

Retinopathy of prematurity screening in the Indian population: It's time to set our own guidelines!

There is an alarming increase in the incidence of retinopathy of prematurity (ROP) in the developing countries including India today, constituting what is referred to as the third epidemic of ROP. While the incidence of ROP is on the wane in the West, thanks to the improvement in neonatal care and screening, in India we are just beginning to face the storm mainly due to increased awareness. The most important determinant of any ROP management program is an effective screening strategy. There are several peculiarities that preclude the application of the effective guidelines that exist in the West to the Indian scenario.

Two questions: Whom to screen? And when to screen? have to be answered in the Indian scenario.

Let us consider the first question of whom to screen? There is a geographic variation in the incidence of ROP in babies born at even similar gestational ages.¹ In the West, ROP at least of the threshold variety is not seen in higher birth weight (BW) babies! Therefore, larger babies generally are not screened since the incidence of treatable ROP is low and these infants have been observed to have a generally good outcome even without treatment. The American Academy of Pediatrics (AAP) recommends screening of infants born at ≤ 28 weeks gestational age (GA) and/or ≤ 1500 g BW (regardless of supplemental oxygen); 1500 to 2000 g BW if supplemental oxygen was administered and the infants had an unstable clinical course.² However, Wright *et al.*³ recommended screening of all infants born at ≤ 32 weeks GA and/or ≤ 1500 g BW (regardless of supplemental oxygen) and predicted that it would lead to savings in excess of 1.5 million dollars annually in the United States; this was approved by Andruscavage *et al.*⁴ A recent study from the US found that no infant with birth weight greater than 1500 g developed treatable ROP.⁵ Similar guidelines exist in the UK as laid out by the Royal College of Ophthalmologists and the British Association of Perinatal Medicine.⁶

In contrast, ROP is seen in larger, bigger BW babies in Asia and other developing countries. In south India, threshold ROP has been seen in babies born with 2000 g birth weight.⁷ While partly this might reflect the failure of very small infants to thrive, other factors such as perhaps the quality of neonatal care that has led to a decline of ROP in the West is lacking here. Of note, a similar scenario existed in Lithuania, wherein ROP was seen in larger infants initially. However, the birth weights of babies with ROP have fallen quickly due to improvements in neonatal care.⁸ A similar swing in the pendulum could be expected to occur in India as well! Nevertheless, it is essential to realize that at least in the present scenario, the cutoff birth weight and the gestational ages of our babies that need to be screened for ROP need to be higher. Hence regionalization of screening criteria needs to evolve. This is important, especially in India, where no auditing of delivery services exists, unlike for instance, in the UK (96% of NICUs in the UK had regular screening for ROP).⁹ We therefore cannot be choosy and restrict ourselves in India where the number of nurseries allowing screening themselves are small. This is another reason to screen even bigger babies till confidence grows and our data become well-established and analyzed. A converse view point is that it would not be a sound economic proposition in India where ophthalmic expertise is sparse. Interestingly, an elegantly performed study has recently compared the efficiency of general ophthalmologists (ophthalmic residents) as well as non-ophthalmologists (pediatric residents and nurses posted in neonatal intensive care units) in screening for ROP on the basis of posterior pole vascular changes and found them to be independently reliable.¹⁰ This if implemented well could decrease the problem of lack of trained manpower in India.

In fact, it has been suggested that as a lower cost option in developing countries, screening infants only under 1200 g BW may be more cost-effective!¹¹ But how many such infants would survive in India has to be kept in mind. There is hence a need for centers to examine the data, especially from larger birth weight infants to develop a strategy that would not only be more cost-effective but also not miss any treatable ROP. The article from post graduate institute Chandigarh in this issue of Indian Journal of Ophthalmology addresses this concern, with the authors encountering a significant percentage of severe ROP in babies weighing more than 1250 gms at birth.¹²

A reasonable guideline of screening babies born at ≤ 34 -35 weeks gestational age (based on the work by Fielder *et al.*)¹³ and/or BW 1500 g (or even up to 1700 g) and/or exposed to oxygen for more than 30 days exists in India.¹⁴ As higher cutoff limit, Jalali *et al.* have recommended screening babies born at ≤ 37 weeks GA and/or BW 2000 g in the presence of a high sickness score in order to prevent missing any infant with threshold ROP.¹⁵

The plot thickens further with the second question of 'When to screen'?

