director and Head ROP services: PBMA’s H. V. Desai Eye Hospital, Pune, India

Tapas Padhi
Consultant: Retina Vitreous Services, Shri Mithu Tulsi Chainrai Campus, LVPEI, Bhubaneswar, India
The role of community health workers in prevention of blindness due to ROP

Community health workers can play an important role in health education and ante-natal care that will help reduce the number of preterm births. As members of their communities, they are best placed to advise and support parents and extended families in reducing the risk of ROP and visual loss.

Preterm births are an important public health concern worldwide due to the resultant morbidities. Survival of premature babies has improved largely due to improved neonatal care services. However, premature infants are at greater risk of cerebral palsy, developmental delays, hearing and vision related issues.

Retinopathy of prematurity (ROP) remains one of the leading causes of childhood blindness worldwide. Recent estimates show that worldwide 32,000 infants become blind or visually impaired due to ROP. Most of the ROP blind infants are born in countries in Asia.1 Although the numbers seem significant, the number of blind years is huge, leading to an immense socio-economic burden to the family, society and country. Currently, ROP is a significant problem even in district and remote hospitals in rural India.2

Community-based interventions help in reducing perinatal and neonatal morbidity and mortality.3 The most promising short-term strategy for providing newborn care entails training and equipping community health workers.

Community health workers in India: role in ROP programmes

Community health workers are members of communities where they provide preventive, promotional and rehabilitation care to other members. The community health workers in India are:

- Auxiliary nurse midwife (ANM)
- Anganwadi worker (AWW) and
- Accredited social health activist (ASHA) worker.

They play a crucial role in the health care system especially in maternal and child health care and thus can help in prevention of blindness due to ROP.

- Auxiliary nurse midwife

Commonly known as ANM, they are a first level female health worker who is the first contact person between community and health services. ANMs are regarded as the grassroots workers in health organisation pyramid.

<table>
<thead>
<tr>
<th>Community health workers</th>
<th>ASHA workers visit a Special Newborn Care Unit (SNCU)</th>
<th>INDIA</th>
</tr>
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</table>

Anganwadi Workers

Anganwadi centers are government run mother and child care center in villages in India. The anganwadi workers ensure antenatal and postnatal care for pregnant women, nursing mothers and immediate diagnosis and care for new born children. Monitoring regular health and medical check-ups for women and children is one of their key responsibilities.

Accredited social health activists

ASHA workers are local women trained to act as health educators and promoters in their communities. Their tasks include motivating women to give birth in hospitals, bringing children to immunisation clinics, encouraging family planning, treating basic illness and injury with first aid, keeping demographic records and improving sanitation.

Community health workers serve as a key communication pathway between the healthcare system and the rural population, especially in reducing preterm deliveries and in prevention of ROP in babies born too soon. Preterm deliveries can be reduced by working on modifiable risk factors such as maternal nutrition, pregnancy planning, birth spacing etc. ROP blindness can be reduced by expanding and improving screening and treatment services at medical colleges and district hospital sick newborn care units (SNCUs) and neonatal intensive care units (NICUs). The community health workers play a key role in preventing ROP blindness in three different stages:

- Reducing preterm deliveries
- Prevention of ROP in preterm babies
- Screening and treatment services for ROP

Table 1 | Do’s and Don’ts to prevent neonatal infections

<table>
<thead>
<tr>
<th>Do’s</th>
<th>Don’ts</th>
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<tbody>
<tr>
<td>Hand hygiene</td>
<td>Excessive use of antibiotics</td>
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<tr>
<td>Aggressive use of enteral feeds</td>
<td>Central lines</td>
</tr>
<tr>
<td>Restricted oxygen</td>
<td>Bundles of care (eg. VAP, CLABSI)</td>
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<tr>
<td>Optimal nurse : patient ratio</td>
<td>Restricted oxygen</td>
</tr>
<tr>
<td>Maternal participation</td>
<td>Central lines</td>
</tr>
<tr>
<td>Kangaroo care</td>
<td>Bundles of care (eg. VAP, CLABSI)</td>
</tr>
<tr>
<td>Good house keeping</td>
<td>Excessive use of antibiotics</td>
</tr>
</tbody>
</table>

Table 2 | Ready reckoner for nurses in prevention and management of ROP

- Identify newborns at risk of ROP at admission to the NICU. Note the expected screening date and time on the case file.
- Encourage communication with the obstetrician for improving the coverage of antenatal steroid usage.
- Restrict oxygen use in the NICU. Monitor saturations in all babies on oxygen and set targets between 90 to 95%.
- Restrict and duration of antibiotics, intravenous fluids, parenteral nutrition and continuous positive airway pressure.
- Encourage mothers of preterm babies to use kangaroo mother care, continue with breastfeeding and aggressive enteral nutrition and developmentally supportive care.
- Co-ordinate with the neonatal and ophthalmology team in timely preparation of the newborn (pain relief and eye dilatation) for ROP screening.
- Monitor the newborn during the screening procedure.
- Play an active part in communication with the parents on screening outcomes and need for treatment when needed.
- At discharge brief the mother on the need for subsequent screening for ROP, hearing and neurodevelopment.
- Ensure follow up on schedule and become part of the extended family of every newborn.

