International Journal of Research in Medical Sciences
Mishra S et al. Int J Res Med Sci. 2020 Apr;8(4):1463-1468
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20201343

Original Research Article

Retinopathy of prematurity in preterm babies in a local medical college and hospital

Shantisena Mishra[1], Anjali Saji[1], Saiprasanna Behera[2]*, Sridhar Mohanty[1]

[1]Department of Pediatrics, MKCG Medical College, Berhampur, Odisha, India
[2]Research Associate, SCB Medical College, Cuttack, Odisha, India

Received: 21 January 2020
Revised: 12 February 2020
Accepted: 28 February 2020

***Correspondence:**
Dr. Saiprasanna Behera,
E-mail: behera.saiprasanna82@gmail.com

ABSTRACT

Background: Retinopathy of prematurity is a multifactorial vasoproliferative retinal disease that increases in incidence with decreasing gestational age and is one of the leading causes of preventable childhood blindness in India. Advances in neonatology have led to dramatic increase in survival of preterm neonates and in turn, to the risk of developing ROP. Since most of the risk factors associated with ROP mentioned above arise in the neonatal intensive care unit (NICU) itself and most of them are avoidable, cautious monitoring of the risk factors, early screening, follow up and surgical intervention have been shown to reduce the incidence and improve the outcome of ROP.
Methods: This was a prospective observational study conducted for a period of 2 years. A total of 151 infants admitted in NICU /SNCU who satisfied the inclusion criteria were enrolled in this study. Initial and follow up screening was conducted in three phases the results were documented in proforma after ethical clearance.
Results: Comparison of risk factors between eyes with and without ROP was done using Chi-square test. A p-value of<0.05 was considered to be statistically significant. Incidence of ROP in centre is found to be 33.8%. Among maternal risk factors, multiple gestation and PROM/PPROM is found to be significant in the development of ROP from this study. However, mode of delivery and gestational hypertension, were found to be not significant in ROP. Among neonatal risk factors, low birth weight, lower gestational age, prolonged oxygen exposure, blood transfusion, mechanical ventilation, sepsis, phototherapy was found to be significant in this study.
Conclusions: ROP, being an emerging cause for potentially blinding visual disability, needs to be diagnosed early. Due to the advancements in neonatology and better survival of preterm babies, timely screening, regular follow up, early detection and intervention is mandatory. A multidisciplinary approach is required in diagnosis and treatment of the disease. Proper counselling and motivation for parents of preterm and low birth weight babies for regular follow up is also essential.

Keywords: Cryotherapy, Light amplification by stimulated emission of radiation, PLUS disease, Premature rupture of membranes, Preterm babies, Retinopathy of prematurity

INTRODUCTION

Retinopathy of prematurity (ROP) which was previously called Retrolental fibroplasia (RLF) in 1940s is a blinding disease of premature infants. The enigmatic findings of the disease, with scar tissue behind the neonate lens associated with retinal detachment, have been responsible for the two largest "epidemics" of blindness in neonates in modern times.

These outbreaks of the disease occurred approximately 25 years apart in the mid-1950s and late 1970s.[1]

It is a multifactorial vasoproliferative retinal disease that increases in incidence with decreasing gestational age (GA).[2] The possible mechanism of injury suggested is vasoconstriction, increase in level of vasogenic factors like vascular endothelial growth factor (VEGF) and compensatory neo-vascularization leading to severe extraretinal fibrovascular proliferation and retinal detachment. ROP is mostly limited to preterm babies with birth weight (BW) of less than 1500 grams or GA of less than 32 weeks, with an incidence varying between 35 to 60%.[3] However preterm infants born at 32 weeks or later can also develop severe ROP if they had a turbulent NICU course or prolonged oxygen therapy.[4]

ROP is emerging as one of the leading causes of preventable childhood blindness in India. Advances in neonatology have led to dramatic increase in survival of preterm neonates and in turn, to the risk of developing ROP.[5,6] Out of 26 million annual live births in India, approximately 8.5% weigh <2000 grams, thus making 2 million newborns at risk for ROP.[7] The overall incidence of ROP varies from 20-52%. 65% of infants with birth weight <1250 grams, 80% of those with birth weight <1000 grams will develop some degree of ROP. Only about 10% of the infants progress to severe ROP implying that the rest regress spontaneously.

