

## An Analysis of Incidence and Risk Factors for Retinopathy of Prematurity in a Tertiary Care Center of Central India

Shalabh Amrawanshi<sup>1</sup>, Sanandan Patel<sup>2</sup>

1(Dept. of Ophthalmology, Bundelkhand Medical College, Sagar, M.P., Medical Science University, Jabalpur, M.P. India)

2(Dept. of Radiation Oncology, Rural Medical College, Loni, Pravara Institute of Medical Sciences India, Loni, Ahamednagar, Maharastra, India)

Corresponding Author: Dr. Sanandan Patel

### Abstract:

**Background:** Retinopathy of prematurity (ROP) is an important cause of childhood visual impairment since the 1940s. Although its incidence and severity have been decreasing in developed countries over the past two decades, both are increasing in developing nations. The aim of this study to analyze risk factors for Retinopathy of prematurity and its incidence, in newborns at risk in SNCU of a tertiary care center of central India.

**Materials and Methods:** Infants with birth weight less than 1500gm and gestation age less than 34 weeks were screened after birth at 4 weeks for ROP or 31-33 weeks post conception age, whichever was later from February 2015 to June 2016. Infants with birth weight 1500gm to 2500 gm and gestation more than 34 weeks with additional risk factors were also screened.

**Results:** The incidence of ROP in this study was 33.70%. Mean birth weight and mean gestational age were significantly low in infants with ROP ( $p$  value  $< 00001$ ). Oxygen supplementation, ventilator support, septicaemia, respiratory distress syndrome, apnoea and asphyxia were found to be significant risk factor for ROP development ( $p$  value  $< 0.05$ ). However single or multiple pregnancies, Blood transfusion and hyperbilirubinaemia were not significant risk factor for ROP development in this study( $p$  value $>0.05$ ).

**Conclusion:** ROP is a multifactorial disease. Timely screening of at-risk neonates and infants can prevent development of advanced ROP which can lead to childhood blindness.

**Key Word:** Oxygen supplementation; respiratory distress syndrome; Retinopathy of prematurity (ROP); Risk factors;

Date of Submission: 18-12-2019

Date of Acceptance: 01-01-2020

### I. Introduction

Retinopathy of Prematurity (ROP) or Terry syndrome, previously known as retrolental fibroplasia is an important cause of preventable childhood visual impairment and blindness after been first described by Terry during an epidemic in 1940s.<sup>1</sup>The WHO'S "Vision 2020 programme" has identified ROP as an important cause of blindness in both high and middle income countries.<sup>2</sup>Retinopathy of Prematurity (ROP) is a proliferative fibro-vascular disorder, affecting the peripheral retinal vasculature in premature infants of low birth weight and young gestational age.<sup>3</sup> The spectrum of outcome findings in ROP extends from minimal sequela with no effect on vision in mild case to bilateral irreversible blindness in advanced case.<sup>4</sup> Many risk factors have been reported to predispose to the development of ROP. Oxygen therapy, gestational age, low birth weight, mode of delivery, respiratory distress syndrome, anemia, double volume exchange, packed cell volume transfusion, septicemia, apnea and clinical sepsis are important risk factors.<sup>5,6,7,9</sup>Recent studies from India report an incidence ranging from 20% to 46%.<sup>8,9,10</sup>

The aim of this study was to find out the incidence of ROP in a tertiary care centre in a developing country. It also attempts to identify the risk factors which predispose to ROP.

### II. Method And Material

A retrospective, observational based clinical study was carried out in newborns admitted in neonatal unit of tertiary care hospital of central india and falling in the inclusion criteria during the study period of one and half years.

#### Inclusion Criteria:

All neonates with

1. Birth weight less than or equal to 1500g

2. Gestational age less than or equal to 34 weeks
3. Neonate with known risk factors for retinopathy of prematurity.

**Exclusion Criteria**

1. Infants with more than 34 weeks of gestational and birth weight more than 1500gms without risk factors.
2. Newborns having family history of exudative vitreoretinopathy, congenital hydrocephalus
3. Parents/ guardians not willing to enrol for study were excluded from the study.

**Sample Size:** 178 eyes of 89 infants were screened for ROP in this study. **Method of Examination:** The initial examination was carried out at 4 weeks after birth or 31 to 33 weeks post conception age, whichever was later. Detailed history was recorded including the gender, gestational age, birth weight, type and mode of delivery. Significant post natal problems such as apnoeic spells, asphyxia, RDS, septicaemia and intraventricular haemorrhages were also noted in prestructured proforma. History regarding need for mechanical ventilation, oxygen support and blood transfusion was also asked.

**Screening:** Parents were explained about the procedure. Initial ocular examination was done without dilating pupil and anterior segment was examined for corneal opacities, non-dilating pupil, persistent tunica vasculosalentis, and plus disease of the iris. Two drops each of 2.5% phenylephrine and 0.5% Tropicamide are instilled at an interval of 15 minutes and a lid speculum was used to open the lids.

