Early presentation of severe ROP in Sri Lanka

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Abstract

Introduction: *Retinopathy of Prematurity (ROP) is a major blinding condition in immature neonates. Early diagnosis and treatment of ROP is critical in saving the vision in these children. This study was designed to find out the timing of the presentation of threshold ROP in Sri Lanka.*

Method: *Retrospective analysis of patient records of neonates screened for ROP at the Eye Unit of the Lady Ridgeway Hospital for Children during 1st June 2013 to 31st May 2014.*

Results: *Any Zone 1 ROP with plus disease, Zone 2 Stage 2 ROP with plus disease and Zone 2 Stage 3 ROP with or without plus disease were considered as threshold for treatment. Of the total 568 babies screened during the period 106 babies were in the above categories. All the babies diagnosed to have Threshold ROP were given 532nm Green Laser and 54 (50.94%) babies received Intravitreal Bevacizumab injections additionally. Mean age at the diagnosis of Threshold disease was 4.51 weeks postnatal with a range of 2-13 weeks. 32 babies (5.6% from total screened and 30.2% from all the babies with Threshold ROP) developed threshold ROP during the first 2-4 weeks of life.*

Conclusions: *Significant proportion of threshold ROP present before 4 weeks of age in Sri Lanka. If the first screening of ROP not done before 4 weeks of age, the diagnosis will be delayed in these cases which will lead to blindness.*

Introduction

Retinopathy of prematurity (ROP) is a major blinding condition in the premature infants[1-9]. Development of ROP has been associated to the Post Menstrual Age (PMA) according to the studies done on the natural history of the condition[7,8]. Therefore, guidelines for screening for ROP throughout the world aim to start screening with the onset of the disease. In most neonatal units first screening examination is carried out at a PMA of 30-31 weeks or 4 weeks post natal[1-9]. In Sri Lanka, it was noted that few babies went blind with tractional retinal detachment when ROP screening was carried out in accordance with the above criteria. This was noted mostly, but not exclusively in babies who were born at a PMA less than 30 weeks. Therefore, the current study was designed to find out whether a proportion of babies develop severe ROP sooner than 4 weeks of chronological age.

Materials and methods

Eye Unit at the Lady Ridgeway Hospital for Children (LRH) serves as a tertiary level referral centre for ROP management. In addition the staff at the Eye Unit also carry out screening in the local Premature Baby Units in the De Zoysa Maternity Hospital (DMH), Castle Street Hospital for Women (CSWH) and the LRH. Each baby screened is registered separately in a register which is exclusively reserved for premature babies.

Criteria to screen for ROP includes babies born on or before 32 weeks of gestation, birth weight 1500g or less and the babies who had acute illnesses such as septicaemia, meningitis or major surgeries during the first few weeks of life[10]. Screening examination was carried out at the premature baby unit or in the Eye Clinic. Pupils were fully dilated with 0.5% Tropicamide and 2.5% Phenylephrine solution. Dilatation begins approximately 30 minutes before the intended time of examination. Dilatation drops were repeated 3-4 times. proparacaine 0.5% drops were instilled 5 minutes before the examination and soon before the insertion of the speculum. Baby is wrapped in warm cloth and held by a trained nursing officer to minimise the movement of the limbs and the neck. 'V' Shaped paediatric speculum is inserted without touching the cornea. Retinal indenter is used to manipulate the globe very gently to get the full view of the retina up to Ora Serreta. Indirect ophthalmoscopy is done with the 20D bio-microscpe lens. Findings are recorded in the patients' clinic notes and handed over to the parents or caretaker and an identical entry is made in the clinic register. Important clinical findings were photo-graphed in the RETCAM wide field paediatric retinal imaging system.

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Table 1 summarises the indications for treatment of ROP in Sri Lanka, herein referred as "Threshold ROP".

Table 1.

Criteria to Treat (Threshold ROP)
Any Zone l ROP with Plus Disease
Zone ll Stage 3
Zone ll Stage 2 with Plus Disease

If laser treatment was required it was carried out on the same day under topical anaesthesia. If there was an indication to give intravitreal bevacizumab injection, RETCAM photos are e-mailed to the vitreoretinal surgeon's opinion. Injection of intravitreal Bevacizumab was also done on the same day under topical anaesthesia.

Current study used the patient records during May 2013 and June 2014. Following parameters were extracted from the patient register. Post menstrual age (PMA) at birth, PMA at diagnosis, birth weight, ROP Stage, Zone and presence of plus disease, type of treatment and the referring centre was recorded.

Results

Total number of babies screened at the Eye Unit of the Lady Ridgeway Hospital for Children during June 2013 and May 2014 was 568, of which, 136 babies were tertiary referrals from other hospitals. Rest of the 432 babies was from the Premature Baby Units of LRH, DMH and CSHW. 214 (37.6%) babies had some degree of ROP. From this group, only 106 (18.66%) had Threshold ROP (Table 1) and required treatment according to the local guidelines. Most of the treated ROP was Zone 2 disease (Table 3). All the babies with Zone 1 ROP with Plus disease received Laser and Intravitreal Bevacizumab (IVB) treatment. All the babies with Zone 2 Stage 3 ROP received Laser treatment, and in addition 54% of them received IVB.

