RESEARCH PAPER

Initiating Retinopathy of Prematurity Screening before Discharge from the Neonatal Care Unit: Effect on Enrolment in Rural India

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Objective: To compare the benefits of initiating Retinopathy of Prematurity (ROP) screening at first contact with the admitted infant prior to hospital discharge ('early screening') with screening performed between 21 and 28 days after birth ('conventional screening') in rural India.

Design: Prospective study.

Setting: Two Level II neonatal intensive care units (NICU), from two district headquarters in Karnataka state.

Participants: 329 infants admitted in the two NICUs.

Intervention: One NICU was randomly selected for 'early' and the other for 'conventional' screening. Infants <2000 g at birth were targeted for enrolment. Both centres were visited once a week by a dedicated ROP team.

Main Outcome Measure(s): The yield of enrolment, and the magnitude of treatment-requiring cases that would be missed in each scenario were estimated and compared.

Results: 107 of 329 admitted infants were eligible for ROP screening. In the study period of 4 months, 42 and 65 infants were eligible for enrolment in the early and conventional group, respectively. In the early group, 88.1% of eligible infants got screened, compared to 38.5% in the conventional group (*P*=0.03).

Conclusion: Early enrolment of infants for ROP screening in the NICU itself ensures a superior yield compared to conventional age of initiating screening. The recorded information of mothers allowed pre-counselling, improved enrolment and better compliance to the scheduled examinations. These results suggest the need to re-look at the screening guidelines in India and other regions with similar demographics.

Keywords: *Diagnosis, Neonatal screening, Premature Infant*.

Retinopathy of prematurity (ROP) is one of the leading causes of preventable blindness in children, particularly in middle-income countries [1], where the 'third epidemic' of blindness from ROP is said to be occurring [2-4]. The recommendation for first screening for ROP in the United Kingdom is between 6-7 weeks chronological age [5]. In the United States, it ranges between 4-9 weeks postnatal age, depending on the postmenstrual age [6]. In India, the first screening is recommended between 2-3 weeks for infants born before 28 weeks gestational age or with a birthweight less than 1200 grams and not later than 30 days or 4 weeks after birth for infants born between gestational age of 28-34 weeks or born less than or equal to 2000 g [7].

Identifying which infants need to be screened for ROP and the date for the first examination must be done when each preterm infant is admitted in the neonatal intensive care unit (NICU). For many infants the date of the first retinal examination is after discharge from the neonatal unit, particularly in India when larger, more mature but less sick infants need to be screened [8-11]. In rural neonatal centres, infants are also often discharged early due to scarce financial and/or infrastructural resources. Scheduling ROP screening 3-4 weeks after birth, especially when the date is after discharge from the unit can be problematic as the parents may not return on the scheduled date or may not comply at all [11].

The effect of modifying ROP screening guidelines to initiate the first screening session before discharge, irrespective of the post menstrual age has not been studied in the Indian context. This study compares the conventional timing of first examination [7] with an 'early' examination strategy of at least one screening examination prior to discharge from the unit.

METHODS

This was a prospective, observational study conducted in two Level II NICUs in two district headquarters in Karnataka State. One was randomly selected for

'conventional' and the other for 'early' screening. In both NICU, the neonatologist identified infants to be screened in compliance with the National Neonatology Foundation ROP guidelines (2010) [7] (those with a BW below 2000 grams), and referred them for screening.

Both centres were visited once a week on a predetermined day by a dedicated ROP team, and a pediatric retina specialist performed the ROP screening. Prior to the study, teams of doctors and nurses were orientated about the study in both NICU. In the early screening NICU, the rationale for early screening was explained to the mothers.

In both groups, maternal contact information was recorded in the database and two alternate mobile numbers were verified. Follow-up cards detailing the retinal condition and the date for the next follow-up were provided to all mothers. Each session was documented on the RetCam Shuttle (Clarity MSI, USA) and the images were shown to the parents who were counselled appropriately. Laser treatment was performed on-site, based on the Early Treatment of ROP recommendations [12].