Today, it is well known that oxygen therapy is not the single causative factor. The pathogenesis involved in the development of ROP is multifactorial. It includes prematurity, low birth weight, multiple gestation, prolonged oxygen exposure, severity of neonatal illness, severe respiratory distress requiring mechanical ventilation, shock, sepsis, hypoxia, apneic attacks, high ambient light, prolonged ventilatory support, need for blood transfusion, intraventricular hemorrhage, acidosis, anemia, high ambient light, vitamin E deficiency whereas breast feeding is proposed to be protective. Infants born to mothers with pregnancy induced hypertension have a reduced risk of developing ROP due to accelerated fetal maturity of retinal vessels.

There is a significant correlation between prevalence of ROP and socioeconomic development. ROP is more prevalent in high income and middle-income countries where preterm and smaller babies have access to tertiary health care facilities, and therefore have a higher chance of survival. This is referred to as a "third epidemic". Unfortunately, in most cases the exposure to high concentrations of oxygen, and poor oxygen saturation monitoring increases the risk of developing ROP. In low income countries, ROP is not as prevalent because of lack of adequate ventilator facilities reducing the chances of oxygen exposure. However, there are low income countries with urbanized areas which have the facilities to support VLBW babies. ROP does occur in these places.

In India with the development of neonatal intensive care units, premature infants with extremely low birth weights are surviving and are at highest risk of developing ROP. Although it has been more than decades since the establishment of safety and effective prophylaxis against ROP blindness using laser photocoagulation or cryotherapy, there is still a lack of uniform agreement and implementation of updated NICU based effective and timely ROP screening program in many neonatal centers in India.

Currently no definitive methods are available for the prevention of ROP. Since most of the risk factors associated with ROP mentioned above arise in the neonatal intensive care unit (NICU) itself and most of them are avoidable, cautious monitoring of the risk factors, early screening, follow up and surgical intervention have been shown to reduce the incidence and improve the outcome of ROP.11n view of paucity of Indian studies on the incidence and risk factors of ROP from Government tertiary care centers. Especially from the eastern parts of India, the present study is undertaken.

Aims and objectives of the study were to study the incidence of retinopathy of prematurity in preterm infants with less than 34 weeks of gestational age or less than 2000 grams birth weight and at least 3 weeks of postnatal life and to study the maternal and neonatal risk factors associated with the development of retinopathy of prematurity.

METHODS

Study design was prospective, cross sectional observational study.

Preterm infants admitted in Sick Newborn Care unit (SNCU), Department of Pediatrics, with the help of Department of Ophthalmology, MKCG Medical College, Berhampur, Odisha

Study period was 2 years (November 2017 - October 2019). Sample size was 151 infants who satisfied inclusion criteria

Inclusion criteria

- Preterm neonates less than 34 weeks gestation and/or less than 2000 grams
- Preterm neonates of at least 3 weeks of postnatal life.

Exclusion criteria

- Neonates with congenital anomalies
- Neonates with congenital cataract or tumours of eye.
- Neonates who died before eye examination.
- Unilateral or bilateral retinal or choroidal disease (other than ROP).

A media opacity obstructing the fundal view (e.g. cataract). Refusal of initial consent by the parent/guardian.

Ethical clearance was obtained from the hospital ethics committee prior to study. Neonates admitted to SNCU, Department of Pediatrics, MKCG Medical College, satisfying the inclusion criteria were enrolled in the study. The purpose of the study was explained to the patient's parents and informed written consent was obtained from the parents. The data were entered on a pre-designed proforma for analysis.

