Setting up an ROP Screening Program in a Developing Country

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INTRODUCTION

Retinopathy of prematurity (ROP) is an avoidable cause of irreversible blindness in babies who are born prematurely where abnormal and proliferative development of retinal blood vessels occurs in preterm babies that are exposed to supplemental oxygen. More and more babies are beginning to develop ROP as more babies survive as the level of neonatal care improves in our hospitals.[1,2] The occurrence of ROP blindness varies dramatically with the socioeconomic development of the country and also may even vary within regions of the same country depending on the facility and expertise available to them. [3] These retinal changes can only be detected if it is looked for, on time and treated appropriately. [4,5] Therefore, health care professionals who care for preterm infants in both neonatal intensive care units and community settings must know who could have ROP, who to screen for it, when to screen for it and how. [6-9]

Importance of ROP screening

ROP is potentially blinding if screening for it is neglected or left until late.[10] A child could actually become irreversibly blind before 6 months of life and remain so for upwards of 70 years life expectancy.[11,12] See Figure 1.

ROP is closely related to Neonatal Intensive Care Unit (NICU) care and survival. [13]

Early screening before proliferative changes occur and prompt treatment of ROP which can be done in NICU has been documented to prevent blindness effectively. Once there is advanced ROP, where the retina becomes thickened and rigid with retinal detachment, even when surgery is carried out, results are often poor. [14-16]

The best is to screen them before it ever happens. Figure 2

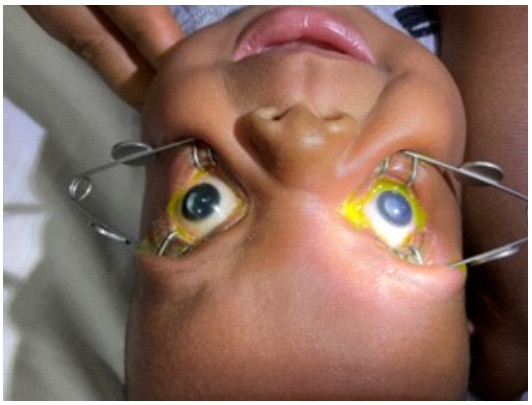

Figure 1: A child blind in both eyes from retinopathy of prematurity

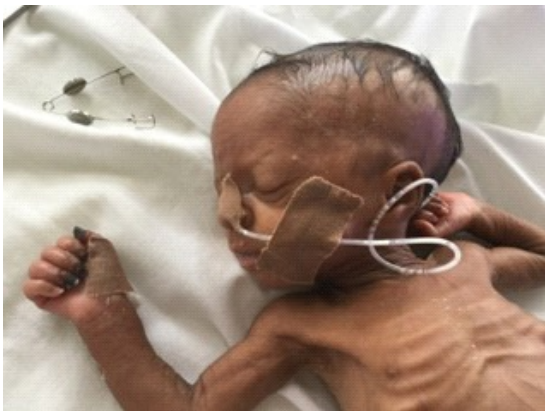

Figure 2: A premature child just after screening for retinopathy of prematurity

Epidemics of blindness

By way of history, 3 epidemics of blindness have happened since the 1940s when the disease was first described by Terry. [17-19]

1st epidemic - 1940s-1950s in industrialized countries primarily due to unmonitored supplemental oxygen.

2nd epidemic - in the 1970s in Industrialised countries due to advances in neonatal care, premature infants survived at earlier gestational ages and lower birth weights.

3rd epidemic – mid 1990s in low and middle income countries due to high rates of preterm births and varying levels of neonatal care.

The stages of ROP

There are 5 stages-

Stage 1*:* Demarcation line separating avascular from vascularized retina.

Stage 2: A ridge arises in region of demarcation line.

Stage 3: Extraretinal fibrovascular proliferation/ neovascularization extending into the vitreous.

Stage 4- Partial retinal detachment

Stage 5- Total retinal detachment

Plus disease – here there is increased vascular dilation and tortuosity of posterior retinal vessels in at least 2 quadrants of the retina.

Pre plus disease-more dilation and tortuosity than usual but still insufficient to make a diagnosis of plus disease.