References


2. Adebo UM, Darville BM, Davis PG. et al. Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants. Cochrane Database Syst Rev. 2017 Apr 11;4


Role of community health workers in prevention of ROP blindness

1. Reducing preterm deliveries
   a. Child marriages and early pregnancy
      Child marriage has lasting consequences on girls, from their health, education and social development perspectives which often last well beyond adolescence. It has been found that teenage mothers are three times more likely to deliver preterm babies and twice as likely to deliver low birth weight (LBW) babies compared to older mothers (21 Yrs to 34 Yrs)\(^1\). Health workers, especially in rural areas can counsel newly weds and public about such age-old harmful practices.
   b. Birth spacing
      It is likely that when the space between births is short, there will be depleted nutrition in new mothers, as these women do not get enough time to recover before getting pregnant again. Therefore, after a birth, the interval before attempting a new pregnancy should be at least 24 months to reduce the risk of adverse maternal and infant outcomes\(^1\). Community health workers can explain that optimally spaced births reduce the infant and maternal morbidity and mortality. They can help in educating their communities about different family planning methods and encourage their use for optimal birth spacing.
   c. Maternal nutrition
      Maternal undernutrition is still a major problem in India. In populations with food insecurity and high rates of maternal undernutrition, balanced protein energy supplementation may improve foetal growth and reduce the risk of foetal and neonatal death\(^2\). Community health workers can monitor and advise on proper dietary intake of balanced energy and protein contents. As anaemia is more common in rural women, iron supplements may be provided to them. The health workers may provide periconceptual folic acid supplements which help in reducing neural tube defects, preterm births and low birth weight. As village health workers are trusted by friendly pregnant women, they can monitor and guide them about their diet and nutritional supplements from time to time.
   d. Stress during pregnancy
      Prenatal maternal stress, depression and anxiety are found to be related to preterm labour\(^3\). A community health worker can explain to the spouse of the pregnant woman and their family members about the ill effects of domestic violence on the outcome of pregnancy.
   e. Antenatal check-ups and hospital deliveries
      ASHA workers can help in educating pregnant women about regular antenatal check-ups and the importance of periodic follow-up. This aids in monitoring for hypertension, diabetes, infections etc, which if properly managed may reduce preterm deliveries. The community health workers play a role in birth preparedness which consists of preparing the mother, family and community for delivery and potential complications. They should encourage and increase the percentage of hospital deliveries which are safe for the mother and child.

2. Prevention of ROP in a preterm infant
   a. Antenatal corticosteroids (ANC) in threatened preterm labour
      A significant reduction in the risks of mortality, respiratory distress syndrome and intraventricular haemorrhage have been confirmed after administering antenatal steroids in babies delivered before before 34 weeks gestation\(^4\). ANMs who are skilled birth assistants should be guided on giving ANC to pregnant women in preterm labour. Guidelines include diagnosis of preterm labour, indications, contraindications and doses of ANC. Thus, the health workers help in prevention of ROP by giving prerferal dose of steroid and arrange for referral to an appropriate facility.
   b. Breastfeeding
      It has been found that exclusive breastfeeding for six months starting within an hour after birth may prevent ROP. Health workers can help in explaining to mothers the importance and advantages of exclusive breastfeeding. There are several significant short term and long term benefits of breastfeeding preterm infants. Neurodevelopmental outcomes are also been proven to improve with early and exclusive breastfeeding\(^5\). The health worker can also be trained to check for proper weight gain.
   c. Infection control
      As sepsis in preterm infants leads to increased risk of ROP, infection control procedures like personal hygiene can be clearly explained to mothers. Small yet significant measures such as bathing regularly and washing all clothes used for the baby can be easily explained to the mothers in the local language. Educating family members along with the mother on washing hands thoroughly before touching the baby and keeping surroundings clean help in keeping infections under control.
   d. Thermal care
      Hypothermia is another concern in the management of preterm infants. Kangaroo mother care (KMC) involves direct and continuous skin to skin contact between infant and mother. It helps in preventing hypothermia, improving weight gain and reducing incidence of infection. The procedure and benefits of KMC when explained clearly to the mothers, help in improving survival and decrease ROP. Along with KMC, the ASHA workers can also show proper swaddling of babies and keeping babies warm.

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Figure 1: Role of community health workers

Role of community health workers
(ANMs, Anganwadi workers, ASHA workers) in creating awareness about

- Prevention of preterm deliveries
  - Child marriages and early pregnancy
  - Birth spacing
  - Maternal nutrition
  - Stress during pregnancy
  - Antenatal check-ups and hospital deliveries

- Prevention of ROP
  - Antenatal corticosteroids in threatened preterm labor before referral
  - Breast feeding
  - Infection control
  - Thermal regulation (KMC)

- Screening and treatment programmes - ROP
  - Screening
  - Treatment
  - Long term follow-ups

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Sensitisation of ASHA workers, INDIA
3. Screening and treatment programmes for ROP

a. Screening for ROP

Community health workers should be made aware that all the babies born too soon (<34 weeks) and small (<2000 grams) who have been admitted to NICU/SNCU should undergo first eye screening for ROP before 30 days of birth. They are best placed to motivate parents to take their preterm infants for ROP eye screening to a trained ophthalmologist nearest to them. Educating parents about the disease with the help of visual aids like flash cards or posters of the disease and how it leads to blindness helps in reaching out to illiterate population in a better way. Health workers can also encourage parents to take the baby for ROP screening before they are 30 days old.

b. Treatment

Community health workers can help parents understand that ROP is a disease with a narrow time period between detection and treatment and that treatment cannot be delayed. Counselling parents and their families about laser photocoagulation can also be done by a community health worker.

c. Long term follow-up

The most common challenge faced in management of ROP is lack of compliance and follow-up. Though the initial screening is done when the baby is in NICU, parents especially in rural areas do not come back for follow-up. As ROP is a disease which requires multiple visits the ASHA workers can help in tracking pre-term infants in their communities and motivating parents to go for follow up visits. Educating parents about long term effects a pre-term birth can have on the eyes is also important, to encourage them to attend for follow up visits. Simple language must be used in training the ASHA workers so they can effectively counsel parents.

Conclusion

Community health workers can play an important role in health education and ante-natal care that will reduce the number of premature babies born. They also have an important role in advising and supporting the mothers of preterm babies in order to reduce the risk of ROP and visual loss.

References


Innovations in technology and service delivery to improve Retinopathy of Prematurity care

A novel method of using mobile screening by non-physician imagers can address a key challenge of lack of ROP specialists in the South Asia region.