Complete clinical, antenatal, natal and postnatal history and demographic data was noted. Detailed history of symptoms and clinical examination of enrolled neonates was obtained. It included detailed birth history, number of days of oxygen exposure, any significant positive investigations (CRP), history of blood transfusion, phototherapy or mechanical ventilation.

ROP screening was done by indirect ophthalmoscopy in SNCU/NICU by ophthalmologist under guidance of neonatologist initially and stable and discharged patients were screened in the outpatient department of Ophthalmology.

The examination of the infants included indirect ophthalmology with sclera indentation with the help of infant speculum and a 20 D lens. The infant was well clothed and wrapped and was fed and burped an hour before evaluation. A quick flashlight examination of the adnexa and anterior segment was done before instilling the dilating drops.

Drops used for dilation included 0.4% tropicamide and 2.5% phenylephrine. The dilating drops were freshly prepared by diluting the available adult dosage drops with tear substitute. Two or three instillations of each of these drops, five minutes apart were usually sufficient to dilate pupils in 10-15 minutes. Care was taken to wipe any eye drop that spilled onto the cheeks, as they can be absorbed through the skin and cause increased heart rate. One drop of local anesthetic 0.5% proparacaine was instilled just before the examination.

The first screening was done between 25-30 days after birth or at 31-33 weeks post-conceptional age whichever is later. Retinopathy was graded into stages and zones as per the ICROP classification. The findings were recorded. Subsequent examinations were conducted according to the findings of first examination.

If the initial examination showed no changes of ROP, the infant was followed up at an interval of 2-3 weeks, until the vessels reached the oraserrata or till 45 weeks of gestation.

If changes of ROP were noted on initial examination the infant was followed up every week or more frequently according to the severity of ROP.

The results were tabulated in a master chart using Microsoft Excel 2013 and statistical analysis was performed using SPSS version 26. Univariate comparison of risk factors between eyes with and without ROP was done using Chi-square test. A p value of <0.05 was considered statistically significant.

RESULTS

Out of the 44 ROP positive infants only 7 (15.9%) were delivered as multiple gestation whereas 37(84.1%) were singleton. Among the 86 ROP negative infants, 29(33.7%) were multiple gestation as compared to 57(66.3%) who were singleton. Statistically this difference is found to be significant (p=0.032) (Table 1).

Table 1: Type of gestation with ROP.

Multiple/singleton	ROP		Total
	Positive	Negative	
Multiple	7	29	36
Singleton	37	57	94
Total	44	86	130
Chi square		4.612	
p value		0.032	

Out of the 44 ROP positive infants, only 8 (18.2%) were delivered by LSCS whereas 36(81.8%) were vaginally born. Among the 86 ROP negative infants, 19 (22.1%) were born by LSC as compared to 67 (77.9%) who were vaginally born. Statistically this difference is found to be not significant (p>0.05) (Table 2).

Table 2: Mode of delivery with ROP.

Mode of delivery	ROP		Total
	Positive	Negative	
Lower segment caesarean section	8	19	27
Percentage	18.2%	22.1%	20.8%
Vaginal delivery	36	67	103
Percentage	81.8%	77.9%	79.2%
Total	44	86	130
Chi square	0.271		
p value	0.603		

Out of the 44 ROP positive infants, 10 (22.7%) had antenatal history of gestational hypertension whereas 34 (77.3%) didn't had gestational hypertension history. Among the 86 ROP negative infants,17 (19.8%) had history of gestational hypertension as compared to 69 (80.2%) who didn't have that history. Statistically it is found to be not significant (p>0.05) (Table 3).

Out of the 44 ROP positive infants, 28 (63.6%) had antenatal history of PROM/PPROM whereas 16 (36.4%) didn't had PROM history. Among the 86 ROP negative infants, 33 (38.4%) had history of PROM/PPROM as compared to 53 (61.6%) who didn't have that history. Statistically it is found to be significant (p=0. 006) (Table 4).

Table 3: Gestational hypertension with ROP.