Risk factors for ROP [20-24]

1. Prolonged oxygen use
2. Multiple apnoeic attacks
3. Blood transfusion
4. Respiratory distress syndrome
5. Necrotizing enterocolitis(NEC)
6. Asphyxia
7. Sepsis
8. Anemia
9. Persistent Ductus Arteriosus(PDA)

The risk for severe ROP is greatest in infants <28 weeks gestational age or weighing <1000g at birth. There are 2 types of ROP that need to be responded to in different ways. [25]

Type 1 ROP -in this type, treatment must be instituted within 2 to 3 days.

Type 2 ROP -here, the baby can still be followed up and there is no reason to offer treatment immediately.

The ROP screening program

This is a very important program that is required to ensure blindness is avoided from ROP. [26] The ROP program therefore requires collaboration between neonatologists, ophthalmologists, nurses and allied health personnel together with parents of the babies. In most cases, the process might need to be jump-started by the ophthalmologist after which when the neonatologists are fully onboarded, it becomes their responsibility to invite the ophthalmologist for screening. [27] Effective ROP screening hinges on this collaboration however, as the babies are domiciled with neonatologists, it must be led by them. More information and advocacy may be required to enable this happen more effectively across board especially in developing countries like Nigeria.

An administrator is required to make the program work properly especially as related to documentation, form filling , care of the equipment including the retinal cameras, BIO and planning date for screening, calling the ophthalmologist, preparing the eye and equipment for the intraocular injections given to treat ROP and other details. To achieve this, ROP training workshops need to be organized where experience and expertise of facilitators who have been trained can be used to plan efficient and effective screening programs (Figures 3,4 and 5).

Advocacy

This is a very key step in setting up an ROP screening programme and involves engaging critical stakeholders on the burden of ROP and the need for a screening programme. Posters, seminars webinars, meetings, repeated visits to the NICU, grand rounds of neonatology, obstetrics etc to speak about ROP may be required before everyone gets on board fully [28,29] (Figure 3).

Target for advocacy

- Caregivers/parents
- Midwives/Obstetricians
- Philanthropists
- Community
- Neonatologist/paediatrician
- NICU nurses
- Ophthalmologists
- Hospital administrators and medical directors

Figure 3: Teaching residents how to screen for ROP

What is the aim of screening ?

The aim of screening is to control ROP blindness. [30] This control requires 2 broad approaches.

- **Primary prevention**-reducing the incidence of ROP through excellent neonatal care like kangaroo nursing, use of individual pulse oximetry, CPAP, medical air blended with oxygen etc (Figure 4).
- **Secondary prevention**-Detecting and treating infants who develop the different stages of disease in addition to follow-up (Figure 6).

Important considerations for screening

- Who to screen?
- When to screen?
- Who does the screening?
- How to screen?
- Who treats?
- Anything to treat with?

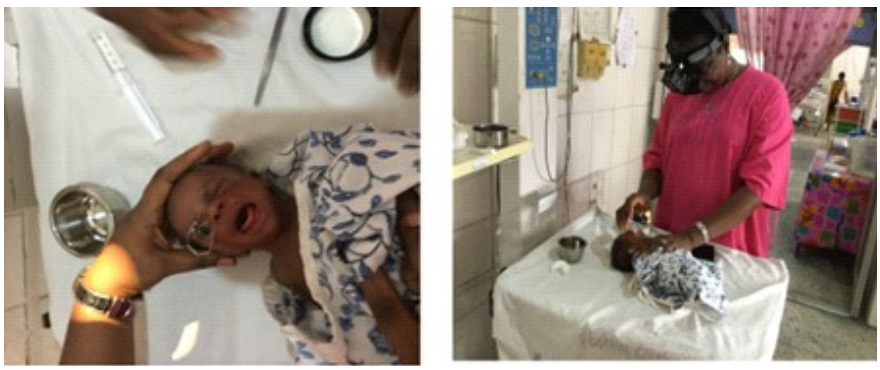

Figure 4: ROP screening going on

Figure 5: Picture of attendees after ROP training in UPTH

- When to treat?
- Follow-up systems
- Who follows up?
- When should screening stop?
- Other ocular co -morbidity checks
- Who records all these/who is responsible?

Who to screen?

The current Nigerian screening guidelines.[29,32]

1. Any baby with birth weight of 1500g or less
2. Any baby delivered at 32 weeks gestational age or less
3. Heavier babies with a turbulent course (eg Sepsis, Anemia, Apnea, Necrotizing enterocolitis etc)
4. When a special request for screening is made by the neonatologist for a baby they think might need to be screened.

