Articles

Retinopathy of prematurity at a University Hospital in Riyadh, Saudi Arabia

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ABSTRACT

Objectives: To prospectively study the incidence and nature of retinopathy of prematurity (ROP) at a University Hospital in Riyadh, Kingdom of Saudi Arabia.

Methods: This study was carried out the Neonatal Intensive Care Unit of King Khalid University Hospital in Riyadh, Kingdom of Saudi Arabia. One hundred and ninety-five consecutive preterm infants with a birth weight of 2000 g or less were screened for ROP. The first examination was performed at 4-7 weeks of postnatal age.

Results: Mean gestational age of all premature infants was 28.4 ± 2.4 weeks (range 22-34), mean birth weight was 1103 ± 302 g (range 520-1960), and mean duration of oxygen therapy was 24.0 ± 32.2 days (range 0-210). Seventy-three children developed acute ROP, giving an overall incidence of 37.4%. The incidence in preterms with birth weight of ≤1500 g and ≤1250 g was 41% and 50.7%. No infants with a birth weight of ≥1500 g developed ROP. Nineteen of the 73 children with ROP (26% or 9.7% of all infants studied) reached threshold ROP, and needed laser treatment or cryotherapy which induced regression in all of patients.

Conclusions: Incidence of ROP in our patients in comparable to other reports. Screening for ROP should be carried out for all preterms of ≤1500 g birth weight. Such screening programs will identify those requiring retinal ablative surgery in order to induce regression of the acute ROP and prevent cicatrizing sequelae with subsequent traction retinal detachment and blindness.

Saudi Med J 2003; Vol. 24 (7): 720-724

Retinopathy of prematurity (ROP), nowadays, is considered to be one of the major causes of childhood blindness.[1] During the past 2 decades, the survival rate of extreme premature infants as well as the frequency of ROP has increased.[2,3] Many reports have been published on the incidence and severity of ROP.[2-12] However, the incidence of ROP in Kingdom of Saudi Arabia (KSA) is not known. We undertook a prospective study to investigate the incidence and nature of ROP among premature infants in the Neonatal Intensive Care Unit of the King Khaled University Hospital (KKUH), Riyadh, KSA.

Methods. A retina specialist (SAA) from January 1995 through to July 1998 examined 195 consecutive preterm infants born at KKUH. Infants with gestational age of ≤34 weeks or birth weight of ≤2000 g were included. The awake premature infants were initially examined in the Neonatal Intensive Care Unit (NICU) at postnatal age of 4-7 weeks. Eyes were dilated with 2.5% phenylephrine and 1% tropicamide eye drops 1-2 hours before examination. Topical anesthesia with 0.4% Benoxinate eye drops was used before inserting the premature eyelid speculum. Examination of the anterior segment was performed looking for remnant of anterior or posterior vasculosa lentis, vitreous haze, and engorged iris vessels. This was followed by indirect ophthalmoscopy with 28 diopter lens and scleral depressor/rotator. The latter was used for ocular rotation rather than indentation that facilitated visualization of

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Received 8th May 2002. Accepted for publication in final form 23rd November 2002.

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the peripheral retina over its entire circumference. All care was taken to examine the posterior retinal vessels before any pressure was put on the globe, as that might deflate any engorged blood vessels and gives false impression of absent plus disease. All pertinent information, including birth weight, gestational age, pre and postnatal medications, oxygen supplementation, and concomitant diseases were recorded. Presence, extension and staging of ROP was documented using the international classification for ROP.[13] Infants without ROP were examined monthly until complete retinal vascularization took place. Infants with Stage one or 2 ROP were re-examined every 2 weeks while those with pre-threshold ROP were re-examined weekly, until resolution or progression to a more advanced stage. Infants with Stage 3 plus (threshold) disease were managed by retinal ablation surgery then followed till regression was complete with no other complications, such as cataract, macular dragging, or retinal detachment. Cryotherapy was used early in the study and later replaced by laser treatment through indirect ophthalmoscope delivery system. The aim of treatment is to ablate the avascular retina anterior to the ridge. Statistical significance was determined using Student's t-test, chi-square, and logistic regression analysis methods; $p < 0.05$ was considered significant.