Improved neonatal care, enhanced preterm survival and a proliferation of neonatal units in middle-income countries has resulted in a steep rise in the number of infants requiring screening for ROP. Unfortunately a gross lack of specialists has resulted in a large gap in the demand and supply equilibrium. A novel method of "task shifting" using mobile screening units manned by non-physician imagers has tried to address this challenge (pp. 9–10). However, there is an unmet deficit that requires innovations in technology and service delivery that can enhance affordability, accessibility and availability of these services even in remote regions. This article focuses on some of these resources especially in the context of middle-income countries.

Affordable technology for ROP screening

The infant retinal camera of choice for ROP imaging has been the RetCam (Natus USA) image of Stage 3 ROP in the right eye. The image is rectangular due to the 1800 x 1600 sensor of the camera.

Recently, an indigenously invented wide-field camera from India for ROP screening, the “Netra Neo” has become available for commercial use.1 The camera provides a 120-degree field of view, is a contact camera with a single, monolithic, hand-held probe. The innovative liquid lens is integrated into the hand-piece and does not require to be removed after each session. The illumination source is a patented warm LED light which has been tested for safety. The image resolution is 2040 x 2040 (compared to 1800 x 1600 of the RetCam) and results in a square image which provides an extra arc of the superior and inferior retina which would be cropped out in the rectangular image of the RetCam (Figure 1a and 1b).

In a pilot study, the “Neo” was evaluated as a ROP screening tool by comparing it with images from the RetCam. Two masked observers reported the diagnosis and decision in over 128 infants, which gave good sensitivity (ability to identify cases) of 97-99%, and good specificity (ability to identify normal eyes) of 75-81%. The study has subsequently been expanded to include over 1,200 infants and the results are encouraging.

From the community aspect, the advantages of the Neo are: first, the cost. Currently, in the Indian market, the Neo is one-sixth the cost of the RetCam and with increased demand the price is likely to reduce further. Second, it is smaller and portable, (Figure 2) allowing easier transport (including a two-wheeler) in rural areas and between centres. Third, the Neo has an
INNOVATIONS

Software innovations and artificial intelligence

Once retinal images are uploaded on to the server, in the current scenario, experts have to review most of them before either providing or confirming the diagnosis. Given the limited number of experts, this could become an important roadblock as an increasing number of centres switch to image-based screening. Innovations in automated software algorithms are becoming refined to bridge this gap. Disease severity

Creating stronger surveillance

ROP has gained medical and legal significance in recent years. After a landmark judgment in 2015 by the Supreme Court of India effectively making ROP screening mandatory, surveillance of ROP screeners and treatment providers has become even more important. The National Task force of ROP in India is now an apex body that regulates and promotes such activity. The Indian Retinopathy of Prematurity (iROP) Society, 5 which comprises of ROP skilled ophthalmologists have united to collaborate on best care practices that are ethical, evidence-based and address local needs.

Conclusion

Innovations in ROP management are constantly improving the accessibility, affordability and availability of care for these tiny and precious babies.

References


Evolution of ROP screening at Aravind Eye Hospital, Coimbatore - Lessons learnt and the way ahead

Through Aravind ROP Tele-screening Project called Retinopathy of Prematurity Eradication Save Our Sight (ROPE-SOS), 8117 babies were screened and 127 babies were treated between 2015 and 2017.

ROP in India

According to World Health Organization (WHO) report, there are 15 million preterm births (<37 weeks) per year in the world, and annually India has the largest number of premature babies (3.5, 100).1 With improving economies, the neonatal care facilities are also improving and consequently survival rate of premature babies has increased. With a birth rate of 23 per 1000 population and about 12% of infants being born prematurely in India, it is estimated that incidence of ROP is 20-30%.2 India also has a highest risk of ROP blindness due to sub-optimal neonatal care and lack of screening facilities.3 ROP is rapidly becoming a public health issue as the screening and treatment services are estimated to be 30% lower than the present need.4

ROP services at Aravind Eye Hospital, Coimbatore

ROP screening was started at Aravind Eye Hospital, Coimbatore in the year 2000 by the paediatric ophthalmology department. Initially screening started covering a single neonatal intensive care unit (NICU) once a week. Babies who needed laser treatment were treated with green laser (532 nm). From 2002 the retina department took over the ROP screening services and since then, on a weekly basis a retina specialist visited the NICU. From 2003 more NICUs were added and currently Aravind Hospital covers eight major NICUs in Coimbatore.

Aravind Coimbatore was the first institute in India to get the RetCam 120 digital fundus imaging camera in 2003 and infra-red diode (810 nm) laser was also added in the following year. Use of intra-veital injection of anti-vascular endothelial growth factor (VEGF) was introduced in 2006. As the number of ROP cases increased over a period of time, a separate Paediatric Retina Clinic was inaugurated. A month-long ROP training programme was initiated, wherein candidates are trained to examine infants using indirect ophthalmoscopy and practice indirect laser on the RetiEye Model eye (Aurolab, Madurai, India) (Figure 1). So far 54 candidates from India and abroad have been trained under this programme, 41 from India, five from African countries and eight from a variety of other countries.

To serve the unreached in rural areas, Aravind ROP Tele-screening Project called Retinopathy of Prematurity Eradication Save Our Sight (ROPE-SOS) was launched in August 2015. The project aimed to screen 2000 babies per year in the sub-urban and rural areas. Technicians are trained to capture fundus images of pre-term babies with help of digital retinal camera (RetCam). The team comprises of one manager, two trained technicians, one mid-level ophthalmic assistant and a driver. The team covers 56 NICUs of 18 cities in 12 districts of Tamil Nadu and Kerala (Figure 2). The team visits scheduled district NICU on specified days in a customised van with a Retcam shuttle. The technicians enter the details of the babies in RetCam and obtain fundus images. The digital images of the fundus are then transmitted to the base hospital through broadband internet.

The independently developed Aravind Diabetic Retinopathy Eye Screening (ADRES) software was used to transmit these images. The ADRES software was modified for ROP. At the base hospital, images are graded by a ROP expert (retinal specialist) and the report is sent back immediately to the NICU. The 4G network (which is now available in remote parts of India) is used to transfer these images. The family is explained about the baby’s eye status and given a follow-up date. The whole process for screening and counselling parents takes about 12-15 minutes per baby. If a baby requires treatment and if the baby is stable systemically, the baby is transferred to Aravind Eye Hospital Coimbatore for management. If the baby is not stable for distant travel, the ROP expert visits the NICU within three days to provide treatment. With the help of tele-screening, various other eye conditions like cataract, corneal opacity and even retinoblastoma have been diagnosed and promptly managed by early referral.

