Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublisher.com/sjams/

OPEN ACCESS

Pediatrics

Prospective Clinical Study on Incidence, Risk Factors and Management of Retinopathy of Prematurity in Preterm Babies Admitted in NICU, GGH, Kakinada

N Madhavi[1], V V Vijayalakshmi[2*], P Shanthi Priya[3], M N V Poushya SAI[4], D Manikyamba[5], A Krishna Prasad[6], P S S Aparna[7]

[1]Professor, [2]Assistant Professor, [3,4]Post Graduate, [5]Professor And Head of The Department, [6]Professor, [7]Undergraduate, Department of Pediatrics, Government General Hospital, Rangaraya Medical College, Kakinada
From Neonatal Intensive Care Unit, Department of Pediatrics, Government General Hospital, Kakinada 533001, India

DOI: 10.36347/sjams.2020.v08i01.037 | **Received:** 10.01.2020 | **Accepted:** 17.01.2020 | **Published:** 23.01.2020

***Corresponding author:** V V Vijayalakshmi

Abstract **Original Research Article**

This study was done to study the incidence, risk factors, severity and interventions done for ROP in preterm babies. This was a Hospital based prospective study done in Neonatal intensive care unit for a period of 18 months. Inclusion criteria, exclusion criteria and timing of screening were taken according to NNF guidelines. ROP screening was done using RETCAM and timely intervention was done whenever needed with laser and/or intravitreal bevacizumab. Out of 576 screened preterm babies, 124 (21.4%) had ROP and among them 64 (51%) babies had type1 ROP, 48 (38%) had type2, 12(9.6%) had Aggressive posterior ROP. ROP incidence was higher in babies with birth weight <1000gms (75%), 1001-1250gms (63%),1250-1500gms (35%) with mean weight being 1310gms. 90% of babies with ROP were of < 34 weeks of gestation with mean GA of 31weeks. Most common risk factors identified on univariate analysis apart from birth weight and gestational age were oxygen therapy, CPAP, RDS, sepsis, duration of stay, apnea and hyperbilirubinemia (with p values < 0.0001). Multivariate analysis showed oxygen therapy, CPAP, RDS, sepsis and hyperbilirubinemia were significantly associated with ROP. Among 29 babies with blood transfusion, 44. 8 % had ROP and of which 77% had severe ROP (type 1 ROP or APROP). Laser treatment was given for 43 (56.6%) babies and intravitreal bevacizumab for 28 (36.8%) babies and 5(6.6%) babies received both. This study identified increased incidence of APROP. Severe ROP higher among babies who received blood transfusion.

Keywords: retinopathy of prematurity, special new born care unit, national neonatal forum, aggressive posterior ROP, vascularized retina.

INTRODUCTION

Retinopathy of prematurity (ROP) is a vasoproliferative disorder that affects the developing retinal vessels of premature infants. Premature retina exposed to high oxygen concentration, followed by abrupt withdrawal, easily undergoes uncontrolled vascular proliferation, fibrosis and eventually results in retinal detachment. In 1942, Terry [1] first described retrolental fibroplasia with implication of oxygen therapy as the causative agent [2, 3].

The aim of the present study was to identify the incidence, risk factors and severity of ROP in at risk preterm babies and refer them for early intervention whenever needed.

MATERIALS AND METHODS

This was a hospital based prospective study done in Neonatal Intensive Care Unit, Department of Pediatrics, Government General Hospital, Kakinada for a period of 18 months from January 2017 to June 2018. As per National Neonatal Forum guidelines babies born <34weeks gestational age and/or <1750 grams birth weight and infants between 34 to 36 6/7 weeks gestational age or a birth weight between 1750 and 2000 grams with risk factors for ROP were screened.

The first retinal examination was done at 4 weeks of postnatal age or 30 days of life in infants born ≥ 28 weeks of gestational age. Smaller babies born <28 weeks of gestational age or < 1200 grams birth weight were screened early at 2-3 weeks of age.

All the eligible preterm babies admitted in NICU were enrolled in this study, of which babies who died before the scheduled time of screening and babies with > 34weeks gestational age and/or >1750 grams of birth weight without risk factors for ROP were excluded.