Results. One hundred and ninety-five consecutive preterm infants were enrolled in the study. There were 106 (54.4%) girls and 89 (45.6%) boys. The distribution of infants among different gestational age and birth weight categories is shown in **Tables 1 and 2**. The mean birth weight ± SD was 1103 g ± 302 (range, 520 - 1960 g), and the mean gestational age ± SD was 28.4 ± 2.4 weeks (range, 22-34 weeks). Retinopathy of prematurity is the 2nd most common disease affecting our preterm infants, with lung diseases being the first. The overall incidence of ROP was 37.4% (73/195). However, the incidence was 41% (73/178) and 50.7% (71/140) in babies with birth weight ≤1500 g and ≤1250 g. No infants with birth weight of >1500 g developed ROP. Incidence of ROP decreases significantly with increasing birth weight and gestational age ($p<0.001$) **Table 1**. Retinopathy of prematurity developed in 72 of 189 infants with gestational age ≤32 weeks (38.1%), with odds ratio of 3.08 and 95% confidence interval (C.I.) 0.33-147.5. The mean birth weight and gestational age were significantly lower, whereas duration of oxygen therapy was significantly longer in infants who developed ROP compared to those who did not **Table 3**. This association is more prominent for those infants who had laser treatment (which is the group with worse ROP stage), **Table 4**. Both duration of mechanical ventilation and oxygen therapy were significantly related to birth weight ($P<0.001$), **Table 5**. The duration tended to be inversely related to birth weight, which is babies with very low birth weight (<750g) having the longest duration and average duration declined as birth weight increased.

Table 1 - Birth weight distribution of the study population.

Birth Weight (gm)	Retinopathy of prematurity		Total (n=195)	
	Yes (N=73)	No (N=122)		
≤750	23 (95.8)	1	**24**	**(12.3)**
751-1000	37 (68.5)	17	**54**	**(27.7)**
1001 - 1250	11 (17.7)	51	**62**	**(31.8)**
1251 - 1500	2 (5.3)	36	**38**	**(19.5)**
1501 - 2000	0	17	**17**	**(8.7)**
Overall	**73 (37.4)**	**122**	**195**	**(100)**

Table 2 - Gestational age distribution of the study population.

Gestational Age (weeks)	Retinopathy of prematurity		Total (n=195)	
	Yes (N=73)	No (N=122)		
22-23	4 (100)	0	**4**	**(2)**
24-25	13 (92.9)	1	**14**	**(7.2)**
26-27	29 (61.7)	18	**47**	**(24.1)**
28-29	21 (30)	49	**70**	**(35.9)**
30-32	5 (9.3)	49	**54**	**(27.7)**
33-34	1 (16.7)	5	**6**	**(3.1)**
Overall	**73 (37.4)**	**122**	**195**	**(100)**

Table 3 - Comparison of birth weight, gestational age, and duration of oxygen therapy between preterm infants with and without retinopathy of prematurity.

Variables		Retinopathy of prematurity		
		Yes	No	p value
Birthweight (g)	Range Mean ± SD (n)	520-1340 856.5 ± 177.3 (73)	720-1960 1250.4 ± 264.1 (122)	p<0.001
Gestational age (wks)	Range Mean ± SD (n)	22-33 26.8 ± 2.2 (73)	25-34 29.4 ± 1.9 (122)	p<0.001
Oxygen therapy (days)	Range Mean ± SD (n)	1-200 44.0 ± 37.9 (73)	0-180 11.9 ± 20.5 (122)	p<0.001

Table 4 - Comparison of birth weight, gestational age, and duration of oxygen therapy between preterm infants who received laser treatment and those who did not. Note that the latter group includes some patients with retinopathy of prematurity who did not need laser treatment.

Variables		Laser treatment		
		Yes	No	p value
Birthweight (g)	Range Mean ± SD (n)	520-1130 787.4 ± 166.7 (19)	580-1960 1137.0 ± 294.3(176)	p<0.001
Gestational age (wks)	Range Mean ± SD (n)	22-33 26.0 ± 2.7 (10)	23-34 28.7 ± 2.2 (176)	p<0.001
Oxygen (days)	Range Mean ± SD (n)	6-240 66.7 ± 59.0 (19)	0-180 19.3 ± 24.0 (176)	p<0.001

Table 5 - Relationship of duration of mechanical ventilation and oxygen therapy with birth weight (n=195).