Through this mode of screening from August 2015 to June 2017, 8117 babies were screened and 127 babies were treated. By including anterior segment photography 10 babies underwent cataract surgery which was diagnosed by tele-screening.

With this process about 127 babies were prevented from going blind due to ROP in the last two years. The total growth of ROP screening from 2003 to 2017 is shown in Figure 3. As part of the ROPE-SOS project, awareness of ROP and the importance of screening is spread by means of continued medical education (CME) programmes conducted in the districts screened. The CME programme spread awareness of ROP, the impact of external factors like oxygen on disease, the ideal time for screening and indication for screening. The neonatal nurses and neonatologist are targeted in all CME programmes. So far CME programmes were held in 11 cities sensitising 711 NICU staff. Of these 233 were nurses and 31 were paediatricians and neonatologists. Patient information posters and brochures were displayed and distributed widely. With the success of ROPE-SOS project, it is now being replicated at Aravind Eye Hospital, Tirunelveli. Vitrectomies for advanced ROP are done using the 25 or 27 gauge instruments. With lack of surgical training in ROP, at one year long term training Surgical Paediatric Retina Fellowship was also launched in 2016.

Conclusion

The journey of starting ROP services at Aravind Eye Hospital, Coimbatore has been quite satisfactory and with the tools for screening and management in place, mentoring other upcoming institutes in India and abroad is on-going. Developing automated diagnosis of ROP using computer assisted deep learning is the next goal.5

References

Retinopathy of prematurity in Bangladesh: an overview

Bangladesh is the eighth most populous country in the world and currently a lower middle income country. The improvement in the country's economy has led to a visible improvement in its health systems and a noticeable decline in the incidence of childhood blindness.

National ROP guidelines, database for monitoring, evidence-based policy making, and provision of infrastructure and equipment are critical to prevent a ROP epidemic in Bangladesh.

Approximately 3.75 million infants are born in Bangladesh each year. About 25,000 of these weigh 1,500 grams or less (and hence at risk for ROP). From 1,500 grams or less to 2,000 grams or less (and hence at risk for ROP), approximately 500,000 infants are born each year, representing 13% of all newborns. In 2013, ORBIS International in collaboration with IIEI&H organised a stakeholders' awareness and sensitisation programme for ophthalmologists and other personnel. This support from ORBIS included human resources development, infrastructure and equipment. The goal of the collaboration was to ensure that no premature baby would be left out of the screening net in the NICUs of Dhaka within the next five years.

Through this programme, three retina specialists were trained in ROP at the LV Prasad Eye Institute (LVPED) in India. ORBIS also supported the training of a ROP programme manager and technicians. The ROP programme manager is responsible for communication between the NICUs and ROP team of IIEI&H. According to a protocol, the ROP team visits NICUs to screen and treat babies before discharge. This collaboration has led to an increase in the number of babies screened. It has also reduced the proportion of babies with blinding ROP at presentation.

Currently, there are 20 NICUs in Dhaka and only three are government owned. In a survey carried out by ORBIS in 2014 at 12 NICUs of Dhaka, 2962 preterm infants were managed over a six-month period in 2014. IIEI&H screens ROP babies who are referred to the hospital from the NICU centers. Additionally, the ROP programme manager is responsible for坏境之间的communication between the NICUs and ROP team of IIEI&H. According to a protocol, the ROP team visits NICUs to screen and treat babies before discharge. This collaboration has led to an increase in the number of babies screened. It has also reduced the proportion of babies with blinding ROP at presentation.

In January 2013 and March 2017 staff in IIEI&H screened 2000 preterm infants. 40% of the babies had birth weight (BW) between 1500-2000g and 38% had BW > 1500g (Figure 1). About a third of these babies had different stages of ROP. Stages 1 and 2 constituted 45% of the ROP cases, stage 3 was 23%, stage 4 was 5% and stage 5 was 9%.

The incidence of ROP in premature eyes is higher in NICUs where there is a lack of effective medical check-ups. This supports the need for a national screening programme to prevent the incidence of childhood blindness. The incidence of ROP in premature eyes is higher in NICUs where there is a lack of effective medical check-ups. This supports the need for a national screening programme to prevent the incidence of childhood blindness.

Lack of adequate trained human resources, infrastructure and equipment are major challenges. Level of awareness is still low, especially outside Dhaka. A greater level of participation from the government, better coordination between the existing centres and increased awareness of the condition, especially about the appropriate time of referral are the need of the hour.

Future strategies
ROP training is now incorporated into retina and paediatric ophthalmology long-term fellowship programmes at IIEI&H. Short term training in ROP management is also available for ophthalmologists.

We hope to develop a national ROP screening guideline in conjunction with relevant stakeholders. A national database on ROP for monitoring and evidence-based policy which will be owned by the government forcontinuity is imperative. We look forward to government participation in the area of infrastructure and equipment provision. Current stakeholders (both private and NGOs) should identify a model for future government programmes in light of current achievements and failures in management of ROP.

There should be adequate incentives for all levels of personnel involved to sustain morale and encourage specialists at the district level.

Figure 1 Total babies screened.

<table>
<thead>
<tr>
<th>Total 2154 babies screened</th>
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<tr>
<td>ROP (669) 31%</td>
</tr>
<tr>
<td>No ROP (1485) 69%</td>
</tr>
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</table>

Table 2 Distribution of ROP.

| ROP (669) 31% |
| No ROP (1485) 69% |

| ROP 31% |
| No ROP 69% |

Table 3: Distribution of ROP.