Mode of delivery	ROP		Total
	Positive	Negative	
Yes	10	17	27
Percentage	22.7%	19.8%	20.8%
No	34	69	103
Percentage	77.3%	80.2%	79.2%
Total	44	86	130
Chi square	0.154		
p value	0.694		

Table 4: PROM/ PPROM with ROP.

Mode of delivery	ROP		Total
	Positive	Negative	
Yes	28	33	61
Percentage	63.6%	38.4%	46.9%
No	16	53	69
Percentage	36.4%	61.6%	53.1%
Total	44	86	130
Chi square	7.460		
p value	0.006		

Out of the 44 ROP positive infants, 24 infants (54.5%) were males and 20 (45.5%) were females. Among the 86 ROP negative infants, 40 (46.5%) were males and 46 (53.5%) were females. Statistically it is found to be not significant (p>0.05) (Table 5).

Table 5: Gender with ROP.

Gender	ROP		Total
	Positive	Negative	
Male	24	40	64
Percentage	54.5%	46.5%	49.2%
Female	20	46	66
Percentage	45.5%	53.5%	50.7%
Total	44	86	130
Chi square	0.752		
p value	0.386		

The weight of the infants studied in the study was between 800-1970 gms with a mean weight of 1390.23 gms with a standard deviation of 253.64 gms (Table 6).

Among the 130 studied, 11 (8.5%) were less than 1000 grams, 77 (59.2%) were between 1000- 1500 grams and 42 (32.3%) were more than 1500 grams.

Out of the 44 ROP positive infants,7 infants (15.9%) were less than 1000 gms, 29(65.9%) between 1000-1500 gms and 8 (18.2%) more than 1500 gms. Among the 86 ROP negative infants, 4 (4.7%) were less than 1000 gms,48 (55.8%) between 1000-1500 gms, and 34 (39.5%) more than 1500 gms. Statistically it is found to be significant (p=0.011).

Table 6: Birth weight with ROP.

Baby weight	ROP		Total
	Positive	Negative	
≤1000 gms	7	4	11
Percentage	15.9%	4.7%	8.5%
1001-1500 gms	29	48	77
Percentage	65.9%	55.8%	59.2%
>1500 gms	8	34	42
Percentage	18.2%	39.5%	32.3%
Total	44	86	130
Chi square	8.969		
p value	0.011		

The gestational age range of studied population was between 26-36 weeks with a mean of 31.35 weeks and standard deviation 2.25 weeks (Table 7).

Table 7: Gestational age with ROP.

Baby weight	ROP		Total
	Positive	Negative	
≤30 weeks	20	29	49
Percentage	45.5%	33.7%	37.7%
30-32 weeks	19	21	40
Percentage	43.2%	24.4%	30.8%
>32 weeks	5	36	41
Percentage	11.4%	41.9%	31.5%
Total	44	86	130
Chi square	12.977		
p value	0.002		

Among the 130 infants studied, 49 (37.7%) were less than 30 weeks, 40 (30.8%) were 30-32 weeks, 41 (31.5%) were more than 32 weeks. Out of the 44 ROP positive infants, 20 infants (45.5%) were less than 30 weeks, 19 (43.2%) between 30-32 weeks and 5 (11.4%) more than 32 weeks. Among the 86 ROP negative infants, 4(4.7%) were less than 1000 gms,48 (55.8%) between 1000-1500 gms, and 34 (39.5%) more than 32 weeks. Statistically it was found to be significant (p=0.002).

Out of the 44 ROP positive infants, 8 infants (18.2%) received oxygen for less than 3 days whereas 36 (81.8%) received oxygen for more than 3 days. Among the 86 ROP negative infants, 54 (62.8%) received oxygen for a duration less than 3 days whereas 32 (37.2%) received oxygen for more than 3 days. Statistically it is found to be highly significant (p<0.001) (Table 8).

Out of the 44 ROP positive infants, 35 infants (79.5%) had CRP positive sepsis whereas 9 (20.5%) didn't had CRP positivity. Among the 86 ROP negative infants, 38(44.2%) had CRP positive sepsis whereas 48(55.8%) didn't had CRP positivity. Statistically it is found to be highly significant (p<0.001) (Table 9).