The AAP recommends screening of all eligible babies at four to six weeks chronologic age (CA) or 31-33 weeks postconceptional age (PCA) whichever is later.² Initial examinations are usually not needed within the first four weeks after birth. The Royal College of Ophthalmologists and the British Association of Perinatal Medicine suggests screening of the infants between six to seven weeks of CA (there is no mention about PCA).⁶ It has been recommended with regard to the Indian scenario to screen at 31 weeks PCA or three to four weeks CA¹⁵ whichever is earlier (in contrast to the AAP guidelines that mentions later, when it is to be decided between choosing the PCA and the CA). Initial examinations are usually not needed within the first two to three weeks after birth.

What is the rationale behind earlier screening in the Indian population? As per the CRYO-ROP study, Stage I ROP begins at around 34 weeks PCA, although it could be delayed till the 39th week as well, while threshold ROP is usually seen at 36.6 weeks PCA, (32-42 weeks, variation).¹⁶⁻¹⁷ In Asian countries the entire sequence of events occurs one to two weeks earlier.¹⁴ Hence if the first exam is at 32 weeks PCA, it is the earliest age (even by Indian and Asian standards) for early significant ROP to occur and hence could be detected prior to its reaching the threshold stage.

Moreover, since ROP is seen in heavier and larger babies in India that have consequently a shorter window period for development of ROP earlier examinations are essential, in contrast to the West wherein threshold ROP is seen in smaller babies

that have a longer window period to develop ROP. Hence, an examination carried out later would suffice in the West but would lead to missing of early stages of ROP in our country.

There are some more peculiarities in the Indian scenario.

Ideally both CA and PCA have to be considered since if CA is used alone, there is a risk of missing out threshold disease in larger birth weight babies. Conversely, usage of PCA alone would increase the risk of missing the onset of threshold disease in smaller BW babies. Usually screening protocols are mainly based on PCA, since ROP onset and progression are mainly determined by it. However, in India, accurate GA and hence PCA (GA+CA) estimation is not possible many a time that results in babies with intrauterine growth retardation (IUGR) cluttering up the screening program, leading to a lot of unnecessary screenings. Hence, it is a good idea to have the first screening within Day 30 of an infant's life.¹⁵ Of note, if an infant is 1500 to 2000g BW and also if an infant is very small, receiving a lot of oxygen, an earlier screening at perhaps two to three weeks of CA is essential to prevent missing the onset of threshold ROP in the former, and to have a good baseline fundus picture and prevent the missing of the detection of Type II ROP (ROP that does not manifest the fibrous landmarks of classical ROP and which is seen more commonly in Asian countries) in the latter.

What is the bottom-line?

All screening programs are time-consuming and labor-intensive, uncomfortable to the infants, cause anxiety to the parents and sometimes lead to an extended stay at nurseries. All these factors have to be weighed against missing a child with treatable ROP. In fact an average of 39 screening examinations and 19 hours of an ophthalmologist's time is necessary to detect one single case of threshold ROP.¹⁸ Additionally, all the current screening strategies are directed at detecting threshold ROP. In the light of ETROP results that advocate treatment for even high-risk pre-threshold ROP,¹⁹ earlier screening becomes necessary. Efforts are already underway in the UK to modify the existing guidelines. Region-specific screening criteria modified according to recent developments in the understanding and management of ROP need to be evolved in India as well. This could be made possible by a concerted and cooperative effort between the major eye institutes with an analysis of pooled data and auditing of delivery services to constitute "The Indian ROP screening guidelines".

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