In the conventional screening, NICU infants were first screened between day 21 and 28 after birth irrespective of their gestational age. This included infants who were still admitted as well as those who had returned after discharge for their first screening. In the 'early screening' group, the first screening was performed at the first opportunity after admission irrespective of the post menstrual age, unless the child was systemically unstable.

The primary outcome of the study was to compare the yield of babies getting successfully enrolled into the ROP screening program and to estimate the number of cases that would have been missed in each method. The secondary outcome was to compare the number of screening sessions between the two groups.

The study was approved by the Institutional Ethics Committee, and informed consent was obtained from either of the parents or guardians in all cases of screening, and a special consent prior to the treatment.

Statistical analysis was performed using the IBM Statistical Package for Social Sciences (SPSS) Ver. 23 (IBM Corp, NY). Chi square tests were done to analyze the incidence of ROP, treatment-requiring disease and gender distribution between the early screening and conventional screening groups. One sample T-test was performed to assess the difference in the mean age of screening and the number of follow up visits between the two groups.

RESULTS

During the study period of four months, 107 infants with a birthweight below 2000 g from the two NICU were included in the analysis, 42 of whom were in the early screening group and 65 in the conventional group. Both groups were comparable for gender, birth weight and gestational age (***Table* I**). The incidence of any stage ROP and treatment-requiring disease were also comparable.

The mean age at first screening was 7.1 (3) days in the early group and 24.2 (2) days in the conventional group ($P<0.001$). Of the 42 infants identified for screening in the early group, 37 (88.1%) underwent first screening. Among the five who missed screening, the neonatologist did not refer three infants, and two infants had died. In the conventional group, of the 65 infants identified for

TABLE I DEMOGRAPHIC DATA OF THE STUDY INFANTS (N=107)

	Early screening	*Conventional screening*	*P value*
*Babies with birthweight <2000g (%)	42 (32.8)	65 (32.3)	
Babies enrolled for screening (%)	37 (88.1)	25 (38.5)	0.003
Gender (M:F)	23:19	27:38	0.2
Birthweight (g), mean (SD)	1550.9 (290)	1598.2 (274)	0.3
Gestational age (wks), mean (SD)	32.2 (2.5)	32.3 (2.1)	0.4
No ROP (%)	24 (24/37, 64.9)	14 (14/25, 56)	0.7
Mild ROP (%)	10 (10/37, 27)	8 (8/25, 32)	
ROP requiring treatment (%)	3 (3/37, 8.1)	3 (3/25, 12)	
Age at screening (d), mean (SD)	7.1 (3)	24.2 (2)	<0.001
Age at discharge (d), mean (SD)	13 (6)	14 (6)	0.1
Number of screening sessions, mean (SD)	3.4 (1)	3.6 (1)	0.6

**Number of babies admitted during the study period was 128 and 201 for the early screening and conventional screening groups, respectively.*

screening, only 25 (38.5%) underwent first screening, which was significantly lower than in the early screening group (P=0.03). All 40 babies who were not screened had been counselled by their treating pediatrician to return to the NICU for screening, but none did. All infants in both groups completed all the follow-up screening examinations. The average number of screening examinations needed before ROP screening could be discontinued was comparable in the two groups.

Of the 37 infants screened in the early group, 6 babies (16.2%) with a birthweight range between 1350-2050 grams and a gestational age range between 29-34 weeks needed only one examination and hence did not require further screening visits.

Timing of discharge and enrolment: The vast majority (86.5%) of the 37 infants examined in the early screening group had been discharged before completing 21 days in the NICU and would not have been screened during admission if the conventional protocol had been followed. In the conventional group, half (52%) of the 25 infants screened were discharged before 21 days, and were screened because they came back after discharge as advised by the neonatologist. The other 12 (48%) were screened between 21-28 days while they were still inpatients. There were no adverse results in the examination of any of the infants, especially in the early screening cohort, during or within 24 hours of the screening session having been concluded.