A predesigned proforma was used to collect data for risk factors such as birth weight, gestational age , multiple gestations, gender, duration of hospital stay, duration of oxygen given with hood or nasal prongs, duration of CPAP, duration of mechanical ventilation, blood transfusions, complications during hospital stay like jaundice, apnea, sepsis, hypoglycemia, polycythemia and interventions done like phototherapy and exchange transfusion.

Ethical clearance was obtained from the hospital ethics committee and informed consent of the parents was also obtained.

PROCEDURE OF SCREENING

An hour before screening, pupils of babies were dilated with 0.5% tropicamide + 1.25% phenylephrine drops one drop in each eye, 3 times 10 minutes apart. Screening was done in NICU by technician by using RETCAM. Images were interpreted by retina specialist. Retinopathy was graded into stages and zones as per the ICROP classification [12].

Infants with fully vascularized retina were not examined again. Those babies with zone I-stage 1 or 2 and zone II - stage 3 were reviewed after one week.

Babies were followed till complete vascularization. Babies with zone I – stage 3 or any stage with plus disease and zone II – stage 2 or 3 with plus disease and APROP were treated with laser or intravitreal bevacizumab within 48 hours under local anesthesia. All the treated babies were reviewed after 3days and then weekly for regression.

STATISTICAL ANALYSIS

Analysis was performed using SPSS version 24. Univariate analysis was conducted using Chi square test and odds ratio. Multiple logistic regression analysis was performed to study the predictors of ROP using independent variables which were significant in the univariate analysis.

RESULTS

As per NNF guidelines 690 babies were eligible for screening of which 42 did not come for screening even for the first time. Of the remaining, 72 did not come for subsequent follow up in spite of repeated reminders. A total of 576 babies completed their screening. Out of the 576 screened preterm babies, 124 had ROP and the incidence of ROP was 21.6% .69 out of 295 males and 55 out of 281 females developed ROP.

The incidence of ROP according to gestational age is shown in Table 1. Mean gestational age of babies with ROP was 31 weeks gestation. As the gestational age decreased, the incidence of ROP increased.

Table-2: Distribution of study population based on birth weight

Birth Weight	ROP+	ROP-	Total
<1000gms	6(75%)	2	8
1000-1249gms	45(63%)	26	71
1250-1499gms	44(35%)	80	124
1500-1749gms	21(8.5%)	225	246
1750-2000gms	8(6%)	119	127
Total	124	452	576

The chi-square value is 140.9577. The *p*-value is < 0.00001.

The incidence of ROP according to birth weight is shown in Table 2. Mean birth weight of babies Babies with lower birth weight had higher chances of getting ROP.

Table-2: Distribution of study population based on birth weight

Birth Weight	ROP+	ROP-	Total
<1000gms	6(75%)	2	8
1000-1249gms	45(63%)	26	71
1250-1499gms	44(35%)	80	124
1500-1749gms	21(8.5%)	225	246
1750-2000gms	8(6%)	119	127
Total	124	452	576

The chi-square value is 140.9577. The *p*-value is < 0.00001.

A univariate analysis was initially done taking each risk factor. Chi square values were calculated for duration of oxygen therapy (Chi; 305.3464), duration of hospital stay (Chi: 239.8715) and odds ratios were calculated for RDS (OR: 15.2062, CI: 9.2328 to 25.0441), sepsis (OR: 19.0189, CI: 6.3061 – 57.3602) hyperbilirubinemia (OR: 11.7191, CI: 6.6134 – 20.7665) and apnea (OR: 9.6667, CI: 5.1748 -18.0576) showed statically significant association with incidence of ROP with p values < 0.0001.Babies who received Oxygen for longer duration had higher incidence of ROP as shown in Table 3. None of the babies (261) who did not receive oxygen, developed ROP.

Table-3: Relation between duration of oxygen and ROP

Duration of oxygen	ROP+	ROP-	TOTAL
1-3days	13(8.6%)	139	152
4-7days	87(63%)	52	139
8-14days	24(100%)	0	24
No oxygen	0	261	261
Total	124	452	576

The chi-square value 305.3464. The *p*-value is < 0.00001.

