



RETINOPATHY OF PREMATURITY – A CLINICAL STUDY

Paediatrics

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ABSTRACT

Retinopathy of prematurity (ROP) is a multifactorial vaso-proliferative disease of premature retina affecting preterm neonates, that increases in incidence with decreasing gestational age and birth weight. A prospective clinical study was done from October 2019 to July 2021 in 150 preterm babies less than 36 weeks of gestational age (GA) or less than 2000 gm of birth weight (BW) to determine the incidence and outcome of ROP at BTGH AND STGH, attached to MRMC, KALABURAGI. After having obtained an informed consent, detailed history and risk factors were documented using a structured proforma. ROP screening was performed using wide-field digital imaging on a Retcam Shuttle (Clarity MSI, USA). If ROP was found the details were noted down regarding the stage, zone and extent of disease. **Results:** Among 150 neonates, 31 (incidence of 21.7%) developed ROP with 17(54.8%) being male and 14(45.2%) female. Among the 31 babies 20 had the disease bilaterally and 11 showed ROP in one eye alone, so total 51 eyes had ROP. Of the 31 ROP babies, majority were between 30-32 weeks GA (52%) and BW between 1500gm-1750gm (56%). Of the 51 eyes with ROP, majority showed stage 2 and zone 2 involvement. Majority of the ROP babies on follow up showed spontaneous resolution and 2 neonates of stage 2 plus disease were treated with laser photocoagulation. In the postnatal period oxygen supplementation ($p < 0.001$), hyperbilirubinemia ($p = 0.003$) and Patent Ductus Arteriosus ($p = 0.047$) were found to be significant risk factors. **Conclusion:** ROP screening is recommended to all babies ≤ 34 weeks GA and/or ≤ 1750 gm BW at 4 weeks after birth. Screening should be intensified in the presence of risk factors. Judicious use of oxygen in premature infants is important. Thorough screening, close monitoring and frequent follow ups are essential to prevent the blindness due to ROP.

KEYWORDS

Retinopathy of Prematurity, Staging, Zone, Gestational Age.

INTRODUCTION:

Retinopathy of prematurity (ROP) is a multifactorial vaso-proliferative disease of premature retina affecting preterm neonates, that increases in incidence with decreasing gestational age and birth weight. It can range from mild, transient changes in the retina showing regression, to severe progressive vaso-proliferation, scarring, detachment of retina and blindness.¹ Approximately 65% of infants with a birth weight of < 1250 gm, and 80% of infants with a birth weight < 1000 gm, will develop some degree of ROP.

In view of ongoing trend for resuscitation of smaller infants with lower gestational age along with increased survival of very low birth weight (VLBW) & extremely low birth weight (ELBW) babies, an increase in incidence of ROP is expected.^{2,3} Out of 26 million annual live births in India, nearly 2 million are < 2000 g in weight and are at risk of developing retinopathy of prematurity (ROP).⁴

In India, the incidence of ROP is between 38% and 51.9% in low-birth-weight babies.⁵ Oxygen supplementation is identified to be an important risk factor for the development of ROP.⁶

Babies who have received oxygen need not necessarily develop ROP. ROP can develop without oxygen supplementation.⁷ Early gestational age (GA), low- birth weight, hyperoxia, apnea, intraventricular hemorrhage, blood transfusions, and maternal bleeding are other risk factors associated with ROP. Large refractive error mainly myopia, strabismus, impaired vision, and blindness may occur following severe ROP.⁸

Treatment of ROP includes cryotherapy, laser photocoagulation, and intravitreal injection of anti-VEGF (Vascular Endothelium Growth Factor). Each has their merits and demerits. During recent years, blindness due to ROP has also been increasing in middle income countries, giving rise to a third epidemic.⁹ ROP is responsible for approximately 3-10% of all new cases of childhood blindness in high income countries, while in middle income countries ROP accounts for up to 60% of such cases.¹⁰

ROP is therefore now considered a major health problem and it has been included in the World Health Organization program for prevention of childhood blindness.