Aggressive posterior ROP occurred in 18% of all ROP cases seen at this center (Figure 2). During this period, 274 babies were managed with laser, 69 with intraocular bevacizumab injection and 53 babies had ROP surgery for stage 4 or 5 ROP.

The mean gestational age of babies with ROP was 31.09 ± 2.28 weeks (range: 26-36 weeks) and mean birth weight was 1354.13 ± 266.38g (range: 700 - 1900g). Even though our screening protocol is for babies to be screened between 20 and 30 days after birth, the mean chronological age at screening is unfortunately still very far from ideal (mean 46.63 ± 25.37 days, range: 20-150 days).

Existing challenges
The current staff in Bangladesh includes three retinal surgeons who are proficient in ROP surgery, and 16 ophthalmologists who can diagnose and treat ROP. Four other ophthalmologists who can only screen for ROP are in districts outside Dhaka.

Five centers have equipment for laser treatment and two centers offer ROP surgical services. All these centers are located in Dhaka and are either private or NGO driven. The only RetCam in Bangladesh is in IIEI&H.

Lack of adequate trained human resources, infrastructure and equipment are major challenges. Level of awareness is still low, especially outside Dhaka. A greater level of participation from the government, better coordination between the existing centers and increased awareness of the condition, especially about the appropriate time of referral are the need of the hour.

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There should be adequate incentives for all levels of personnel involved to sustain morale and encourage specialists at the district level.

Conclusion
ROP is rapidly attaining public health significance in Bangladesh. There is a significant gap between the increasing need and the limited resources. The current efforts are mainly driven by the private and NGO sectors. More government involvement and commitment is required for a nationwide sustainable programme.

References
The restless retina in aggressive posterior retinopathy of prematurity: prevention is better than cure

Aggressive Posterior Retinopathy of Prematurity (APROP) is a severe variant of ROP that usually affects the smallest and sickest babies. Following the best neonatal care practices is a good way to prevent it.

Case Report

A male baby was born at 29 weeks gestational age with birth weight of 1100g. The baby’s twin did not survive. The baby suffered from neonatal sepsis and apnea that required a stay at neonatal intensive care unit (NICU) for 33 days. Supplemental oxygen was given to the baby for a duration of 20 days including three months of continuous positive airway pressure (CPAP) via the non-invasive route. NICU Blood transfusions were performed twice. As per records, timely screening was performed at 32-week post menstrual age (PMA). The ophthalmologist noted a poorly dilating pupil, a small zone of vascularisation and presence of diluted and tortuous vessels at the posterior pole suggestive of zone 1 APROP. Uneventful laser photocoagulation of anterior avascular retina was performed using 532nm green laser, but the disease worsened and the child was referred to us for management.

At PMA 41 weeks, good disease regression is observed in both eyes (a, b).

Figure 1 Fundus images of the right (a) and left (b) eyes showing very small zone 1 ROP with poor vascularised margins, plus disease, sub-hyaloid hemorrhages and peripheral laser spots.

At 34 weeks PMA, the pupils were still poorly dilating. Intravitreal examination revealed a very small zone 1 APROP, with media haze and markedly diluted and tortuous vessels indicating severe plus disease with patches of sub-hyaloid bleed in both eyes (Figure 1). Intravitreal Bevacizumab (0.625mg/0.025ml – half adult dose) injections were given in both eyes under aseptic conditions in the same sitting in the operation theater.

Figure 3 a & b 50 wks PMA, developing recurrences of plus disease with progressive FVP and TRD (black arrows) in the laser treated regions in both eyes (a, b).

The following day, the child was brought for a prolonged follow up period. The report stressed the need for better neonatal care which can prevent development of APROP and avoid the challenges for its treatment.

Figure 4 One month after LV5 in both eyes, resolution of plus disease and regressed FVP is noted in both eyes (a, b).

At 54 weeks PMA, bilateral pupillary dilation, improved media clarity, significant reduction in plus disease and partial resolution of the sub-hyaloid bleed. 7 weeks after injection (PMA 41 weeks), good disease regression was observed in both eyes (Figure 2).

However, at 48-50 weeks PMA, both eyes started developing dilation and tortuosity of vessels (plus disease) with progressive fibrovascular proliferation (FVP) and tractional retinal detachment (TRD) suggestive of stage 4A ROP (Figure 3). At 54 weeks PMA, bilateral

25G suture-less lens sparing vitrectomy (LSV) was performed. One month later, both eyes showed near complete disease regression (Figure 4). At the last follow up, the retina was attached with no evidence of retinal traction. The parents were counselled regarding a need for close and long term follow up for retinal status and detection of refractive errors.

Discussion

This case study demonstrates the aggressive disease in APROP, a severe ROP variant which required treatment with laser, Anti-VEGF drugs and surgery in both eyes, a prolonged follow up with active treatment over a period of months in a sick preterm baby.

Emerging role of Anti-VEGF drugs in APROP

Laser treatment of avascular retina has been the gold standard for ROP treatment. However, laser treatment scars the avascular retina with limited prospects of further retinal growth. In small zone 1 ROP/ APROP, this can lead to constriction of visual fields and high incidence of plus disease. Anti-VEGF drugs like Bevacizumab/Ranibizumab are now emerging as a good alternative treatment in zone 1 ROP. The BEAT-ROP study showed significantly better outcomes of Bevacizumab in cases of zone 1 ROP compared with laser, with decreased chances of recurrences and progression of normal retinal vascularisation, leading to future prospects of better visual fields.

Anti-VEGF pharmacotherapy also has the added benefit of absence of need for higher dose, but is often complicated by delayed recurrences requiring much longer follow up, and laser treatment may be needed. The ideal dose for preterm babies, choice of Anti-VEGF drug, the role of multiple injections, and long-term safety (due to systemic absorption and VEGF suppression) still remains unclear due to lack of relevant data.1

1 Anti-VEGF agents are especially useful in cases with severe plus disease with rigid non-dilating pupils, where laser treatment is not possible. It leads to rapid papillary dilation in a few days, that allows laser treatment to be completed. Currently, many use them as adjunct before or after laser treatment as well.

