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Epidemiology of ROP update – Africa is the new frontier

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TITLE PAGE

Epidemiology of ROP update – Africa is the new frontier

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ABSTRACT

Several epidemics of blindness due to retinopathy of prematurity (ROP) have been described, with the most recent (the third) occurring in middle income countries in Latin America and Eastern Europe initially, and more recently in the more advanced economies in Asia. In these settings, which are characterized by variation in the quality of neonatal care and inadequate coverage of ROP screening and treatment, larger, more mature infants are affected as well as extremely preterm infants. In 2010 the annual incidence of blindness and visual impairment from ROP globally was estimated to be 32,300, with the lowest incidence in sub-Saharan countries. However, ROP is likely to become an increasingly important cause of blindness in children in sub-Saharan Africa as neonatal care expands unless policies and programmes for control are included at the outset.

INTRODUCTION

Retinopathy of prematurity as a cause of blindness in children

Two epidemics of vision impairment and blindness from retinopathy of prematurity (ROP) have been described in high income countries (HICs)(Figure 1), starting in the 1940s. In the mid-1990s the third epidemic was described, initially in the upper middle income countries (MIC) of Latin America and Eastern Europe.[1] The epidemic is now affecting countries in East and South Asia, following an increase in the provision of care for sick newborns, including those born preterm.[2-4] The third epidemic has already started in South Africa,[5] which like many countries in Latin America and Eastern Europe, is an upper MIC. Some of the more advanced economies in Africa, such as Ghana, Nigeria and Kenya are beginning to establish ROP screening and treatment services as intensive neonatal care starts to expand.

Visual impairment and blindness from ROP was estimated to affect 32,300 infants globally in 2010, with marked regional variation.[6] The incidence varies markedly, with countries falling into three groups: those with very low rates of visual loss (<10 affected/100,000 live births);

moderate rates (10-<45/100,000) and higher rates (≥45/100,000)[7](Figure 2). Most countries with very low rates are low income countries in sub-Saharan Africa (excluding southern Africa) where neonatal intensive care is generally not in place and preterm infants have very high mortality rates. HICs have moderate rates as visual loss due to ROP is largely being controlled by high quality neonatal care, and good access to screening and treatment. Countries with high rates of vision loss are those where intensive neonatal care has recently expanded, but where the quality of care is variable, with inadequate coverage of ROP screening and treatment.[8-9]

Variation in the characteristics of infants with severe ROP

The predominant risk factor for ROP is prematurity, with an inverse relationship between gestational (GA) and the incidence and severity of ROP. Other risk factors are discussed in another paper in this issue.[10,11]

In HICs only extremely low birth weight (BW) infants develop ROP requiring treatment (i.e., Type 1 ROP). For example, in the United Kingdom, the median gestational age (GA) of infants treated in 2014 was 25 (interquartile range (IQR) 24.3-26.1) weeks, and the median BW was 706 (IQR 620-821) g.[12] Data from 29 neonatal units in the US are similar: mean GA of infants with Type 1 ROP ranged from 24-25 weeks, and the BW ranged from 604-741 g.[13] However, in countries experiencing the 3rd ROP epidemic, the BW and GA of infants with Type 1 ROP can be far higher,[14] as in Bangladesh (Figure 3). In this eye hospital study, infants were either screened in neonatal units nearby or were referred for examination or treatment, or for a second opinion from a large number of eye hospitals or neonatal units. Over two years 283 babies were treated, most by laser photocoagulation, or had vitreoretinal surgery for Stage 4 or 5 ROP. The median GA was 31.4 (range 24-36) weeks and the median BW was 1,400 g (range 600-2,500). 20% had a GA of >32 weeks and a BW of >1500 g. Similar findings have been reported from a programme in India where technicians

visit a large number neonatal units on a weekly basis to screen for ROP using retinal imaging (Figure 4).[15]

These findings have important implications. Firstly, the quality of neonatal care needs to improve to reduce the incidence of ROP. Second, ROP programmes in LMICs need to have screening criteria which are wide enough to detect the majority of infants developing Type 1 ROP. There are no universally applicable criteria.[16]

ROP in South Africa

ROP screening started in South Africa in the early 1980's, largely in private neonatal units and tertiary academic institutions (Medical Schools) in large cities. Infants were managed using HIC guidelines with comparable outcome.[17,18,19,20] Many babies born in lower level hospitals in rural areas did not survive, but those who did were transferred for tertiary, high quality care with a low incidence of ROP. The National Guideline on the Prevention of Blindness (2002)[21] included ROP screening guidelines, based on those from the UK and USA.