The incidence of ROP and the population at risk of developing ROP are dependent on the availability, access to, and quality of neonatal care. Guidelines and screening programs that take into consideration the characteristics of local populations therefore have to be designed.¹⁰

Hence, the current study was undertaken to study the incidence and associated risk factors of ROP among all preterm infants born in a tertiary care hospital. This study also examines short term outcome in preterm infants with ROP.

MATERIALS AND METHODS:

- Study Type and Design – prospective observational study
- Study Population- Preterm neonates between 28-36 weeks and birth weight less than 2 kgs admitted in BTGH and STGH attached to MRMC, KALABURAGI.

- Sample-size-150
- Study Duration -October 2019 to July 2021 or till desired sample size is attained, whichever is earlier.

Inclusion Criteria

- Preterm infants < 36 weeks of gestation, and
- Preterm infants weighing < 2000 gm

Exclusion Criteria

- Newborns with congenital anomalies, syndromes, congenital cataract and tumours of eyes
- Term babies born with less than 2 kgs.

Objectives of the study

To determine the **incidence and outcome of retinopathy of prematurity [ROP]** in neonates between 28-36 weeks and birth weight less than 2 kgs.

Data Collection Method

- Informed parental consent was taken from all cases.
- In all cases detailed history, physical examination and assessment of all risk factors was done and recorded in study proforma.
- All the data is compared and stored in form of excel sheet for further references.

METHOD:

All Preterm infants who will be born in NICU of BASAVESHWAR AND SANGAMESHWAR TEACHING AND GENERAL HOSPITAL (BTGH AND STGH) attached to M R MEDICAL COLLEGE (MRMC), KALABURAGI will be screened for Retinopathy of Prematurity (ROP), after 3 weeks of postnatal life, by an ophthalmologist. Result of Retinopathy of Prematurity will be interpreted as those requiring regular follow up, until retina matured like that of term, or those requiring intervention. All the risk factors related to ROP will be compared.

ROP screening will be done by an experienced ophthalmologist, with indirect ophthalmoscopy using 20 D or 28/30 D lens. After instilling a topical anaesthetic drop like Proparacaine, a wire speculum is inserted to keep the eye-lids apart. First the anterior segment of the eye is examined to look for tunica vasculosa lentis, pupillary dilation, and lens / media clarity; followed by the posterior pole to look for plus disease; followed by sequential examination of all clock hours of the peripheral retina. A scleral depressor is often used to indent the eye externally to examine areas of interest, rotate and stabilize the eye.

Statistical Methods:

Linear variables will be summarized as mean and standard deviation whereas nominal/categorical variable will be analysed by Chi square test and Fisher exact test. SSPS version 22 software will be used for all statistical calculations.

RESULTS:

Among 150 neonates, 31 (incidence of 21.7%) developed ROP with 17(54.8%) being male and 14(45.2%) female. Among the 31 babies 20 had the disease bilaterally and 11 showed ROP in one eye alone, so total 51 eyes had ROP. Of the 31 ROP babies, majority were between 30-32 weeks GA (52%) and BW between 1500gm-1750gm (56%). Of the 51 eyes with ROP, majority showed stage 2 and zone 2 involvement. Majority of the ROP babies on follow up showed spontaneous resolution and 2 neonates of stage 2 plus disease were treated with laser photocoagulation.

As depicted in Table 1, of all the various risk factors that were observed, oxygen supplementation, hyperbilirubinemia and PDA were found to be statistically significant.