When to screen?

The disease is not present at birth but develops slowly so that by the time the baby is age 3 to 4 weeks post delivery, the disease would already be detectable [33] (Figures 4 and 7).

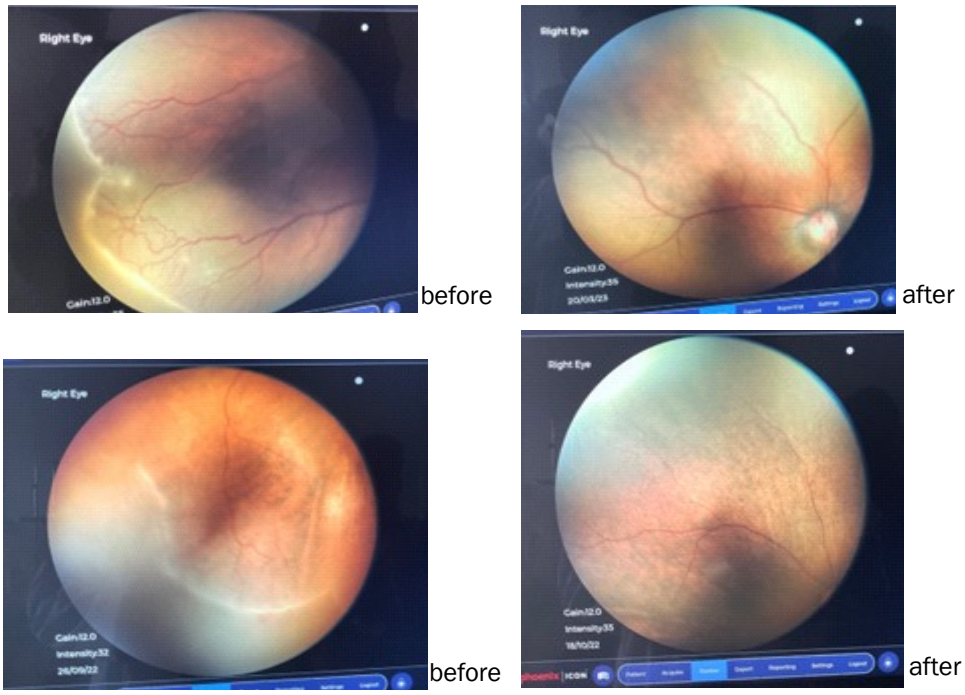

Figure 6: Retinal images of patients who developed ROP and the appearance of the retina after treatment with anti VEGF

Therefore, this age is recommended for the first initial screening or any time before discharge home from the NICU or SCBU for the condition. All eligible babies within the Nigerian guidelines for screening should be examined at least once before discharge irrespective of gestational age. [29,34,35]

Who does the screening?

The pediatric ophthalmologist, retina surgeon, general ophthalmologist who is interested and experienced and technicians who can mainly assist to take fundus pictures. [35,-37] (Figures 4 and 7)

Figure 7: Screening with the ICON retinal camera

Some important issues to take note of and to have ready or available for the screening are:

1. 2.5% phenylephrine and tropicamide drops to dilate the pupils to enable better view when screening the child.
2. Control of pain eg topical local anesthesia, sucrose drops, breastmilk, pacifiers, swaddle the child with warm blankets.
3. Be on the lookout of the possibility of apnea and use pulse oximeters for each child routinely and also when screening for ROP. (Figure 8)
4. Once the ophthalmologist is well trained in the use of these devices, then ensure that fundus pictures using the ICON retinal camera (similar to what we have in UPTH). See Figures 4 and 7. Retinal camera if available,20D and smartphone are taken for record purposes and for review of recovery after treatment is instituted.

How to screen?

