

ORIGINAL ARTICLE

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Criteria for the timing of the initial retinal examination to screen for retinopathy of prematurity

ABSTRACT

Objective

To determine the applicability of a modified criteria for initiating retinal examinations to screen for retinopathy of prematurity (ROP).

Methods

All ROP charts of babies who had initial retinal examination to screen for ROP from January 1, 2005 to December 31, 2008 at the neonatal-intensive-care nursery and eye center of a tertiary hospital were reviewed. Date of birth, sex, age of gestation (AOG), birth weight (BW), postnatal age (PNA), postconceptional age (PCA), and ROP classification were recorded. Descriptive statistics and Student's t-test were used to analyze the data.

Results

A total of 690 eyes of 345 babies, 174 males and 171 females, were included in the study. At the initial retinal exam, the mean AOG was 31.39 ± 2.46 weeks; BW, $1,268.77 \pm 317.12$ grams; PNA, 4.56 ± 2.95 weeks; and PCA, 35.94 ± 3.26 weeks. Immature retinas in both eyes were seen in 175 (50.72%) babies, while 113 (32.75%) had ROP of any stage in both eyes and 51 (14.78%) had immature retina in one eye and ROP of any stage in the other eye. Among the 113 babies with ROP, 33 (29.2%) were assessed to have pre-threshold ROP.

Conclusion

This study supported the applicability of the modified criteria which are in agreement with the Joint Statements of the American Academy of Pediatrics, American Academy of Ophthalmology and American Association of Pediatric Ophthalmology and Strabismus, and the United Kingdom Royal College of Pediatrics and Child Health for initiating retinal exams to screen for ROP.

Keywords: *Retinopathy of prematurity, Screening criteria, Initial retinal exam*

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IN BABIES at risk, performing a well-timed initial examination to screen for retinopathy of prematurity (ROP) can detect the onset of retinal changes before they become permanently destructive. As knowledge and experience increase, criteria have been recommended and adjusted for the initial, follow-up, and concluding retinal exams. Because neonatal care and ophthalmologic technology vary around the world, each center is encouraged to determine the applicability of screening criteria to their local settings.

The International Classification of Retinopathy of Prematurity study (ICROP)¹ recommended a method for classifying the stages, location, and extent of ROP. The classification made it possible for multicenter, large population studies and the establishment of guidelines for ROP screening.

The Multicenter Trial of Cryotherapy for ROP (CRYO-ROP Study)² used the ICROP classification and documented the benefit of retinal ablation in reducing the proportion of infants who progressed to retinal detachment. The criteria for babies at high risk for ROP had birth weights (BW) of <1,251 grams. The initial retinal exam was performed at postnatal age (PNA) 4 to 7 weeks. No data regarding age of gestation (AOG) were mentioned.

The Light Reduction in ROP (LIGHT-ROP) study³ evaluated the effects of ambient-light exposure on the incidence of ROP and found no significant difference between babies with and without goggles. This study included babies with AOG <31 weeks and BW <1,251 grams. Retinal examinations were initiated at PNA of 4 to 9 weeks.

Wright et al.⁴ proposed that the initial retinal exam be performed in babies who were born <32 weeks AOG, with a higher limit for BW at <1,500 grams in order not to miss ROP in the less severe stages.

In 2001, the American Academies of Pediatrics (AAP) and Ophthalmology (AAO) together with the Association of Pediatric Ophthalmology and Strabismus (AAPOS)⁵ jointly recommended that ROP screening be done for all babies born at AOG of <28 weeks and with birth weight of 1,501 grams, with the first retinal exam performed at PNA of 4 to 6 weeks or postconceptional age (PCA = PNA + AOG) of 31 to 33 weeks, whichever was later.

Gonzales et al. (Retinopathy of prematurity in the Philippine General Hospital; 2002; unpublished) reported preliminary data on the profile of ROP at the University of the Philippines–Philippine General Hospital. They used a combined criteria of BW <1,500 grams as recommended by the Joint Statement of AAP, AAO, AAPOS⁶ with an older AOG of <32 weeks as suggested by Wright and colleagues⁴ in order not to miss babies with earlier, less severe stages of ROP. Older and larger babies with unstable perinatal courses, assessed to be at risk by their

neonatologists, also underwent ROP screening. The initial retinal exam was performed at PNA of 4 to 6 weeks and PCA of 31 to 33 weeks.

This study assessed the applicability of the modified criteria used by Gonzales and colleagues to initiate retinal fundus examinations in babies at risk for ROP. It also described the estimated AOG, BW, PNA, and PCA used in the criteria, and the general fundus findings at the initial retinal examination.