Birth Weight (g)	Mechanical ventilation (days) Mean ± SD (n)	Oxygen therapy (days) Mean ± SD (n)
<750	57.6 ± 29.8 (24)	63.0 ± 39.9 (24)
751-1000	30.0 ± 21.2 (54)	31.1 ± 33.0 (54)
1001-1250	13.8 ± 14.8 (62)	12.6 ± 13.4 (62)
1251 - 1500	8.8 ± 9.5 (38)	13.3 ± 30.2 (38)
1501 - 2000	4.4 ± 4.9 (17)	3.0 ± 3.1 (17)
Overall	**22 days (range 0-154)**	**24 days (range 0-210)**

Table 6 - Distribution of retinopathy of prematurity cases among different stages.

Stage	n	(%)
1	17	(23.3)
2	20	(27.4)
3 (early	17	(23.3)
3 (threshold)	19	(26)
Total	**73**	**(100)**

The incidence of different stages of ROP is shown on **Table 6**. The incidence of severe ROP (Stage 3 or more) was 49.3% (36/73) in infants with ROP (or 18.5% of the total study population). However, 26% (19/73) of infants with ROP (or 9.7% of the total study population) reached an advanced stage (threshold disease) that needed cryotherapy or laser treatment to induce regression. Five infants received cryotherapy, whereas 14 infants were treated with laser after binocular indirect ophthalmoscope laser became available. This ablative treatment was carried out at a mean postnatal age of 12.5 weeks (87.1 days) (range 8.6-16.3 weeks), which induces regression of the disease in all patients. Spontaneous regression took place in all infants with early stages of ROP (Stages 1, 2, and early 3). The disease was bilateral in all infants with ROP. Both eyes were at the same stage of disease involvement in 93.6% of infants with ROP. In 98.3% of infants with ROP, both eyes had the same zone affected. The incidence of ROP was slightly higher in female infants compared to males (39.6% and 34.8%), but the difference was not statistically significant (P=0.5892).

Discussion. The reported incidence of ROP in the population of infants at risk (≤1500 g birth weight) ranges from 16-56%.[4-12] It was estimated that approximately 546 babies were blinded by ROP in one year in the United States of America.[2] The incidence of ROP in infants of ≤1500 g birth weight in our study is 41%. Our incidence is on the higher side of the reported incidence range. Possible explanations for this include our rigorous examination protocol with the use of speculum and scleral depressor/rotator, earlier screening, and that 40% of our study population are ≤1000 g birth weight who are known to have higher incidence of ROP. Another possible explanation is based on population differences on ethnic and socio-economic grounds, as it has been shown that blacks have a less risk of developing ROP,[14] and that ROP incidence is more in inner-city hospital where patients are of low socio-economic status.[15] However, in our study 54 of 73 infants (74%) with ROP only had mild to moderate disease which regressed spontaneously.

Since there is an effective treatment for threshold ROP with cryotherapy[16-18] and more recently with laser[19,20] attention should be paid to ophthalmic screening in all NICU. Timing of the first examination is important as there is a narrow window of opportunity to deliver a timely treatment which is after developing threshold disease and before progression to retinal detachment and other blinding complications. In designing a general screening program for a particular population one should take into consideration the specifics and the behavior of the disease in that particular population, and should not base recommendations on a single study. In a clinical (not research) setting, one fundus examination should be enough to confirm or rule out the presence of ROP in

most infants.[21] Research oriented trials suggest an earlier screening for example at 4-6 postnatal weeks suggested by cryotherapy-ROP group,[16] whereas clinical studies usually recommend a later age for screening for example 7-9 and 8-10 postnatal weeks recommended by Palmer[22] and Flynn.[23] In our study the youngest age at which laser treatment was needed for threshold disease was 8.6 postnatal weeks. We recommend, based on the results of our study, to perform the first dilated fundus examination by an experienced ophthalmologist at 6-8 weeks of postnatal life (or 32-35 weeks postconceptual age). Earlier examinations will be stressful to the infant and insufficient by themselves since the mean age of onset of ROP has been shown to be 7.9 (range 3-16) postnatal weeks or 36 weeks (range 31-43) postconceptual age.[14, 24]