Combination drops of 2.5% phenylephrine and tropicamide are usually used in our setting.[38] In other places, cyclopentolate drops are used. [39] For pain control, either topical local anesthetic drops are used or sucrose, breastmilk drawn in a 1 ml syringe and administered using a piece of gauze in the mouth of the baby soaked periodically with breastmilk or sucrose . Pacifiers or firm swaddling can also be used.[40,41]

Figure 8: A baby in the incubator with a pulse oximeter attached and blender supplying medical air and oxygen mixed together

There is also the possibility of the occurrence of apnea during screening especially in the very small babies, therefore a pulse oximeter is advised during and even after screening them. [42] (Figure 8)

In the interest of the patient, it's better for the ophthalmologist to have completed a training course in ROP evaluation and management. For record purposes, a retCAM (like the ICON retinal camera similar to what we have in UPTH) Figure 7, or at least the use of 20D lens and smart phone is much better than just the use of the BIO and the 20D lens though this may be necessary when no other facility is available.[43] (Figures 3 and 4)

It is advocated for there to be quality neonatal care, kangaroo nursing, blended oxygen(both oxygen and medical air mixed together using blenders and dedicated pulse oximeter for each baby available in the NICU/SCBU with a storage tank of medical air and oxygen separately for use as a reservoir in case there are power outages. (Figure 8)

Indications for treatment (type I ROP): is based on the Early treatment for retinopathy of prematurity trial (ETROP) [31,44,45]

Zone I- any stage ROP with plus disease
Zone I- stage 3 ROP without plus disease
Zone II- stage 2 or 3 ROP with plus disease

Who treats when ROP is found?

This should either be the ophthalmologist, who could be a pediatric ophthalmologist, retinal specialist or an experienced general ophthalmologist who is interested.

Treatment -ROP often goes away on its own without permanent damage to the baby's retina or vision. However severe cases of ROP need treatment typically within 72hours for type 1 ROP.[46,47]

Treatment options- include laser therapy- here small burns are created on the outer edge of the baby's retina. These burns prevent abnormal blood vessels from forming. It treats ROP successfully 90% of the time (Figure 9).

Anti-VEGF therapy-this involves injections into the baby's eye designed to stop abnormal blood vessel growth (Figure 10).

But once the baby has a retinal detachment(stage 4 or 5 ROP), they need specialized surgical treatment(vitrectomy) which may not always be successful (Figure 1).

What is the goal of treatment?

Conventional treatment of ROP is retinal ablation, directed towards the avascular part of the retina with the goal of decreasing production of angiogenic growth factors to inhibit intravitreal angiogenesis and facilitate vascularization of the previously avascular retina which include supporting neural and vascular development of the premature infant and retina with laser or anti VEGF. [48] (Figures 9 and 10)

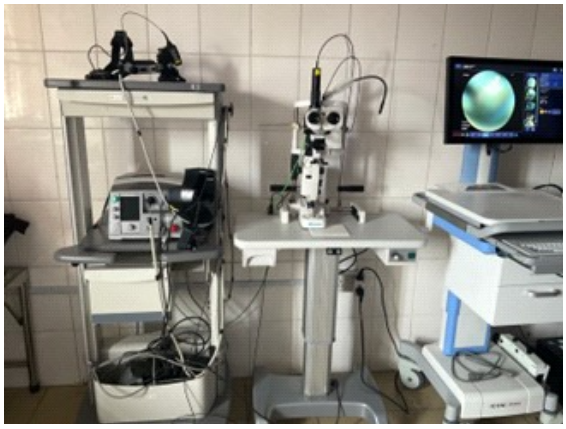

Figure: 9: Laser equipment both indirect and slit lamp guided in the university of Port Harcourt teaching hospital Screening room

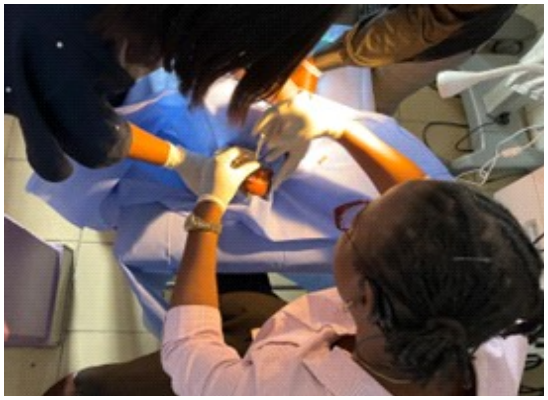

Figure 10: Giving intravitreal injections to a premature baby

Things to note when following up

The neonatal team must include arrangements for any indicated ophthalmological examinations in discharge planning and ensure the parent or caregiver understands the importance of follow-up. [49] The baby may need additional screenings every 1 to 3 weeks. All premature babies should be followed whether they develop ROP or not as they could have other eye conditions that need to be checked on as the child grows older. [50]

In addition, when treatment was given with Anti VEGF injections, the child could have a rebound or recurrence as late as 5 years after and must be followed up. [51-53]

When should screening stop?