Mutiplevariate analysis showed oxygen therapy (OR: 0.060, p: 0.007), CPAP (OR: 0.0236, p: .000), RDS (OR: 0.310, p: .000), sepsis (OR: 0.15, p: .000) and hyperbilirubinemia (OR: 0.337, p: 0.004) to be significantly associated with ROP as depicted in Table 4.

Table-4: Multivariate analysis of risk factors of ROP

Risk factors of ROP	ROP +Ve (n=124) %	ROP -Ve (n=452) %	P Value	Multi variant Analysis Odds ratio 95% CI
O2(315)	124(39.3%)	191(60.7%)	.007	0.060
CPAP(112)	78(58%)	42(8.8%)	.000	0.236
RDS(197)	100(50%)	97(50%)	.000	0.310
SEPSIS (509)	115(22.7%)	394(77.4%)	.000	0.159
NNJ(282)	109(38.6%)	173(61.4%)	.004	0.337
APNEA(51)	34(66.6%)	17(33.4%)	.010	0.346

Both eyes were affected in all infants having ROP. Zones and stages were shown in the Figure 1 and 2.

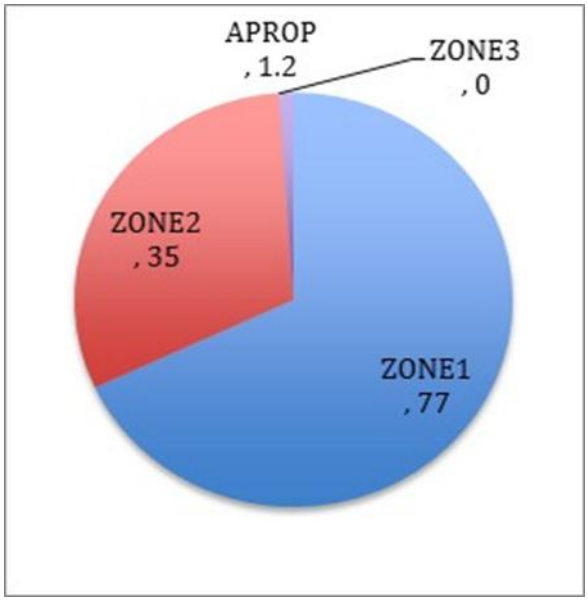

Fig-1: Showing zones of ROP

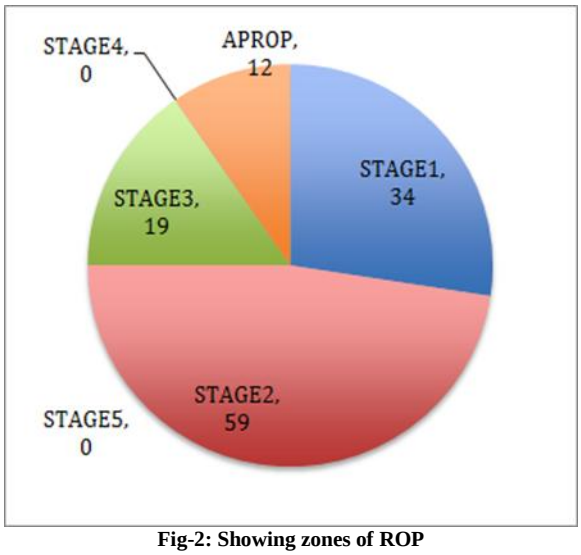

Fig-2: Showing zones of ROP

Out of 124 babies with ROP, laser photocoagulation was done in 43(56.6%) babies and intravitreal bevacizumab was instilled in 28 (36.8%) babies and 5 (6.6%) babies received both. All babies withstood the procedure well and there were no post-laser complications other than reddening of the conjunctiva, which disappeared in 2-3 days.

DISCUSSION

In the present study all babies having birth weight <1750g, gestation ≤34 weeks were screened. Infants with birth weight between 1750 to 2000 gms, gestation 34 to 36 6/7 weeks were screened only if they had additional risk factors [4-6,13]. As reported by Palmer, *et al*. [15], incidence and severity of ROP was closely related to lower birth weight and lower gestational age, as was seen in the present study. The incidence of ROP of 21.4% in this study was much lower than that reported by Gopal, *et al*. [16] in 1995. In more recent studies, incidence of ROP reported is similar to the present study incidence [17, 18].