METHODOLOGY

All ROP charts of babies admitted into the Department of Pediatrics Neonatal Intensive Care Unit (NICU), University of the Philippines–Philippine General Hospital (UP–PGH) from January 1, 2005 to December 31, 2008 were reviewed. Data collected included date of birth, sex, age of gestation (AOG), birth weight, postnatal age (PNA), postconceptional age, and ROP classification.

All babies were referred and cleared by their attending neonatologists for retinal examination to screen for ROP. Consent for the procedure was obtained from the parents or guardians, or in the case of abandoned babies from the pediatrics resident in-charge. Eyes were dilated with tropicamide 0.5% and phenylephrine 0.5% combination eye drops (Sanmyd, Santen, Osaka, Japan). Binocular indirect ophthalmoscopy was done with the aid of an eyelid speculum and scleral indenter suitable for neonatal use, with swaddle restriction and topical anesthesia (Proparacaine hydrochloride 0.5%, Alcaine, Alcon Laboratories Inc., Fort Worth, TX, USA). Examination was done by the medical-retina fellows of the Vitreoretina Service, Department of Ophthalmology and Visual Sciences of UP–PGH, corroborated by one faculty ophthalmologist. Classification and recording of ROP followed the guidelines set by the International Classification of ROP:

Table 1. Screening criteria used for initial retinal examination (N = 345).

Criteria	Mean	Range
Age of Gestation (weeks)	31.39 ± 2.46	21 to 41
Birth weight (grams)	1268.77 ± 317.12	500 to 2500
Postnatal Age (weeks)	4.56 ± 2.95	0 to 24
Postconceptional age (weeks)	35.93 ± 3.26	28 to 51.86

Table 2. General retinal findings in babies at initial retinal examination.

Retinal Findings	Number of Babies	Percent
IR: OU ¹	175	50.72
ROP: OU ²	113	32.75
IR/ROP OD/OS ³	51	14.78
Mature: OU	5	1.45
Mature/ROP OD/OS	1	0.28

¹Immature retina, both eyes

²Retinopathy of prematurity, both eyes

³Immature retina one eye, ROP other eye

Table 3. Criteria used to initiate retinal exams in babies with immature retina or retinopathy of prematurity of any stage in both eyes.

Criteria N = 339 ² /345 (98%)	OU:IR N = 175 51%	OU:ROP any stage N = 113 33%	OD/OS:IR/ROP ¹ N = 51 15%
<i>Age of gestation (weeks)</i>			
Mean	31.62 ± 2.33	30.85 ± 2.40	31.51 ± 2.31
Range	21 to 38.57	24 to 38	26 to 36
<i>Birth weight (grams)</i>			
Mean	1325.08 ± 313.31	1,192.30 ± 301.50	1,231.37 ± 319.68
Range	650 to 2500	550 to 2,300	500 to 1,950
<i>Postnatal age (weeks)</i>			
Mean	3.88 ± 2.04	5.98 ± 3.68	3.59 ± 2.42
Range	0 to 12.71	0 to 24	0 to 10
<i>Postconceptional age (weeks)</i>			
Mean	35.53 ± 2.81	36.74 ± 3.67	35.11 ± 3.25
Range	28 to 453	28 to 51.86	29 to 42

¹ IR/ROP: Immature retina in one eye and ROP of any stage in the other eye

² Five babies with mature vessels in both eyes and 1 baby with mature retina in one eye and ROP of any stage in the other eye were not included.

Table 4. Comparison of criteria in babies with IR or ROP of any stage in both eyes (N = 288).

Criteria	OU:IR ¹ N = 175 (60.76%)	OU:ROP N = 113 (39.23%)	Mean Difference	p ²
Mean age of gestation (weeks)	31.62 ± 2.33	30.85 ± 2.40	0.77	0.007 ³
Mean birth weight (grams)	1325.08 ± 313.31	1192.30 ± 304.50	132.70	0.004 ³
Mean postnatal age (weeks)	3.88 ± 2.04	5.98 ± 3.68	2.10	0.0001 ³
Mean postconceptional age (weeks)	35.53 ± 2.81	36.74 ± 3.67	1.20	0.001 ³

¹Babies with IR in one eye and ROP in the other were not included

²Student's t-test of significance

³Significant

Table 5. Criteria and test of significance in babies with ROP in both eyes.