Table 8: Oxygen exposure with ROP.

No of days in oxygen	ROP		Total
	Positive	Negative	
<3 days	8	54	62
Percentage	18.2%	62.8%	47.7%
>3 days	36	32	68
Percentage	81.8%	37.2%	52.3%
Total	44	86	130
Chi square	23.219		
p value	<0.001		

Table 9: C-reactive protein with ROP.

C-reactive protein	ROP		Total
	Positive	Negative	
Positive	35	38	73
Percentage	79.5%	44.2%	56.2%
Negative	9	48	57
Percentage	20.5%	55.8%	43.8%
Total	44	86	130
Chi square	14.781		
p value	<0.001		

Out of the 44 ROP positive infants, 16 infants (36.4%) were given blood transfusion during NICU stay whereas 28 (63.6%) were not given any blood transfusion. Among the 86 ROP negative infants, 7 (8.1%) were given blood transfusion whereas 79 (86%) were not given any transfusion. Statistically it is found to be highly significant (p<0.001) (Table 10).

Table 10: Blood transfusion with ROP.

Blood transfusion	ROP		Total
	Positive	Negative	
Yes	16	7	23
Percentage	36.4%	8.1%	17.7%
No	28	79	107
Percentage	63.6%	91.9%	82.3%
Total	44	86	130
Chi square	15.923		
p value	<0.001		

Out of the 44 ROP positive infants, 40 infants (90.9%) received phototherapy during NICU stay whereas 4 (9.1%) were not given any phototherapy. Among the 86 ROP negative infants, 47 (54.7%) were given phototherapy whereas 39 (45.3%) were not given any transfusion. Statistically it is found to be highly significant (p<0.001) (Table 11).

Out of the 44 ROP positive infants, 16 infants (36.4%) received mechanical ventilation during NICU stay whereas 28 (63.6%) were not given any ventilation. Among the 86 ROP negative infants, 3 (3.5%) were given phototherapy whereas 83 (96.5%) were not given any transfusion. Statistically it is found to be highly significant (p<0.001) (Table 12).

Table 11: Phototherapy and ROP.

Phototherapy	ROP		Total
	Positive	Negative	
Yes	40	47	87
Percentage	90.9%	54.7%	66.9%
No	4	39	43
Percentage	9.1%	45.3%	33.1%
Total	44	86	130
Chi square	17.287		
p value	<0.001		

Table 12: Mechanical ventilation and ROP.

Mechanical ventilation	ROP		Total
	Positive	Negative	
Yes	16	3	19
Percentage	36.4%	3.5%	14.6%
No	28	83	111
Percentage	63.6%	96.5%	85.4%
Total	44	86	130
Chi square	25.209		
p value	<0.001		

DISCUSSION

Table 1 describes the relation of type of gestation and ROP and found that multiple gestation is statistically significant in development of ROP. This is similar to the reports of Sood et al, and Snigdha Sen et al, in which multiple gestation was confirmed as an independent risk factor.[8,9]

Table 2 describes the relation of mode of delivery and ROP and was found to be not significant. Thus, this study did not report any association of mode of delivery with development of ROP. This is similar to the studies of Hakeem AH et al.[10]

Table 3 describes association of gestational hypertension and ROP and found to be not significant. Sei berth and Linder Kamp reported that maternal pre-eclampsia is associated with reduced incidence of ROP.[11]

Table 4 describes association of PROM and ROP and it is found as a significant risk factor. Although maternal PROM was seldom included in the risk factor analysis of similar studies, these findings were consistent with that of Satar A et al.

Table 5 is about relation of gender and ROP and it is found to be not significant. There are no studies till date that found a significant association between gender and ROP. Table 6 describes about association of birth weight

and ROP and it is significant. It is comparable to several other studies conducted globally.

Table 7 describes relation of gestational age with ROP and found that low GA is a significant risk factor. This is comparable to the studies of Higgins R D, Gopal L and Chawla D. Table 8 describes about oxygen exposure and its relation to ROP and is found to be highly significant. The results are comparable to the studies of Gopal L and Hakeem AH.