There are varying screening criteria described by different authors. Maheshwari, *et al*. in 1994 [19] and Gupta, *et al*. in 2004 [18] screened all babies ≤1500g and/or gestational age ≤35 weeks. Vinekar, et al in 2007[20] suggested that the scenario in developing countries is quite different. Larger and gestationally 'older' infants are more likely to develop ROP compared to their counterparts in Western countries. Hence, the application of Western screening guidelines for developing countries has been questioned by Jalali, *et al*. in 2003[21]. As a higher cutoff limit, they recommended screening babies born at <37weeks gestation and/or birth weight <2000g in the presence of a high sickness score, in order to prevent missing any infant with threshold ROP. Based on these studies present criteria of ROP screening was recommended by NNF in 2011.Goble, *et al*. from England [22] felt that they were screening too many babies for ROP and recommended that babies with birth weight above 1250g should not be screened. In present study, we would have missed 29 cases of ROP needing laser or intravitreal bevacizumab if we had used <1500 as

criteria, as per American Academy of Pediatrics (AAP) updated recommendations [16].

Many risk factors have been reported to predispose to the development of ROP. Oxygen therapy, anemia, packed cell volume transfusion [9], septicemia, apnea and clinical sepsis [10,11] are important risk factors [17, 20, 24, 25]. In present study, oxygen administration, septicemia, hyperbilirubinemia, CPAP and apnea were found to be significant risk factors. Vinekar, *et al*. [20] also found that septicemia was a significant risk factor. Aggarwal, *et al*. [17] found apnea, clinical sepsis and male sex to be significant risk factors [7,8].

Of the 690 eligible preterm babies, 42 did not came for screening even for the first time. Of the remaining 72 did not come for follow up in spite of repeated reminders, and many of these babies had incompletely vascularized retina. There is a possibility that these neonates might develop ROP in case normal complete retinal vascularization did not take place.

CONCLUSION

NNF guidelines are appropriate for screening of ROP in developing countries unlike western world. In the present study 8 preterm babies with birth weight 1750 to 2000 grams and 21 preterm babies with birth weight 1500-2000 developed ROP.

Higher duration of NICU stay, sepsis, hyperbilirubinemia, apnea were some of the risk factors for ROP in the present study.

In the present study all babies who received oxygen for > 7days had ROP whereas all preterm babies who were not given oxygen did not develop ROP. Hence oxygen should be used as a drug only for minimal possible duration, with least possible FiO2.

Due to repeated blood samplings these tiny babies are more likely to become anemic requiring blood transfusion. So, it is important to limit the blood investigations as and when required only, which in turn decreases risk of ROP.

As of now ROP screening is included in the RBSK. Screening rates are increasing all over the country. So, measures to decrease the incidence of ROP now take prime importance. In the present study dropout rate for follow up screening of ROP was 19%. This shows the need to emphasize on the parent counseling periodically during hospital stay for regular follow ups till complete vascularization of retina. Predesigned software that can remind the parents and local ANM/ASHA workers regarding ROP screening similar to POSHAN scheme and immunize India may decrease the dropouts.

ACKNOWLEDGMENT

We gratefully acknowledge the help of Dr. Srinivas for doing interpretation of retinal images done by Sivakumar and Dr. Tejkiran for statistical analysis.