Criteria	Before Pre-threshold (No Need LIO) N = 80 (71%)	Pre-threshold (May Need LIO) N = 33 (29%)	Mean Difference	p
<i>Age of gestation (weeks)</i>				
Mean	30.92 ± 2.39	30.68 ± 2.46	0.24	0.63 ²
Range	24.71 to 38	24 to 35		
<i>Birth weight (grams)</i>				
Mean	1,225.70 ± 303.85	1,112.36 ± 295.36	113.33	0.07 ²
Range	600 to 2,300	550 to 1,700		
<i>Postnatal age (weeks)</i>				
Mean	5.71 ± 3.86	6.64 ± 3.52	0.92	0.23 ²
Range	0 to 24	0 to 14.4		
<i>Postconceptional age (weeks)</i>				
Mean	36.49 ± 3.86	37.33 ± 3.13	0.83	0.27 ²
Range	28 to 51.86	29 to 44		

¹ LIO: Laser indirect ophthalmoscopy

² Student's t-test of significance; not significant

ICROP, ICROP: Revisited⁷ and by the Early Treatment of ROP study (ETROP).⁸ All examinations were performed at the Neonatal Intensive Care Unit (NICU) with the NICU or pediatrics staff in proximity.

Descriptive statistics and Student's t test were used to analyze the data.

RESULTS

The ROP charts of 458 babies were reviewed, of which 345 (690 eyes) were included. There were 174 (50.4%) males and 171 (49.6%) females. A total of 113 ROP charts (24.6%) were excluded due to early demise of the infant, inability to obtain consent from the parents or guardians, absence of neonatal clearance for retinal exam, or incomplete data.

The mean AOG at the initial retinal examination was 31.39 weeks. The mean BW was 1,268.77 grams (Table 1). Babies underwent initial retinal exam at a mean PNA of 4.56 weeks and an average PCA of 35.93 weeks.

Of the 345 babies, 175 (50.7%) had immature retinas (IR) in both eyes, 113 (32.8%) had ROP of any stage, and 51 (14.8%) had IR in one eye and ROP of any stage in the other (Table 2). Five (1.4%) babies had mature retinas in both eyes and 1 (0.3%) had ROP in one eye and a mature retina in the other eye.

The babies with IR in both eyes at initial screening had mean AOG of 31.62 weeks, BW of 1,325.08 grams, PNA of 3.88, and PCA of 35.53 weeks (Table 3). The babies with ROP of any stage in both eyes had mean AOG of 30.85 weeks, BW of 1,192.30 grams, PNA of 5.98 weeks, and PCA of 36.74 weeks. Those with IR in one eye and ROP of any stage in the fellow eye had mean AOG of 31.51 weeks, BW of 1231.37 grams, PNA of 3.59 weeks, and PCA of 35.11 weeks.

There were significant differences in the mean differences of AOG, BW, PNA, and PCA of babies who had IR

Table 6. Studies and joint statements recommending criteria for initiating retinal exams in babies at risk for retinopathy of prematurity.

Guidelines/ Studies	Year Published	Recommendation/Criteria Used in Study				Comments
		AOG (Weeks)	BW (Grams)	PNA (Weeks)	PCA (Weeks)	
CRYO-ROP Study	1988 ²	< 32	< 1,251	4 to 7	No data	Upon discharge ^a
AAP, ACOG ^b	1992 ¹³	< 30 < 35	< 1,300 < 1,800	No data	No data	No O ₂ With O ₂
AAP, AAO, AAPOS ^c	1997 ¹⁴	≤ 28	< 1,500	4 to 6	31 to 33	>1,500 grams with unstable course
Hutchinson	1998 ⁹	< 32	≤ 1,500	7 (Whichever is first)	34	Not before PNA=5 weeks
K. Wright	1998 ⁴	≤ 32	< 1,500	5 to 7 (Whichever is first)	34	Upon discharge
LIGHT-ROP Study	1998 ³	< 31	< 1,251	4 to 9	No data	
AAP, AAO, AAPOS	2001 ⁵	≤ 28	< 1,500	4 to 6 (Whichever is later)	31 to 33	1,500 to 2,000 grams in babies with unstable course
J. Gonzalez: UP-PGH (unpublished)	2001 ²	< 32	< 1,500	4 to 6	31 to 33	>1,500 grams with unstable course
Reynolds	2002 ¹⁰	< 31 Light-ROP	< 1,251 Cryo-ROP	No data	No data	
ETROP	2003 ⁸	< 30	< 1,251	6	No data	
AAP, AAO, AAPOS	2006 ⁶	≤ 32	< 1,500	4	31 if AOG < 27	>32 weeks, 1,500 to 2,000 grams with unstable course
UKRCPCH	2008 ¹²	< 32	< 1,501	4 - 5	30 if AOG < 27	
This study	2010	Mean = 31.39	Mean = 1,269	Mean = 4.56		

^aDo retina exam upon discharge

^bAmerican Academy of Pediatrics, American College of Obstetricians and Gynecologists

^cAmerican Academy of Pediatrics, American Academy of Ophthalmology, American Association of Pediatric Ophthalmology and Strabismus

and those with ROP of any stage in both eyes (Table 4).