Multimodal treatment for APROP

The diagnosis of zone 1 APROP needs a high index of suspicion because of a featureless vascular-avascular junction and avascular loops, which confuse the observer. Indeed, prompt aggressive treatment is warranted as the disease can progress rapidly. Multiple treatments are needed with laser or Anti-VEGF drugs, or a combination of both, but the outcome is unpredictable. Our case had delayed recurrence despite combined treatment, and quickly progressed to retinal detachment needing surgical treatment. However, timely surgical management in developing countries is still difficult due to lack of advanced vitreoretinal surgical setups; experienced paediatric retinal surgeons and trained anaesthesia teams willing to provide general anaesthesia to such small babies. Such services are scarce and available in very few apex eye care facilities.

ROP Prevention is better than cure

It is well known that implementation of best neonatal practices and simple measures like strict regulation of oxygen delivery can prevent development of severe ROP.2 In fact, absence of zone 1 APROP is considered an important marker of quality neonatal care. But poor NICU care across the country is leading to severe ROP developing in even larger babies.3 This has led to repeated changes in screening guidelines to include these bigger babies as well. Lack of proper screening and treatment facilities, adds to increase in the number of cases with ROP blindness. Thus, it is recommended to follow the best neonatal care practices to prevent ROP and especially APROP.

References


6 Aihara K, Tsujikawa T, Inui K, Yamada Y, Fujita K, Uchimura K, et al. Long-term safety (due to systemic absorption and VEGF suppression) still remains unclear due to lack of relevant data.1


9 At PMA 41 weeks, good disease regression is observed in both eyes (a, b).

Figure 2 47 wks PMA, developing disease in both eyes (a, b).
Counselling and co-opting parents to get best outcomes

Timely, realistic and appropriate counselling of parents and making them a part of the team at each step is a critical way to get the best vision for the baby.

Resilience of prematurity is one of the leading causes of preventable blindness in preterm babies. The number of preterm deliveries is increasing. Although the survival of these preterm babies is on the rise due to better and more accessible neonatal care, the situation leads to a period of great stress to family members. This includes emotional, monetary, physical and logistical stress to those involved in giving care to the fragile baby (Figure 1).

In such a situation, the ophthalmology care team has to provide the best possible vision and least ocular morbidity. The main factors in preventing blindness due to ROP are timely screening and treatment, as this is a time-bound disease. The disease occurs in at-risk babies around three to four weeks after birth. A timely screening (between 20-30 days after birth) will help in detecting any sight-threatening ROP. Very close follow-up, sometimes every three to seven days is needed during this time which requires close coordination between all stakeholders.

Major factors that need to be tackled at various levels to prevent ROP blindness are discussed below:

Factors responsible for delayed screening of preterm babies for ROP are:

- Non-availability of ophthalmologists trained in laser or surgical treatment.
- Delay in initiating treatment even after detecting treatable disease, due to financial and logistic constraints. Most parents have to travel a long distance with babies to reach specialist doctor for treatment. The expenditure for two to three attendants who may have to accompany the baby becomes unaffordable. This is especially after having spent a major amount of money for NICU care.
- Ignorance among parents regarding the need for regular and long-term follow up and the threat to sight if the treatment is delayed.
- Unlike other diseases, the symptoms of vision loss due to ROP are manifested in the late stage of disease. Unless the parents are made aware of this, they are likely to delay the eye check-up.
- Sometimes parents do not consent to timely treatment as they are not sure of the benefits of treatment. The lack of trust in modern medicine with apprehension that some ‘experiment’ may be done on their baby are a few of the reasons.

Care factors responsible for worsening of ROP or severe ROP:

- Most factors that lead to severe forms of ROP are related to low gestational age and the type of medical care. Parents can help in caring for their infants by:
  - Washing hands regularly.
  - Breast feeding on time.
  - Giving kangaroo mother care.
  - Taking good nutritious food while breastfeeding.
  - Taking proper care of cough and cold episodes in the baby.
- Overall positive communication while interacting with the baby.
- Some of these factors may not have robust evidence in terms of ROP management but are part of good practices and low-cost additions for integrated and improved neonatal care.

Why counsel parents?

Most of the babies, who need eye evaluation and treatment, are either preterm or have significant co-morbidities. It is imperative that team members work in coordination to ensure safe and timely screening.
- Lack of coordination or lack of appreciation of each other’s roles, or lack of faith in the management can lead to needless delays and doubts in the parents’ mind.

In most cases, neither our medical training nor our mainstream ophthalmic or newborn care literature and training address this issue. Over more than a decade, we have personally tried to understand and devise ways to build the team. It has been a continuous learning and refining process and in this article we share our experiences.

We have experienced that despite all the above-mentioned factors, if we educate the parents about the importance of regular check-ups, then every parent will take the effort to prioritise it over their personal and family matters. Health education literature also indicates that parent education can play a significant role in getting them to prioritise health issues.

Timely, realistic and appropriate counselling of parents and making them a part of the team (Figure 2) at each step is a critical way to get the best vision for the baby. If a screening facility is not available in the NICU, the parents should be motivated to take the babies to the nearest available eye hospital. The display of posters and videos of babies showing the sequence of delayed treatment will help to create the awareness. Connecting parents of babies affected with ROP, ones who had timely treatment and ones who had delayed treatment will help to gain the trust of parents.

How to co-opt parents into the team and make the processes more robust?

The team

- The team has to include an ophthalmologist, a paediatrician/neonatologist, a duty doctor (fellow/resident), nursing staff, parents and sometimes extended family like grandparents/uncles etc and the receptionist/administrator at the neonatology and ophthalmology clinics.

Roles

Each person in the team has to contribute to a safe, effective and efficient service. Communication, protocols and procedures must be well-defined and standardised so that everyone is on the same page.

The neonatologist is the first point of contact with the baby and family. He/she has to take complete ownership for the smooth transition of the baby through the process of ROP screening and follow-up until the baby is safely discharged from any risk of blindness. This has to be done while taking care of other critical day-to-day issues of a fragile baby. Parents should be counseled that all delivery and post-natal treatment related documents/discharge summary are essential during ROP management.