In 1997 the White paper on the *Transformation of the Public Health System* was published to improve access to health care for all citizens, which promoted decentralisation of services to district level. By 2006 paediatric services were largely decentralised. An unforeseen casualty of this policy was an increase in ROP in larger babies, as more mature premature babies were referred down to district hospitals which lacked neonatologists or ophthalmologists, and primary health care workers did not know about ROP. There were no oxygen blenders and all infants were given 100% oxygen. At the same time the survival of preterm infants born at secondary level hospitals increased. Both of these factors led to a marked increase in the number of babies needing treatment in KwaZulu-Natal province between 2006 and 2011 (Figure 5), prompting ophthalmologists and neonatologists to collaborate on modifying the

screening guidelines. Legal issues following the increase of blindness due to ROP prompted the professional societies of neonatology, ophthalmology and vitreoretinal surgeons to draw up national prevention, screening and management guidelines for ROP,[5] taking account of the local setting. The guidelines, which were drawn up by a ROP Working Group comprising ophthalmologists and neonatologists, were based on those of the Royal College of Ophthalmologists (UK) and the American Academy of Pediatrics. All provinces now have services for ROP.

In South Africa the guidelines stipulate that following babies are screened: GA <32 weeks or BW <1500g, and those with a BW 1,500-2,000 g with risk factors, including unblended oxygen supplementation. The first screening is at 4-6 weeks chronological age or 31-33 weeks post-menstrual age (whichever is later) but no later than 37 weeks post-menstrual age.

Since these guidelines have been followed, there has been a significant decline in the number of treatable ROP cases at our centre (Figure 5).

ROP in Kenya

Screening for ROP began in Kenya 2010 in private institutions, as a response to improved neonatal care and higher survival of premature infants. A few of these infants presented with stage 4 or 5 ROP, prompting the litigation-conscious private hospitals to initiate screening. The first government hospital to implement screening (in 2014) was the Jaramogi Oginga Odinga Teaching and Referral Hospital in Kisumu, Western Kenya. The Kenyatta National Hospital, the main teaching and referral hospital with a large neonatal unit (120-180 cots), started screening in 2015. In a study in two neonatal units in Nairobi, where the screening criteria were <32 weeks or ≤1500 g or more mature infants at the discretion of the neonatologist, 16.7% of infants developed any ROP.[22] In a further study in Nairobi in which more mature infants were eligible for screening (≤35 weeks or ≤1,750 g), 41.7% developed any ROP and 20.9% developed Type 1 ROP and were treated.[23]

The screening criteria in Kenya are a BW of <1,501 g or a GA of ≤32 weeks. Neonates with a BW 1501-2000 g or GA >32-35 weeks are also screened if they have been exposed to high or prolonged oxygen supplementation, extended assisted ventilation, sepsis and poor postnatal weight gain, on the recommendation of the neonatologist or pediatrician.

National ROP guidelines were launched on 30th November 2018 at the first annual Ophthalmological Society of Kenya Congress in Nairobi. The guidelines were drawn up by a multi-disciplinary technical working group which consisted of technical experts (neonatologists, pediatricians and paediatric ophthalmologists and vitreoretinal surgeons), methodologists and those who would implement the guidelines. Implementers included representatives of the College of Ophthalmology of Eastern, Central and Southern Africa (COECSA), neonatal nurses and program managers. The process involved adapting existing guidelines, considering the availability and access to different interventions. Following extensive consultation a consensus was reached regarding each of the recommendations. Over 200 copies of the guideline have been distributed to ophthalmologists and presented at regional and local conferences.