No infants in our study with a birth weight of >1500 g developed ROP, however, our 2 infants with birth weight >1250 g and <1500 g developed only Stage one ROP, which regressed spontaneously. All those infants who needed laser treatment (have reached threshold disease) are of ≤1250 g. while their gestational age ranges between 22 and 33 weeks. Therefore it is safe to suggest to screen only infants of ≤1500 g in our population. One infant with gestational age of 33 weeks developed threshold ROP, which regressed after laser therapy. His birth weight is 1025 g and had 52 days of oxygen supplementation with multiple medical problems that included respiratory distress syndrome, intraventricular hemorrhage, patent ductus arteriosus, necrotizing enterocolitis, meningitis, and candida albican septicemia. This particular patient illustrates the importance of small birth weight, longer duration of oxygen supplementation, and the presence of concomitant medical problems in the development of threshold ROP even when gestational age is more than 32 weeks.

We used birth weight rather than gestational age, and postnatal rather than postconceptual age in recommending whom and when to screen as birth weight reflects the health of the infant more than gestational age, and in our area gestational age may not be accurate as ultrasonography is not performed routinely at the early stages of pregnancy especially in rural areas of KSA. In addition, determination of birth weight is simple and does not require sophisticated equipment. Moreover, nurses at NICU routinely use postnatal, not post-conceptual, age to calculate infant age. Ideally one should follow preterm infants till normal retinal vessels reach the ora serrata, at which stage the infant is immune to ROP. However, practically, if avascularity or even stage one or 2 ROP is present only in zone 3 with complete vascularization of the nasal retina, the infant will not develop advanced ROP and its complications. In general, retinal vascularization can be considered virtually complete as soon as normal retinal vessels have developed on the nasal side to within one disc diameter of the ora serrata.[25] Therefore, from a practical point of view, if the temporal ora serrata and the ends of the developing retinal vessels look normal, and can be seen in one view of the condensing lens of the indirect ophthalmoscope, it is considered safe to stop following the infant for the sake of acute ROP. Nevertheless, preterm infants need to be followed and checked for strabismus, myopia, amblyopia, and other ocular changes that are more common in these premature infants.

In conclusion, in KSA, ROP is one of the major diseases that affect premature infants and could lead to bilateral blindness. Screening programs for ROP should be implemented in every NICU in the KSA. Screening should be carried out by an experienced ophthalmologist and offered to all premature infants with birth weight of ≤1500 g or gestational age of ≤33 weeks to insure early detection and timely treatment of threshold ROP to prevent its blinding sequalae. Another way of screening, especially in the peripheral NICUs where experienced ophthalmologists are lacking, is to use telemedicine. This is accomplished by taking Wide-angle fundus photos by the nursing staff with the use of a wide angle digital retinal imaging camera which can be sent to a reading center instantaneously via e-mail. Any patient found to have threshold disease is then referred for ablative surgery.

Acknowledgment. The authors would like to thank Mr. Dustan Kangave for his statistical analysis; Mrs. Beverly Elliot for editorial comments, and Ms. Connie Unisa-Marfil for typing the manuscript.

References

1. McNamara JA, Moreno R, Tasman WS. Retinopathy of prematurity. In: Tasman W, Jaeger EA, editors. Duane's Clinical Ophthalmology. Vol. 3, Chap. 10. Philadelphia (PA): Lippincott-Raven; 1996.
2. Phelps DL. Retinopathy of prematurity: an estimate of vision loss in the United States - 1979. ***Pediatrics*** 1981; 67: 924-926.
3. Valentine PH, Jackson JC, Kalina RE, Woodrum DE. Increased survival of low birth weight infants: Impact on the incidence of ROP. ***Pediatrics*** 1989; 84: 442-445.
4. Kingham JD. Acute retrolental fibroplasia. ***Arch Ophthalmol*** 1977; 95: 39-47.
5. Kalina RE, Karr DJ. Retrolental fibroplasia: experience over two decades in one institution. ***Ophthalmology*** 1982; 89: 91-95.
6. Keith CG, Kitchen WH. Ocular morbidity in infants of very low birth weight. ***Br J Ophthalmol*** 1983; 67: 302-305.
7. Tasman W. The natural history of active retinopathy of prematurity. ***Ophthalmology*** 1984; 91:1499-1503.
8. Reisner SH, Amir J, Shohat M, Krickler R, Nissenkorn I, Ben Sira I. Retinopathy of prematurity: incidence and treatment. ***Arch Dis Child*** 1985; 60: 698-701.
9. Flynn JT, Bancalari E, Bachyansky BN, Buckley EB, Bawol R, Goldberg R. Retinopathy of prematurity. Diagnosis, severity and natural history. ***Ophthalmology*** 1987; 94: 620-629.
10. Schulenberg WE, Prendville A, Ohri R. Natural history of retinopathy of prematurity. ***Br J Ophthalmol*** 1987; 71: 837-843.
11. Nissenkorn I, Ben Sira I, Kremer I, Gaton DD, Krickler R, Wielunsky E. Even years' experience with retinopathy of prematurity: visual results and contribution of cryoablation. ***Br J Ophthalmol*** 1991; 75: 158-159.
12. Palmer EA, Flynn JT, Hardy RJ, Phelps DL, Phillips CL, Schaffer DB. Incidence and early course of retinopathy of