Nine babies who received treatment (8%) presented with Threshold ROP during the third week of their lives. Another 23 (22%) babies had threshold ROP during the 4th week of life (Table 2). Therefore, 32 babies (30.2% from all babies who had threshold disease) had their threshold ROP diagnosed and treatment initiated before the 28th day of life. This group of babies who developed Threshold ROP is recognised as "early presentation group" in this paper. The mean PMA of the early presentation group was 30.1 weeks (27-33) with a Standard deviation of 1.72. Out of these 32 babies 20 (62.5%) were born between a PMA of 27 to 30 weeks.

Table 2. Presentation of Threshold ROP according to the postnatal age

Post natal age	*Number of babies*	*%*
Day 14-20	9	8
Day 21-28	23	22
Day 29-34	31	29
Day 35+	43	41
Total	106	100

50% of the babies who had Zone 1 ROP with Plus disease, 31% of the babies who had Zone 2 Stage 3 ROP and 26% of the babies who had Zone 2 Stage 2 ROP belong to the early presentation group (Table 3).

Table 3. Management of threshold ROP according to the Stage

Diagnosis	*No. of Babies*	*Laser Treatment %*	*Intravitreal Bevacizumab Injection %*
Zone I ROP with Plus Disease	6	100	100
Zone II Stage 2 ROP with Plus Disease	46	100	33
Zone III Stage 3 ROP	54	100	54
Total	106		

Comparison of the mean PMA and the Birth Weight of the two groups is summarised in table 4. Application of the Student's t test revealed that there is no statistically significant difference between the maturity of the two groups ($p<0.05$).

Table 4. Characteristics of babies who develop Threshold ROP before 4 weeks of age (early presentation group) and babies who developed Threshold ROP after 4 weeks of age

Presentation <4/52 (Early Onset Group) n=32	*Mean*	*Range*	*Standard deviation*
POG (weeks)	29.9	27-33	1.621
Birth Weight (g)	1214	900-1900	255.65
Presentation >4/52 *n*=74	Mean	Range	Standard Deviation
POG (weeks)	28.8	25-33	1.82
Weight (g)	1164	700-1950	274.8

81% of the babies of early presentation group were from Base Hospitals and General Hospitals away from Colombo. In the group where Threshold ROP developed after 4 weeks of age only 32% from those outstation Hospitals. There was a highly significant statistical difference between the two groups in regards to the place of referral where early onset babies tend to be from Base and General Hospitals away from Colombo ($p<0.005$).

On a separate inquiry, the researchers found that none of these peripheral neonatal centers were manned by a consultant neonatologist. Furthermore, none of these premature baby units had the facility of delivering blended oxygen at the time of the study. In these neonatal centers cumulatively there was only one pulse oximeter for 4.5 babies whom receive oxygen.

Table 5 describes the timing of diagnosis of each individual case according to the new criteria (first visit at 2 weeks post natal) versus previous guidelines (first visit 4 weeks post natal or 31 weeks whichever occur later). Threshold ROP was diagnosed in these early presentation group at a mean 33.3 weeks PMA. According to the previous guidelines, the first visit would have been made at a 34.5 weeks PMA.

Table 5. All early presentation group cases. Advancement of diagnosing threshold ROP by screening for ROP early

Case Number	*Born at PMA weeks*	*Threshold ROP diagnosed PMA weeks*	*First screening according to the previous guidelines*	*Age at the time of diagnosis*
1	27	30	31	3
2	28	31	32	3
3	28	31	32	3
4	29	31	33	2

(Continued)

Case Number	*Born at PMA weeks*	*Threshold ROP diagnosed PMA weeks*	*First screening according to the previous guidelines*	*Age at the time of diagnosis*
5	29	32	33	3
6	29	32	33	3
7	29	32	33	3
8	29	32	33	3
9	29	32	33	3
10	29	32	33	3
11	30	32	34	2
12	30	33	34	3
13	30	33	34	3
14	30	33	34	3
15	30	33	34	3
16	30	33	34	3
17	30	33	34	3
18	30	33	34	3
19	30	33	34	3
20	30	33	34	3
21	31	34	35	3
22	32	34	36	2
23	32	35	36	3
24	32	35	36	3
25	32	35	36	3
26	32	35	36	3
27	33	35	37	2
28	33	35	37	2
29	33	36	37	3
30	33	36	37	3
31	33	36	37	3
32	33	36	37	3

Discussion

Screening for ROP is being carried out as a national policy in most of the countries, albeit the screening protocols slightly differ[1-9]. Most screening protocols would agree that the babies born before 26 weeks of PMA would be seen around a PMA of 30-31 weeks. The babies born at a PMA longer than 27 weeks would have their first ROP screening examination at 4 weeks of age. There was an observation in Sri Lanka that severe ROP was recognised with tractional retinal detachment when the babies seen at 4 weeks of age or 30-31 of PMA. Therefore, screening at the LRH and satellite clinics at DMH and CSWH was advanced to 2 weeks post natal irrespective of the PMA at birth. Soon, the referring centres also adapted this screening protocol.