Four government hospitals have been selected to pilot implementation of the guidelines, with the support of the Ministry of Health. Further dissemination has been planned through resident workshops and local/regional conferences for ophthalmologists, paediatricians and nurses.

ROP activities in Kenya are being coordinated by the Retinopathy of Prematurity Working Group, which was convened with the support of the Ophthalmic Services Unit of the Ministry of Health. COECSA is the lead implementing partner who helps to bring together other local partners.

ROP in Nigeria

The first study of ROP screening in Nigeria was undertaken in Ibadan in 1995.[24] Screening was subsequently discontinued because of the low incidence of ROP and high mortality of

affected infants. Screening started in Ilorin in 2007, but was discontinued due to logistical problems. Screening was undertaken between 2012 and 2014 in other cities, including Ibadan, Lagos, Port Harcourt and Benin,[24-27] but the services were irregular.

During a meeting on ROP for the Africa region in 2016 (organized by the International Pediatric Ophthalmology and Strabismus Council (IPOSC)), the likelihood of an epidemic of ROP blindness in sub-Saharan Africa was raised. Shortly afterwards, three ROP blind infants from different parts of Nigeria presented to our ophthalmology department. This suggested that changes in neonatal care have resulted in more preterm infants surviving, some whom are developing advanced ROP.[28]

In 2017 screening became established in three hospitals in Nigeria, and a national advocacy exercise was launched to raise awareness amongst neonatologists. This included presentations by members of Nigerian Paediatric Ophthalmology and Strabismus Society at the annual scientific meeting of the Nigerian Society for Neonatal Medicine. These initiatives led to the creation of a joint ophthalmologist - neonatologists/paediatrician social media platform to ease communication, and two joint scientific sessions.

In some parts of the country there are specialists in retina and paediatric ophthalmology, and 14 hospitals across Nigeria are now doing some ROP screening and treatment. Capacity to scale up and deliver ROP services have been strengthened in several ways. Firstly, through a partnership between Ilorin and a centre of excellence for ROP in Odissa State, India who have facilitated training workshops. Second, IPOSC members have developed two webinars on ROP for Africa, and third, ophthalmologists with more experience in ROP are making mentoring visits to assist centres who have recently started ROP programmes.

An important next step was to develop a national screening protocol to collect data to inform national screening criteria for Nigeria. The protocol was agreed through a process of consensus and it supersedes the criteria being used previously. It was agreed that between September 2018 and August 2019 all infants with a GA of <37 weeks or BW of <2000 g

would be screened, with the first examination 3-4 weeks after birth or before discharge, whichever is sooner. Screening is taking place in the neonatal unit, and the management decision at each examination follows international recommendations. Infants are being followed up at 3 months after screening and examined for refractive errors and strabismus. After August 2019 the data will be analysed and presented, and decisions made about the optimal screening criteria to inform guideline development.

CONCLUSIONS

Several countries in sub-Saharan Africa have started services to prevent visual loss from ROP. The examples from South Africa, Kenya and Nigeria emphasize the importance of committed local leaders, collaboration between ophthalmologists and neonatologists/ paediatricians, the need to develop locally relevant, evidence based guidelines, and that services can be scaled up with support from professional societies, and input from external experts. The active engagement of Ministries of Health and national coordinating bodies are also very important for policy change and in scaling up services.

Disclosure: None of the authors have any competing interests

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Figure 1. Epidemics of blindness due to retinopathy of prematurity.