prematurity. ***Ophthalmology*** 1991; 98: 1628-1640.
13. The Committee for the classification of Retinopathy of prematurity. An international classification of retinopathy of prematurity. ***Arch Ophthalmol*** 1984; 102: 1130-1134.
14. Schaffer DB, Palmer EA, Plotsky DF, Metz HS, Flynn JT, Tung B et al. Prognostic factors in the natural course of retinopathy of prematurity. ***Ophthalmology*** 1993; 100: 230-237.
15. Lim J, Fong DS, Dong Y. Decreased prevalence of ROP in an inner-city hospital. ***Ophthalmic Surg Lasers*** 1999; 30: 12-16.
16. Cryotherapy for Retinopathy of Prematurity Cooperative Group. Multicenter trial of cryotherapy for retinopathy of prematurity: Preliminary results. ***Arch Ophthalmol*** 1988; 106: 471-479.
17. Cryotherapy for Retinopathy of Prematurity Cooperative Group. Multicenter trial of cryotherapy for retinopathy of prematurity: three-month outcome. ***Arch Ophthalmol*** 1990; 108: 195-204.
18. Cryotherapy for Retinopathy of Prematurity Cooperative Group. Multicenter trial of cryotherapy for retinopathy of prematurity: one year outcome. ***Arch Ophthalmol*** 1990; 108: 1408-1416.
19. Laser-ROP Study Group: Laser therapy for retinopathy of prematurity. ***Arch Ophthamol*** 1994; 112: 154-156.
20. Al-Amro SA, Ahmed AM, Abu El-Asrar A. Laser photocoagulation for threshold retinopathy of prematurity. ***Saudi Journal of Ophthalmology***1998; 12: 12-15.
21. Anon. Retinopathy of prematurity screening study. ***Bulletin of College of Ophthalmologists*** (Autumn) 1990.
22. Palmer EA. Optimal timing of examination for acute retrolental fibroplasia. ***Ophthalmology*** 1981; 88: 662-666.
23. Flynn JT. Optimal timing of examination for acute retrolental fibroplasia [discussion]. ***Ophthalmology*** 1981; 88: 667-668.
24. Holmström G, El Azazi M, Jacobson L, Lennerstraud G. A population based, prospective study of the development of retinopathy of prematurity in prematurely born children in the Stockholm area of Sweden. ***Br J Ophthalmol*** 1993; 77: 417-423.
25. Palmer EA. Current management of retinopathy of prematurity. In: American Academy of Ophthalmology. Focal points 1993; Vol. 11. Chap. 3.

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Title: Laser Photocoagulation for Threshold Retinopathy of Prematurity
Source: Saudi Journal of Ophthalmology 1998; 1: 12-14

Abstract

To report the clinical outcome of threshold retinopathy of prematurity (ROP) treated with laser photocoagulation. Forty-five eyes from 24 infants with threshold ROP (the 3 remaining eyes were not threshold eyes) underwent laser photocoagulation. The follow up period ranged from 2 to 14 months (average 6 months). All eyes showed regression of the disease. One eye developed mild. temporal dragging of the macula. One patients' eyes had peripheral lens burns resulting in stationary peripheral lens opacities. Laser treatment for threshold ROP is successful and effective in causing regression of the disease.