Delay in laser surgery even by a day can cause irreversible damage. It is critical to counsel parents about the urgency of the situation. Studies have shown that if doctor sits down and talks, the perception is more reassuring to the family, than if the doctor stands while talking, even if the same things are said!
Making parents or extended families part of your team is the next crucial step. Stressing on collectively taking care of the baby helps. When you are speaking to a parent, keep in mind that even if you have good intentions, you need to ensure that they have understood what you have said. Words like “damage” or “failure” can be replaced by positive sounding statements such as “may not be as good as we want to achieve” or “we may not succeed in our attempt but can definitely try and do our best.”

Tips for speaking to parents
• The baby is fragile and you know this. The eye condition needs immediate treatment.
• What we need to do is to take care of your baby and attend to his needs.
• If you have any questions about the surgery, please phone or email later too.

If the baby is not going to be discharged soon, give the family few minutes to digest the information. Make sure that they are in safe hands and under the care of the team. If your team has a good safety record, share the information sheet so that it is not missed by the hospital team. Underline important statements on the information sheet that is to be given to the parents. Give information brochures/handouts in local languages to parents at the time of admission. This must include space to write dates of follow-up screening. If the baby is not going to be discharged soon, ensure that screening is done within 20-30 days of birth. If the baby is being discharged early then screening must be done before discharge. This is to ensure that parents are sensitised about need for next follow-up.

Steps for enhanced team work
• Place information posters in local languages about ROP in waiting areas of SNCUs/NICUs.
• Give information brochures/handouts in local languages to parents at the time of admission. This must include space to write dates of follow-up screening.
• Give the family few minutes to digest the information. Make sure that they are in safe hands and under the care of the team.
• If you have any questions about the surgery, please phone or email later too.

Steps for preventing ROP
• Counselling and creating awareness helps to provide a tight net of vision loss prevention around the baby.
• Give information brochures/handouts in local languages to parents at the time of admission. This must include space to write dates of follow-up screening.

Steps for prevention
• The surgery is a difficult one. If it succeeds, I will assure that care is at hand. If it does not, I won’t ask you either.
• Please feed the baby on time and continue to give at least two feeds.
• All those who are handling the baby must wash their hands regularly.

The role of advocacy and communication in reducing ROP in India
Visual loss from ROP will continue to increase unless improvement in neonatal care facilities includes services for the detection and treatment of ROP. This requires strong advocacy efforts, communication and collaboration among all the stakeholders.

Low birth weight (LBW) and prematurity are two major causes of neonatal and infant mortality rates in India. Nearly 7.5 million LBW and 3.5 million preterm infants are born in India every year, making it the country with highest number of preterm births in the world.1 With the aim of lowering perinatal and neonatal morbidity and mortality, the Government of India has formulated policies that require screening of all LBW and preterm babies by neonatologists and ophthalmologists. The policy requires screening of all LBW and preterm babies by neonatologists and ophthalmologists within 20-30 days of birth. This window of opportunity can help in prevention of visual loss which is a “potentially preventable” cause of childhood blindness worldwide. India and other low and middle income countries are facing an epidemic of ROP blindness.2

India accounted for nearly 10% of the worldwide estimated visual impairment due to ROP, with nearly 5,000 children developing severe disease and 2,900 deaths.3 4 Visual loss from ROP will continue to increase unless improvement in neonatal care facilities includes services for the detection and treatment of ROP. This requires strong advocacy efforts, communication and collaboration among all the stakeholders (i.e., neonatologists, nurses, ophthalmologists, parents, social workers and the government) in the following aspects:
• High quality neonatal care including availability of equipment and establishment of appropriate care protocols.
• Mandatory ROP screening of babies at risk.

Advocacy efforts should stress the availability and regular maintenance of essential equipments in the NICUs/SNCUs. Mandatory periodic accreditation of neonatal care facilities by independent empowered organisations can also help to improve quality of care. Uniform protocols should be set up and widely disseminated to:
• monitor oxygen supplementation starting inside the delivery room while moving the baby within the NICU and throughout hospitalisation;
• setting up alarms for oxygen saturation targets;
• control of infection, prevention of hypothermia;
• improving nutrition and monitoring of weight gain.

For this, adequately trained and knowledgeable staff who are aware of ROP and its risk factors (nurses, neonatologists and pediatricians) are required.

References
1 Wigert H, Blom M, Bry K. Parental experiences of communication with neonatal intensive-care staff: an intensive study. BJU Int 2016; 118: 1094
2 Shenkar A, Jayadev S, Dey P. Improving follow-up rates among the survivors of premature birth in rural areas. India Eye 2010; 5: 5-11
Intensive efforts for expanding in-service training and innovative approaches to training are needed. Improvement in neonatal care has a direct impact on reduction in the incidence of ROP.

Vinekar et al. have shown that with interventions such as increase awareness about risk factors of ROP, oxygen regulation protocols, use of pulse oximetry, monitoring postnatal weight gain, nutritional best practices and management of sepsis it was possible to significantly reduce the overall incidence of ROP, incidences of treatment-requiring ROP as well as aggressive posterior ROP over four years in rural neonatal centres in Karnataka, India.

The following aspects of screening for ROP need to be focused upon:

- Enforcement of the national ROP screening guidelines at district level SNCUs
- Making ROP screening mandatory at all NICUs/SNCUs
- The original SNU toolkit, which guides the establishment of new SNCUs in India must specifically mention ROP screening as an essential requirement. The accreditation criteria for level II and III units should have ROP-screening facility as an essential requirement.
- Availability of equipment for ROP screening such as indirect ophthalmoscope, a 20 or 28 dioptre lens, infant eye speculums, infant scleral depressors in the district level hospitals and possibly retinal imaging systems such as the low cost wide field fundus cameras in the future.