REFERENCES

1. Terry TL. Extreme prematurity and fibroblastic overgrowth of persistent vascular sheath behind each crystalline lens. Am J Ophthalmol. 1942; 25: 203-204.
2. Hammer ME, Mullen PW, Fergusson JG, Poi S, and Cosbox C. Jackson KL. Logistic analysis of risk factors in acute retinopathy of prematurity. Am J Ophthalmol. 1986; 102: 1-6.
3. Seiberth V, Linderkamp O. Risk factors in retinopathy of prematurity. A multivariate statistical analysis.Ophthalmologica. 2000; 214: 131-135.
4. Zafer A, Tamboli BL, Bhatnagar R, Ameta KD. Immunization Coverage-A Comparison between Tribal, Non-Tirbal and Urban Areas of Udaipur District. Indian Journal of Community Medicine. 1996 Jan 1;21(2):47.
5. Hellström A, Ley D, Hansen- Pupp I, Niklasson A, Smith L, Löfqvist C, Hård AL. New insights into the development of retinopathy of prematurity–importance of early weight gain. Acta paediatrica. 2010 Apr;99(4):502-8.
6. Chen M, Çitil A, McCabe F, Leicht KM, Fiascone J, Dammann CE, Dammann O. Infection, oxygen, and immaturity: interacting risk factors for retinopathy of prematurity. Neonatology. 2011;99(2):125-32.
7. Darlow BA, Hutchinson JL, Henderson-Smart DJ, Donoghue DA, Simpson JM, Evans NJ. Prenatal risk factors for severe retinopathy of prematurity among very preterm infants of the Australian and New Zealand Neonatal Network. Pediatrics. 2005 Apr 1;115(4):990-6.
8. Lad EM, Hernandez-Boussard T, Morton JM, Moshfeghi DM. Incidence of retinopathy of prematurity in the United States: 1997 through 2005. American journal of ophthalmology. 2009 Sep 1;148(3):451-8.
9. Giannantonio C, Papacci P, Cota F, Vento G, Tesfagabir MG, Purcaro V, Lepore D, Molle F, Baldascino A, Romagnoli C. Analysis of risk factors for progression to treatment-requiring ROP in a single neonatal intensive care unit: is the exposure time relevant?. The Journal of Maternal-Fetal & Neonatal Medicine. 2012 May 1;25(5):471-7.
10. Tolsma KW, Allred EN, Chen ML, Duker J, Leviton A, Dammann O. Neonatal bacteremia and retinopathy of prematurity: the ELGAN study. Archives of ophthalmology. 2011 Dec 1;129(12):1555-63.
11. Chen M, Çitil A, McCabe F, Leicht KM, Fiascone J, Dammann CE, Dammann O. Infection, oxygen,

and immaturity: interacting risk factors for retinopathy of prematurity. Neonatology. 2011;99(2):125-32.
12. An international classification of retinopathy of prematurity. II. The classification of retinal detachment. The International Committee for the Classification of the Late Stages of Retinopathy of prematurity.
13. NNF guidelines on retinopathy of prematurity, 2011
14. American Academy of Pediatrics. Screening Pediatrics. 2001; 108: 809-8
15. 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.
16. Gopal L, Sharma T, Ramachandran S, Shanmugasundaram R, Asha V. Retinopathy of prematurity: A study. Indian J Ophthalmol. 1995;43: 59-61.
17. Aggarwal R, Deorari AK, Azad RV, Kumar H, Talwar D, Sethi AI. Changing profile of retinopathy of prematurity. Trop Pediatr. 2002; 48: 239-242.
18. Gupta VP, Dhaliwal U, Sharma R, Gupta P, Rohtagi J. Retinopathy of prematurity – risk factors. Indian J Pediatr. 2004; 71: 887- 892.
19. Maheshwasri R, Kumar H, Paul VK, Singh M, Deorari AK, Tiwari AK. Incidence and risk factors of retinopathy of prematurity in a tertiary newborn unit in New Delhi.Natl Med J India. 1996; 92: 211-214.
20. Vinekar A, Dogra M, Sangtam T, Narang A, Gupta Retinopathy of prematurity in Asian Indian babies weighing greater than 1250 grams at birth: ten year data from a tertiary care center in a developing country. Indian J Ophthalmol. 2007; 55: 331-336.
21. Jalali S, Anand R, Kumar H, Dogra MR, Azad RV, Gopal L. Programme planning and screening strategy in retinopathy of prematurity. Indian J Ophthalmol. 2003; 51: 89-99.
22. Goble RR, Jones HS, Fielder AR. Are we screening too many babies for retinopathy of prematurity? Eye. 1997; 11: 509-514.
23. Screening examination of premature infants for retinopathy of prematurity. Section on Ophthalmology, American Academy of Pediatrics. American Academy of Ophthalmology. Pediatrics. 2006; 117: 572-576.
24. Rekha S, Battu RR. Retinopathy of prematurity: incidence and risk factors. Indian Pediatr. 1996; 33: 999-1003.
25. Dutta S, Narang A, Dogra MR, Gupta A. Risk factors of threshold retinopathy of prematurity. Indian Pediatr. 2004; 41: 665-671.