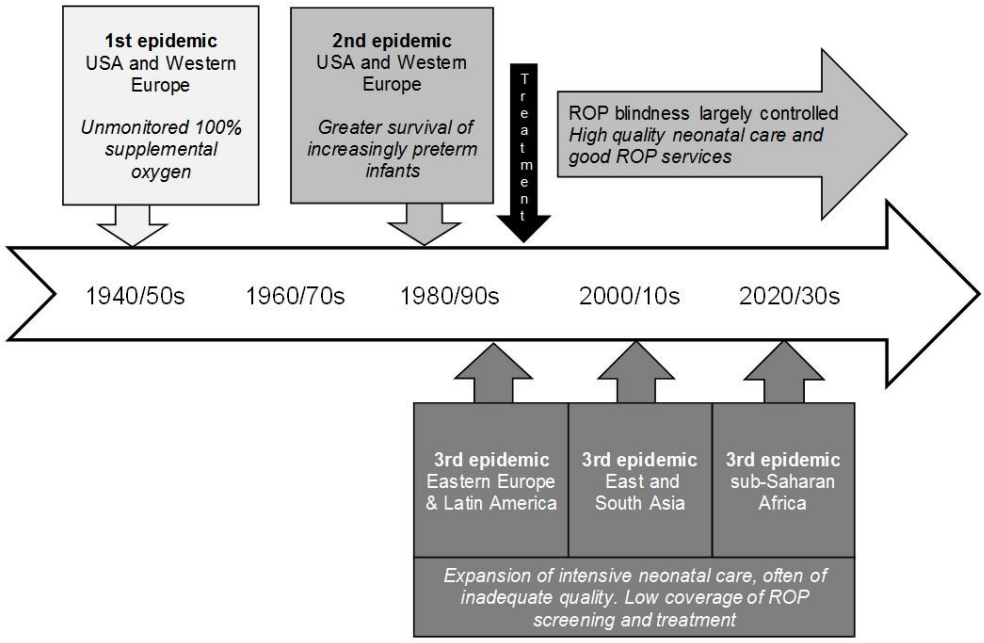

Figure 2. Estimated incidence of vision impairment and blindness from ROP per 100,000 live births in 2010.[6]

(From Blencowe H, et al. Preterm-associated visual impairment and estimates of retinopathy of prematurity at regional and global levels for 2010. Pediatr Res 2013;74 Suppl 1:35-49; with permission.)

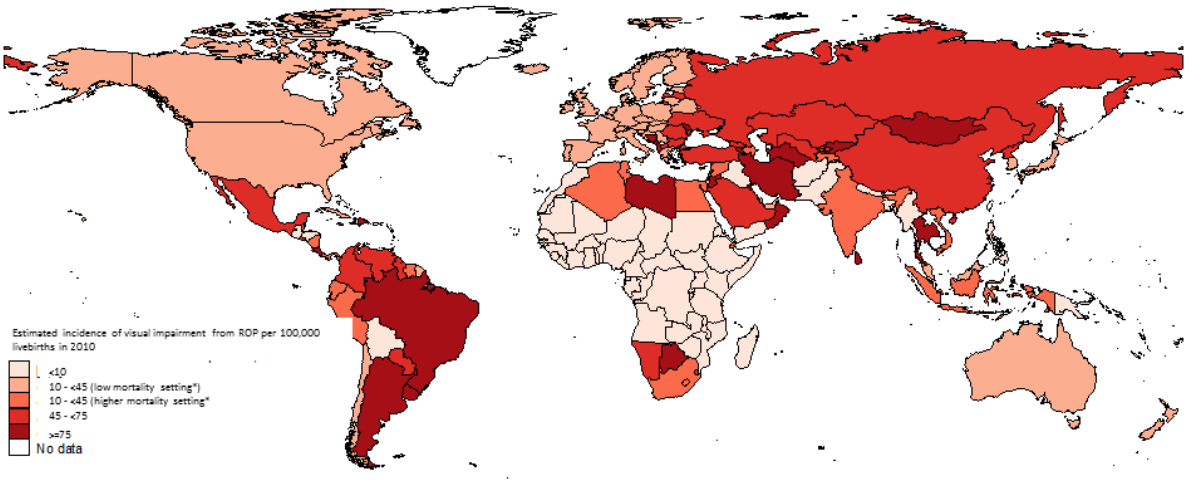

Figure 3. Gestational age and birthweight of babies treated for ROP in an eye hospital in Bangladesh in 2016 and 2017.