Training human resources (neonatologists, nurses) who are the first point of contact for the following aspects of screening in the SNCUs/NICUs:

- Time of first screening: within the first 20 to 30 days of life.
- Who to screen: Wall charts need to be displayed in all NICUs on whom to screen and nurses must be trained to dilate pupils, administer drops and assist in screening.
- Ensure that once an ‘at-risk’ baby is identified, it is important that the baby gets enrolled into the screening programme and completes the required follow-up examinations as per protocol.

Counseling parents on presence of risk factors and the expected date of next screening is essential.

A simple information leaflet in local language can help in educating parents about ROP and its complications. At-risk babies can be marked with color-coded wrist bands or colored stickers applied on their files/cots for easy identification and as a reminder to the treat them.

The National Programme for Control of Blindness (NPCB) along with various non-government organisations (NGOs) such as the Queen Elizabeth Diamond Jubilee Trust, Public Health Foundation of India (PHFI) have been pivotal in advocacy and communication efforts with the Government of India in formulating national guidelines and policy regarding ROP. A National ROP Task Force has been constituted under NCPE and the Ministry of Health. It brings together leading ROP experts, who advise on the direction of the programme and provide impetus to help bring about change in policy.

Available training ophthalmologists

There is a huge lacuna as far as availability of trained ophthalmologists well-versed with indirect ophthalmoscopy and laser treatment. The Indian Retinopathy of Prematurity (ROP) Society was formed in July 2016 to bring together ophthalmologists who are involved in ROP treatment from across India (Figure 1). The current membership of this society is a mere 113.

Future policy

Planning and prioritisation of policies should be based on data about local needs and the country’s geopolitical scenario. A system for data collection and monitoring to track the number of new borns screened and treated for ROP from various SNCUs and NICUs in medical colleges across the country is needed.

Conclusion

The ROP epidemic can be controlled by concerted efforts of all the people involved in the management and care of preterm infants. There is a need for national policy, legislation and strong advocacy. Advocacy with the government would require strong evidence and a clear message to integrate ROP services with neonatal care. A strongly committed leadership is the key for policy change.

References

Questions and Answers on ROP

This page is designed to help you to test your own understanding of the concepts covered in this issue, and to reflect on what you have learnt.

We hope that you will also discuss the questions with your colleagues and other members of the eye care team, perhaps in a journal club. To complete the activities online – and get instant feedback – please visit www.cehjournal.org

Tick ALL that are TRUE

Question 1
Which of the following factors can increase the risk of ROP during the first 4 weeks of life?

- a. Infection
- b. Poor weight gain after birth
- c. Oxygen saturations that are above 95%
- d. Gestational age of 36 weeks or above
- e. Low body temperature

Question 2
Screening for retinopathy of prematurity

- a. The ophthalmologist should identify which babies should be screened
- b. The first screening should take place as soon as the neonatologist says the baby is well enough
- c. An ophthalmologist should visit the unit every two weeks to screen
- d. Babies with plus disease should be screened again in a week
- e. Screening is usually undertaken using an indirect ophthalmoscope

Question 3
Treatment of ROP

- a. Laser treatment is painful
- b. ROP in zone 3 has a worse prognosis than ROP in zone 1
- c. The laser spots should be confluent
- d. Stage 2 ROP in zone 2 with plus disease should be treated
- e. After treatment, babies should be seen again in 4 weeks

Question 4
Follow-up of babies who developed ROP

- a. Babies who have been treated for ROP have more complications than babies who had ROP that did not need treatment
- b. Strabismus should be operated on as soon as it is detected
- c. High myopia can occur within a few months of laser treatment
- d. Occlusion therapy may be required to prevent or treat amblyopia
- e. Children born preterm may be developmentally delayed

ANSWERS

1. a, b, c and e are true. Gestational age of less than 36 weeks is a risk factor.
2. a, c, and d are true. Zone 1 ROP has a worse prognosis, and babies should be seen within 1–2 weeks of laser to ensure that the disease is regressing.
3. e is true. The neonatologist should identify which babies need to be screened, and screening must be done before 30 days after birth. An ophthalmologist should visit the unit once a week, and all babies with plus disease require treatment.
4. a, c, d, e are true. In children with strabismus who were born preterm, the degree of misalignment can vary so the decision about when to operate is more difficult.

Answer to picture quiz

Tick ALL that are TRUE

Question 1
What could be done to improve the care of this preterm baby?

- a. Monitor blood oxygen saturation
- b. Kangaroo care
- c. Feed the baby with the mother's breast milk
- d. Support the baby's limbs
- e. Keep the baby cool

Question 2
How is ROP classified?

- a. Aggressive posterior ROP
- b. 5 zones
- c. 5 stages
- d. Posterior ROP
- e. 3 zones

Question 3
Screening for ROP

- a. Can be done at any time as long as the baby is stable
- b. Can cause the baby stress
- c. Is never needed after the baby is discharged from the neonatal unit
- d. Should include babies at risk even if they are sick
- e. Should be done by 30 days after birth

Question 4
Follow-up of children born preterm

- a. Refractive errors are uncommon after laser treatment for ROP
- b. Babies less than 12 months of age should not be given spectacles
- c. Some preterm babies are developmentally delayed
- d. A normal eye examination means the child can see normally
- e. Strabismus is easy to manage
Babies born before 36 weeks (preterm) are at risk of retinopathy of prematurity (ROP)

- The more preterm they are, the greater the risk
- Poor neonatal care increases the risk, even in less premature babies

It is possible to prevent ROP from causing visual impairment and blindness. This requires:

- High quality neonatal care. If there is not enough equipment to safely deliver and monitor oxygen, this must be strongly advocated for
- Screening: All babies at risk must be screened before 30 days after birth
- Treatment: Laser treatment should be given urgently, with confluent spots
- Follow-up: All children born preterm are at risk of visual impairment and must be followed up by an ophthalmologist and/or optometrist

Parents are important members of the eye care and neonatal team

- Involve parents in the day-to-day care of the baby and encourage kangaroo care
- Keep parents informed of the need for screening and the results of screening, and the need for urgent treatment, if required
- Ensure parents understand the need for follow-up visits