Among the 113 babies who were found to have ROP, 80 (71%) were assessed to be at the earlier (before pre-threshold) stages of ROP, not in any imminent need of retinal ablation, and 33 (29%) were classified to have pre-threshold ROP which may need laser indirect ophthalmoscopy (LIO) at a future time (Table 5). The babies assessed to be at the earlier stages of ROP had a mean AOG of 30.92, BW of 1,225.70, PNA of 5.71, PCA of 36.49. Those determined to have pre-threshold ROP had mean AOG of 30.68 weeks, BW of 1,112.36 grams, PNA of 6.64 weeks, and PCA of 37.33 weeks. There was no statistically significant difference between the means of AOG, BW, PNA, and PCA of these two groups ($p > 0.05$).

DISCUSSION

The screening criteria used in this study (Table 1) suggested that retinal exams to screen for ROP should be initiated for all babies born at AOG < 31.39 weeks and BW < 1,268.77 grams, as well as for older and larger babies at risk for ROP. At a mean PNA of 4.56 weeks and mean PCA of 35.93 weeks, 50% of the babies were assessed with IR (51%) or mature retinas (1%) in both eyes and a third with ROP (33%) of any stage (Table 2).

As in other studies,^{2,3,7} this study found more babies to

have ROP of any stage at lower AOG and BW (Tables 3 and 4). The mean PNA (5.98 weeks) and mean PCA (36.74 weeks) at initial examination were significantly higher ($p < 0.05$) in babies found to have ROP in both eyes compared to those with IR (Table 4). This suggested that conducting the initial retinal exam at a mean PNA of 3.88 weeks would allow monitoring of fundus changes starting at IR.

There were no significant differences ($p > 0.05$) between the criteria for babies who were assessed to be in no imminent need for LIO and those with pre-threshold ROP who may need LIO (Table 5). This implied that AOG, BW, PNA, and PCA alone were not sufficient to predict the onset of ROP fundus changes that may need LIO at a future time. The data suggested that the initial retinal exam should be conducted at PNA earlier than 6.64 weeks or at PCA less than 37.33 weeks to catch the earlier stages of ROP. This finding was in agreement with those of Hutchinson and associates⁹ who cautioned against performing the initial retina exam at PCA of 35 weeks, noting that by this time there could be a few babies in the threshold disease missed by as long as 1 week.

Reynolds and colleagues¹⁰ reported on evidence-based screening criteria for ROP using the data from the CRYO-ROP and LIGHT-ROP studies. He noted a “time window”

for the development of serious ROP at PCA range of 30.9 to 46.3 weeks and PNA range of 4.7 to 18.7 weeks. Our study found a PCA range of 29 to 44 weeks and PNA of 0 to 14.4 weeks in babies with pre-threshold “time window” through which the beginning of serious ROP could be detected.

Table 6 presented a tabulation of the criteria recommended as guidelines for screening babies at risk for ROP and the means of this study. The changes through the years were evident. The data suggested that the mean AOG and BW of this study were within the criteria recommended by Gonzales et al. (2001: unpublished data) and those recommended by the joint statements of the AAO, AAP, Aapos (2006)⁶ and the UKRCPCH (2008).¹² The PNA range of 3.88 to 5.71 weeks between babies found to have IR (Table 4) and babies who were assessed to be in the earlier stages of ROP (Table 5) implied that the initial retina exam should be done between PNA of 4 to 6 weeks in order to intercept ROP at a time before laser treatment was needed or before more serious ROP was present.

In summary, the means of this study were within the criteria used by Gonzales et al. which were in agreement with the joint statements of the AAP, AAP, Aapos (2006)⁶ as well as with UKRCPCH (2008).¹² Thus, babies born with AOG <32 weeks and birth weight <1,500 grams or babies born >32 weeks or >1,500 grams with “stormy” perinatal courses^{6,12} would need initial retinal exams by PNA of 4 weeks.

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