DISCUSSION

The study results demonstrate that infants qualifying for ROP screening may be first screened 'earlier' than the conventional time period. Earlier first ROP screening led to a higher proportion of infants being screened for ROP than those examined at the time recommended in the NNF Guidelines. In addition, earlier screening did not increase the total number of screening sessions required or cause any systemic complications in these babies despite the earlier age at which these screening sessions were carried out. The first 'early' screening allowed the second visit to be scheduled at a more 'physiologically appropriate corrected age' instead of examining every baby every week. Hence, this does not increase the burden of return visits to the NICU than screening at the recommended time.

This study also highlights that the yield of detecting ROP cases needing treatment would be more in the early screening group. By using a large multi-centre, rural community study [13] as a measure of treatment-requiring disease burden and extrapolating the 'missed babies', we found that an eight times higher yield would have been obtained if the babies had been screened 'earlier' rather than according to the conventional NNF guidelines.

The study also demonstrates the advantage of counselling parents using retinal images [9,11,13,14] of their own baby when the child is still admitted, as all infants examined early returned for all their screening examinations whereas only around a third of parents who were instructed to bring their infant back for screening after discharge actually did so. Our initial interaction with the mother also provides a unique opportunity to build rapport, and confirm the mothers' contact information including alternate mobile numbers and convincing other key family members who may be responsible for taking decisions. This helps to improve compliance with follow-up.

The limitations of the study are that it was performed in only two NICUs and the number of babies is relatively small. Hence, the findings cannot readily be generalized as regional differences and local factors could play a role in influencing compliance. Although the two NICUs were comparable in relation to the demographics of the babies they admit and the incidence of ROP, subtle differences in neonatal care practices between the NICUs were not studied. Patients were treated free at both centres. The impact of charging a fee on the uptake of screening or on acceptance of treatment is not known and could influence the findings. A detailed assessment of the adverse effects while screening very low birthweight or preterm infants in the early screening group was not evaluated, even though bradycardia and apnea were not observed in both groups during the screening sessions. Furthermore, the estimate of the number of infants who would miss treatment-requiring ROP among those who were not screened is not a generalizable measure.

Conventionally, the timing of the first screening for ROP is delayed for a few weeks after birth, based on the natural history and correlates more closely with the post-menstrual age rather than gestational age [15,16]. In India, the first screening is recommended not later than 30 days after birth [7] and in the West, even later. Adherence to these guidelines will often prompt the first screening between 4-6 weeks or later after birth. In most instances, especially in rural areas, owing to a lack of financial resources, infrastructure or both, infants are often discharged prior to this date, which necessitates that they return to the NICU for ROP screening leading to poor compliance. Even in the West, infants whose appointments were scheduled by hospital personnel before discharge were more likely to return for a follow-up as compared to when their appointment was not

WHAT IS ALREADY KNOWN?

- ROP screening in India begins between 3-4 weeks after birth for infants weighing between 1200-2000 grams at birth, or 2-3 weeks for infants <1200 grams at birth.

WHAT THIS STUDY ADDS?

- Initiating ROP screening prior to NICU discharge irrespective of the postmenstrual age increases the enrollment into an ROP screening program compared with the conventional age of initiation without any increase in the total number of sessions.

scheduled at all, or after discharge. Support staff from the office was required to remind and ensure better compliance with follow-up [17]. In another study from the US, infants not screened for ROP in the NICU were more likely to miss follow-up appointments than infants who had their first retinal examination in the NICU. This study also reported that infants transported back to a community hospital were significantly more likely to miss follow-up eye care compared to infants discharged from the regional centre [18].

In conclusion, this study suggests that in a rural setting one NICU screening prior to discharge, *vis*. 'early screening', irrespective of the postnatal age or post-menstrual age, leads to a higher proportion of infants at risk of ROP being screened than infants screened at the recommended postnatal age. This impact needs serious consideration while revising the national screening guidelines, since the majority of infants who require screening in our country are from the rural areas.

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