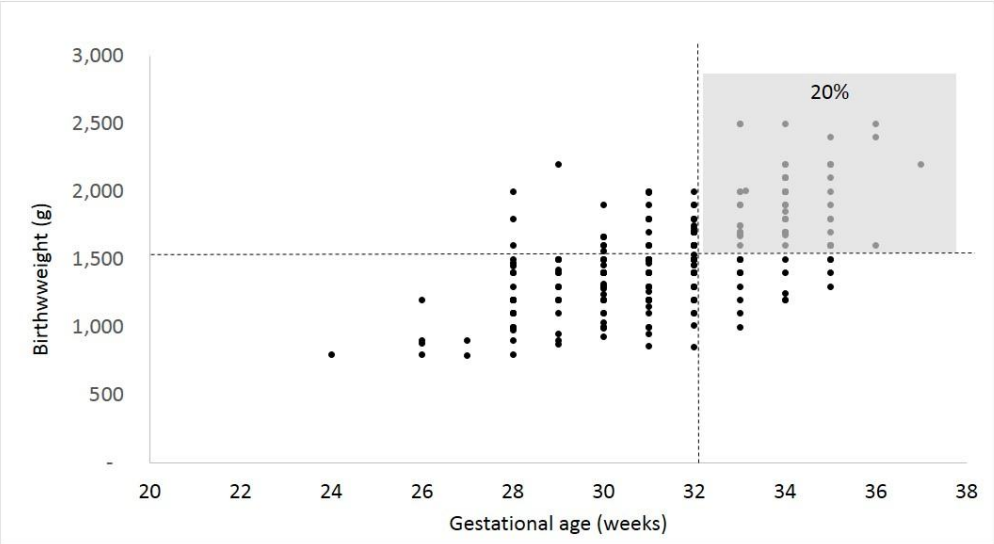

Figure 4. Birthweight and gestational age of infants screened and treated for ROP in a telemedicine programme (KIDROP) in India.[15]
(Reprinted from Vinekar A, Gilbert C, Dogra M, et al. *Indian J Ophthalmol* 2014; 62(1): 41-9; with permission. The original figure being in colour)

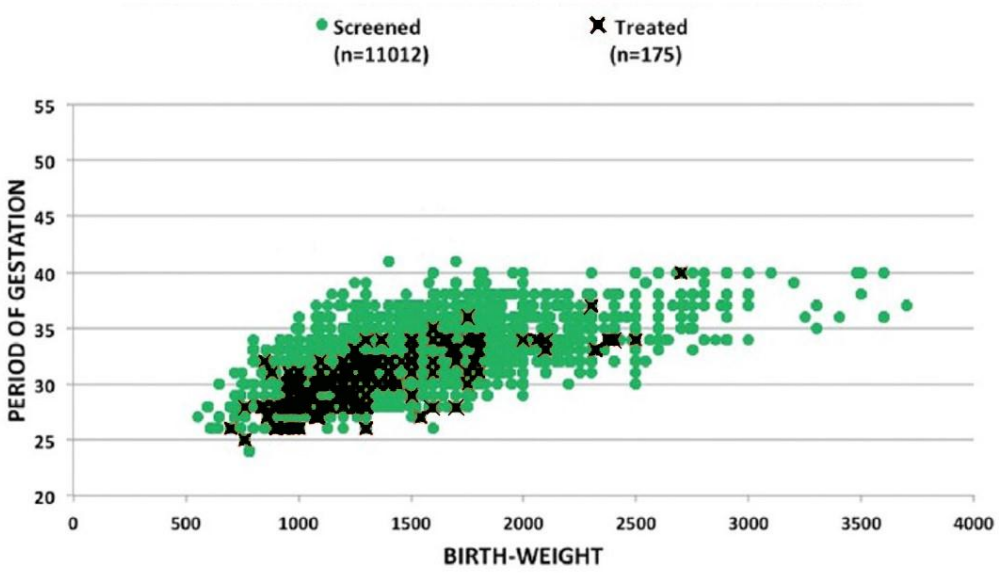

Figure 5. Number of babies treated for ROP in KwaZulu-Natal between 2008 and 2015