Table 9 describes about relation of CRP with ROP. In this study, CRP positivity(sepsis) is identified as a highly significant risk factor. This was in agreement with Gupta VP Chawla D and Hakeem AH which may be dueto effect of endotoxins on retinal blood vessels.

Table 10 describes relation of blood transfusion and ROP and in this study it is found to be highly significant. Recent studies of Oscar Onyango and Snigdha Sen also have identified blood transfusion as a significant risk factor for ROP.

Table 11 describes relation of ROP and phototherapy and it is identified as a significant risk factor, though the risk caused by phototherapy in ROP is yet to be proved.

Table 12 describes about relation of mechanical ventilation and ROP and found to be highly significant. This is consistent with the findings of Karna et al and Seiberth et al.

CONCLUSION

ROP, being an emerging cause for potentially blinding visual disability, needs to be diagnosed early. Due to the advancements in neonatology and better survival of preterm babies, timely screening, regular follow up, early detection and intervention is mandatory. A multidisciplinary approach is required in diagnosis and treatment of the disease. Along with regular screening, each neonatal unit should have a policy on oxygen administration. Pulse oximeters and blended oxygen should be used in delivery rooms and neonatal units to guide oxygen therapy. Judicious oxygen therapy can greatly help in the reduction of incidence of this disease. Proper counseling and motivation for parents of preterm and low birth weight babies for regular follow up is also essential. Prompt referral of diagnosed babies requiring laser photocoagulation or vitreoretinal surgeries, to higher centres is mandatory to reduce the burden of childhood blindness.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee of MKCG Medical College

REFERENCES

1. Terry TL. Extreme Prematurity and fibroplastic overgrowth of persistent vascular sheath behind each crystalline lens. Preliminary report. Am J Ophthalmol. 1942;25:203-4.
2. Vanderveen DK, Zupancic JAF. Retinopathy of Prematurity. In: Cloherty JP, Eichenwald EC, Stark AR, eds. Manual of neonatal care. 6th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2010:640-644.
3. Singh M. Miscellaneous conditions: Retinopathy of prematurity In: Care of the newborn. 8th ed. New Delhi: CBS Publications; 2014:533-536.
4. Paul VK, Deorari A. In: Agarwal R, eds. AIIMS Protocols in Neoanatology. Vol. II. Noble publishers and distributors; 2019:468-481
5. Charan R, Dogra MR, Gupta A, Narang A. The incidence of retinopathy of prematurity in a neonatal care unit. Ind J Ophthalmol. 1995 Jul 1;43(3):123.
6. Gopal L, Sharma T, Ramachandran S, Shanmugasundaram R, Asha V. Retinopathy of prematurity: a study. Ind J Ophthalmol. 1995 Apr 1;43(2):59.
7. Kliegman RM, Stanton B, Geme J, Schor NF. Nelson textbook of pediatrics. 20th ed. Elsevier; 2015:3888.
8. Sood V, Chellani H, Arya S, Guliani BP. Changing spectrum of retinopathy of prematurity (ROP) and variations among siblings of multiple gestation. Ind J Pediatr. 2012 Jul 1;79(7):905-10.
9. Sen S. To study the prevalence and risk factors of retinopathy of prematurity at a tertiary care centre in Agra. Inter J Sci Res. 2018;7(2):350-3.
10. Hakeem AH, Mohamed GB, Othman MF. Retinopathy of prematurity: a study of prevalence and risk factors. Middle East Afri J Ophthalmol. 2012 Jul;19(3):289.
11. Seiberth V, Linderkamp O. Risk factors in retinopathy of prematurity. Ophthalmologica. 2000;214(2):131-5.

Cite this article as: Mishra S, Saji A, Behera S, Mohanty S. Retinopathy of prematurity in preterm babies in a local medical college and hospital. Int J Res Med Sci 2020;8:1463-8.