Table 1: Risk factors

	Risk factors	No ROP		ROP present		p-value
		Number	%	Number	%	
Prenatal	PIH	8	7.2	5	17.2	0.097
	Multiple gestation	12	9.9	1	3.4	0.268
	APH	3	2.7	0	0	0.371
	Antenatal Steroid	6	5.4	0	0	0.201
	PROM	11	9.0	1	3.4	0.322
	GDM	3	2.7	0	0	0.371
Post natal	LSCS	24	19.8	4	13.8	0.457
	Asphyxia	9	8.1	1	3.4	0.386
	MAS	2	1.8	0	0	0.467
	HIE	7	6.3	0	0	0.165
	Hyaline Membrane Disease/ RDS	25	21.6	7	24.1	0.771
	Surfactant	2	1.8	1	3.4	0.586
	Oxygen	21	18	24	75.9	<0.001
	Ventilation	3	2.7	2	6.9	0.279
	Pneumonia	5	4.5	0	0	0.244
	Sepsis	4	3.6	3	10.3	0.138
	Polycythemia	0	0	0	0	
	Anemia	2	1.8	2	6.9	0.143
	Thrombocytopenia	2	1.8	0	0	0.467
	Transfusion	3	2.7	1	3.4	0.830
Hypoglycemia	3	2.7	1	3.4	0.830	
Hyperbilirubinemia	16	13.5	12	37.9	0.003	

Phototherapy	15	12.6	3	10.3	0.739
Ascites	1	0.9	0	0	0.608
Shock	1	0.9	0	0	0.608
PDA	1	0.9	2	6.9	0.047
IVH	2	1.8	0	0	0.467
DIC	1	0.9	0	0	0.608

DISCUSSION:

Among 150 babies, 31 had ROP. The proportion of ROP among premature neonates was found to be 21.7%. Various Indian studies show incidence ranging from 17.5% to 46%.

Table 2: Comparison of incidence of ROP with other Indian studies

Indian Study	Gestational age (weeks)	Birth weight (grams)	Incidence (%)
Mantri 2017 ¹⁶	<34	<1500	13.6
Basani 2016 ¹⁷	≤34	≤1750	2.3
Kaul 2021 ¹⁵	<32	<1500	28
Gupta 2014 ¹³	≤35	≤1500	21.7
Chaudhari 2009 ¹	≤32	<1500	22.3
Present study	<36	≤2000	21.7

Supplemental oxygen:

The causal link between ROP and supplemental oxygen has been confirmed by controlled trials and clinical studies.^{11,12} In our study oxygen administration was a significant risk factor for development of ROP (p=<0.001). Of 150 babies, 45 (30%) received supplemental oxygen. 24 of the 45 developed ROP i.e., nearly half of the babies who had received oxygen developed ROP. This correlates well with studies by Gupta et al¹³ and Agarwal et al¹⁴ who also showed that 50% of babies on oxygen developed ROP.

Also it can be noted that of the 31 ROP babies, 24(75.8%) had received oxygen. Since oxygen supplementation has been found as a significant risk factor it is important to have a continuous oxygen monitoring.

Hyperbilirubinemia:

There was a significant (p=0.003) correlation between babies who had hyperbilirubinemia and ROP. Of the total 150 babies, 28 had hyperbilirubinemia. 12 babies (42.3%) among these developed ROP. Similar results were seen in Chaudhari¹ et al study.

A retrospective analysis on preterm babies showed that prolonged phototherapy and variations in serum bilirubin levels contributed to blindness attributable to ROP.¹⁸ Hence more research and multicentric trials are necessary to confirm these associations as important risk factors.

PDA:

In our study, 75% of the babies with PDA had developed ROP suggesting it as a significant (p=0.047) risk factor. Among the very few studies on associations of PDA and ROP the one conducted in New South Wales, Australia, and ROP was seen in 79% of PDA babies.

CONCLUSION:

1. Among the postnatal factors, supplemental oxygen still stands to be the major risk factor. This mandates judicious oxygen supplementation of utmost importance.
2. Other postnatal factors hyperbilirubinemia and patent ductus arteriosus were also found to be significant.
3. Majority of the babies had milder stages of the disease at presentation. Hence frequent follow up is necessary to check for any progression.
4. Despite increasing survival with improved neonatal intensive care, the incidence of ROP does not appear to be increasing.

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