Once there's no risk of retinal detachment, screening can stop.

Specifically, when there is:

a. vascularization in zone III without previous zone I or II ROP
b. Full retinal vascularization in close proximity to the ora serrata for 360°
c. Postmenstrual age of 50 weeks and no prethreshold or worse ROP
d. Regression of ROP (no abnormal vascular tissue capable of reactivation and progression present in zone II or III)

Other ocular co morbidity checks

Discharged infants with ROP often are at risk of ophthalmologic problems such as strabismus, cataracts, glaucoma, amblyopia and refractive errors. Regardless of whether ROP treatment was required they should be followed up by a pediatric ophthalmologist. Even preterm infants without ROP are more likely than term infants to experience visual problems. Follow-up programs should include visual examination for all preterm infants who have been screened as part of the follow-up process especially during early childhood.

Who is responsible for what in the team?

All nurseries that provide care for preterm infants at risk for ROP must have criteria and procedures to ensure appropriate ROP screening by an ophthalmologist skilled in its identification. [29,54] See Figure 4. Parents should be made aware that there is a chance of poor visual outcome even with therapy. When infants are transferred from one unit to another, arrangements must be made by the neonatal team for appropriate ophthalmological follow-up at the receiving centre. Results of ROP screening and the plan for ongoing screening must be accurately communicated to receiving health care providers. Most importantly, have an administrator/coordinator-usually a nurse coordinating the screening and ensuring that tabs are kept on all admissions, babies eligible for screening and missed screening. See Figure 11. Screening should be done on regular days. Have a screening team available each day on standby. Feedback must be provided to stakeholders by the coordinator while collaborations with other hospitals must be cultivated.

Figure 11: The ICON retinal camera with the ROP coordinator in University of Portharcourt teaching hospital ROP screening room

Audit/Research

It is important that regular audit of the screening program is made.

Records in both soft copies and hard including internet software packages for storage (eg ROP check) must be kept.

Continuous reviews and research on ROP, risk factors, outcome and genetics are encouraged.

Follow-up team in every NICU and Eye clinics with dedicated staff should be set up to ensure seamless follow-up- no waiting time, immediate access to the ophthalmologist when they appear at the eye clinic. It's also better to have a national policy like the one Nigeria has, which will help to streamline the process. [29]

Other aspects to consider

Doctors, ophthalmic imagers, optometrists, nurses and paramedics can be trained to take wide field retinal images and then forward them to ROP specialists in case there's no one trained. See Figures 3 and 12 This has gradually gained popularity in South Asia and has significantly improved the ROP screening program in these areas. But if retinal cameras are unavailable, the BIO and 20D lenses can be a good place to start until you can get one (Figures 3 and 4).

An ROP screening program should therefore

- Keep ROP consciousness in NICU staff minds constantly
- Ensure Team based training of ROP care.
- Keep Training more ophthalmologists on ROP management. Figures (3 and 12)

Figure 12: Teaching trainees how to give intravitreal injections

- Keep Training ROP coordinators
- Have joint scientific/educational meetings on ROP screening at local, national and international levels. (Figure 5)

Steps to setting up an ROP screening team

1. Advocacy
2. Collaboration
3. Coordination by dedicated personnel
4. Training of all Stakeholders. (Figures 5 and 12)
5. Role description
6. Audit and research – refine guidelines.
7. Nigerian or your country's national policy for ROP program.[29]

Figure 13: After screening a premature baby for ROP-baby free of ROP

Figure 14: Handing over a baby to her mother after screening for ROP

CONCLUSION

It is important to develop screening programs in each hospital, at the very minimum regionally. A successful ROP screening program will greatly reduce the incidence of blindness from ROP. Neonatologists are the chief drivers of a successful ROP screening program, however ophthalmologists may have to kickstart the vehicle. A good ROP screening program should be individualized to suit the environment where it is being used- You may not need to pattern it after another program elsewhere, better to do what works for you. The important take home message is to be responsible about the screening of these babies as their entire future lies literally in our hands.

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