Presence of severe ROP at such an early age has never been described in the literature. Those children who developed ROP early were from peripheral hospitals where the service of a consultant neonatologist is unavailable and the oxygen delivery and monitoring facilities are limited.

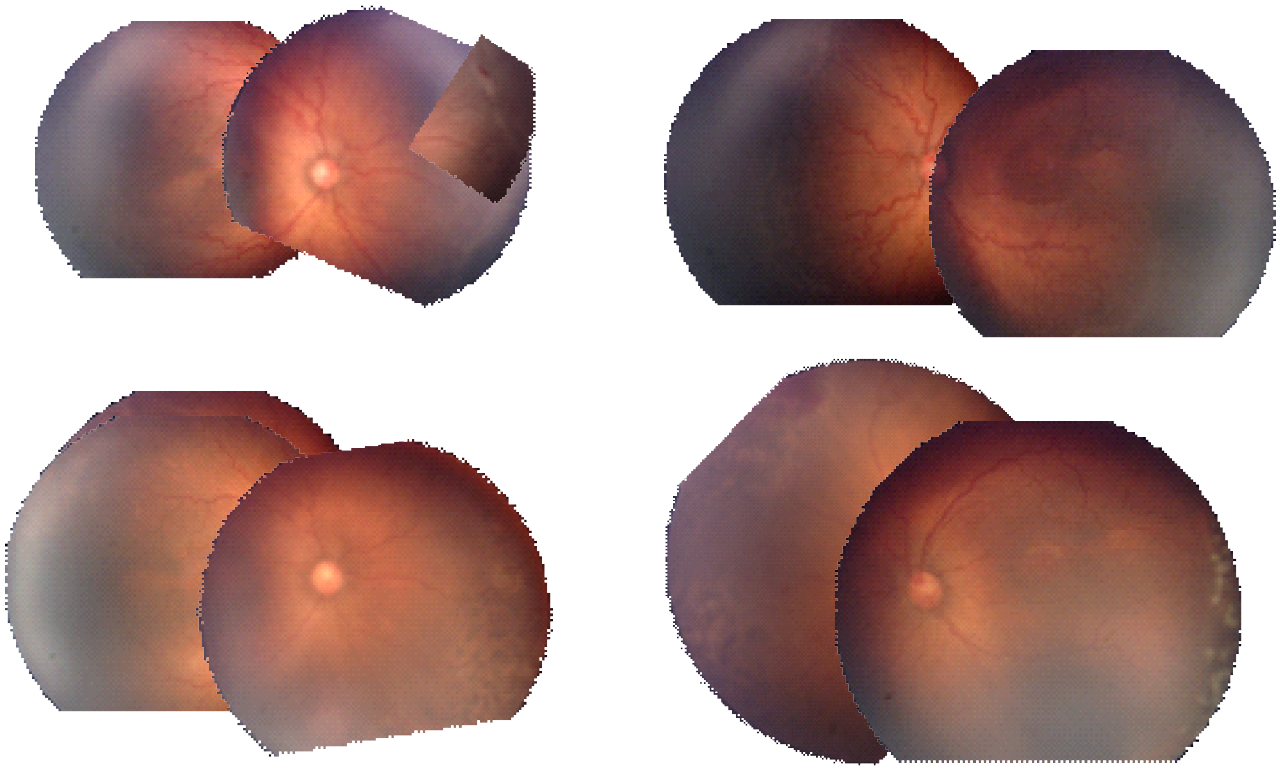
It was difficult to analyse all the risk factors for the development and progression of ROP due to the retrospective nature of the study.

Majority of the early presentation ROP babies were born at a PMA between 27 to 30 weeks and the only statistical difference between the early onset group from the rest of the babies who developed Threshold ROP was the place of referral.

If the babies seen at 30 weeks or 4 weeks post natal, these early onset group babies would be seen at a PMA of 34.5 weeks. Since the first screening was advanced to the 3rd week of life, the diagnosis of Threshold disease was made at a PMA of 33.3 weeks. Therefore, in these babies, the diagnosis of Threshold ROP was also advanced by 1.2 weeks.

Conclusion

Threshold ROP was present within the first four weeks of life in a significant proportion of ROP cases. These early onset ROP cases were mostly from Premature Baby Units away from Colombo. Vast majority of the babies in the early onset ROP group were born at a POA between 27 and 30 weeks. These babies developed threshold ROP within the first 2-4 weeks of life. Herein, we recommend carrying out first ROP screening in premature babies during the third week of their life to prevent these early onset babies going blind. Once the Premature Baby Units develop better oxygen delivery and monitoring facilities this guideline can be revised in few year's time.



Case No: 21 (Table 5) POG 31 weeks Birth Weight 1280g. Seen at 23rd day of life. Posterior Zone 2 Stage 3 with Plus disease. 532nm Green Laser and Intravitreal Bevacizumab injection done.

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