Funds examination was performed with an indirect ophthalmoscope and a 20D or 2.2 pan retinal Lens. Posterior pole is examined without depression for plus disease. Sclera depressor is then used to examine the temporal retina followed by nasal retina, to establish the proximity of the retinal vessel at the ora serrate.

After complete examination, speculum was removed gently and antibiotic eye drop was instilled.

**Precaution:** Examination should be carried out after washing hands with beta dine and rinsing with water. Neonatologist should be present while examination is carried out. There should not be over spilling of eye drop. After instilling eye drop, lacrimal punctum should be occluded so as to prevent systemic absorption of drug. Infant should not be fed immediately prior to examination as child may aspirate or vomit.

**Statistic Analysis**

Data was analysed by the Statistical Package for the Social Sciences. Descriptive statistics included the mean and standard deviation for numerical variables, and the percentage of different categories for categorical variables. The incidence rate of ROP was described in simple proportion. Group comparisons were done by the chi-squared ( $\chi^2$ ) test for categorical variables. A probability (P) of less than 0.05 was considered significant.

**III. Results**

The present study was done prospectively at Department of Ophthalmology in a tertiary care centre of central India and study duration was one and half years. The study included 178 eyes of 89 infants in which 49 were male and 40 were female. Birth weight of infants screened ranged from 980 gms to 2600 gms ,mean B.W was 1518.539±397.2989gms. Gestational age range from 28 wks to 35 wks with a mean G.A of 31.39±2.009 wks. Most of the infants screened were single pregnancy (92.13%). Only 7.83% (n=7) were multiple pregnancy (twins/triplet). In this study Out of 178 eyes of 89 preterm infant screened, who had met the inclusion criteria, 60 eyes showed some stage of ROP. Hence, incidence of ROP in this study is 33.70%. (Table 1)

**Table – 1: Patients Characteristics**

Characteristics		Number	%
Sex	Males	49	55.05%
	Females	40	44.94%
	Males (Eyes)	98	55.05%
	Females (Eyes)	80	44.94%
Type of Pregnancy	Single Pregnancy	82	92.13%
	Multiple (Twins/Triplet)	7	7.86%
Gestational Age (weeks)	<=28	11	12.4%
	29-30	18	20.2%
	31-32	39	43.8%
	33-34	16	18.0%
	>=35	05	5.6%
	Mean	31.39±2.009	
Birth weight (grams)	<=1000	04	4.5%
	1001-1499	45	50.6%
	1500-2499	39	43.8%
	>=2500	01	01.1%
	Mean	1518.539±397.2989	
Retinopathy of prematurity	Present (Eyes)	60	33.70%
	Absent (Eyes)	118	66.70%

(ROP)			
-------	--	--	--

**Table – 2: Incidence Of ROP According To Gestational Age**

G.A	TOTAL EYES N=178	ROP N=60	%
</=28	22	16	72.27%
29-30	36	17	47.22%
31-32	78	20	25.64%
33-34	32	7	21.87%
>/=35	10	0	0

With increase in G.A, incidence of ROP decreased in this study.72.72% eyes of 11 infant with G.A </=28 wks and 47.22% eyes of 18 infant (n=36 eyes) with G.A 29-30 wks were found to have ROP on examination. The incidence of ROP reduced further in infants with G.A 31-32 wks and 33-34 wks to 25.64% and 21.87% respectively.No infant with G.A >35 week were found to have ROP. (Table 2)

**Table – 3:INCIDENCE OF ROP ACCORDING TO BIRTH WEIGHT**

BW gm	N=178	ROP	%
</=1000	8	8	100%
1001-1499	90	38	42.2%
1500-2499	78	14	17.9%
>/=2500	2	0	0

With increase in birth weight, Incidence of ROP decreased in this study.All the infants with B.W </= 1000 gm developed some stage of ROP in their eye. Incidence of ROP in infant with B.W 1001-1499 gm and 1500-2499 gm was 42.2% and 17.90% respectively. No ROP was found in infant with B.W >2500 gm. (Table 3)

**Table – 4: Correlation of MEAN Birth Weight and MEAN Gestational Age OF ROP+ and ROP- INFANT**

	ROP+	ROP-	P value
Mean B.W	1321±315.1093 gm	1629.661±373.5506 gm	<.00001
Mean G.A	30.2833±1.9406 wks	31.9576±1.8041wks	<.00001

The mean B.W of ROP + infant was 1321±315.1093 gm. The mean B.W of ROP- infant was 1629.661±373.5506 gm. Using student t test, the t value is -5.48302. The p value is <.00001.

The mean G.A of ROP + infant was 30.2833±1.9406 wks and of ROP - infant was 31.9576±1.8041wks. Using student t test, the t value is -5.70488. The p value is <.00001.Hence the mean B.W and mean G.A. were significantly low in infants with ROP. (Table 4)

**Table – 5: Incidence of ROP according to ICROP Stage**

Stage	ROP (n=60)	%
1	7	11.6%
2	20	33.3%
3	29	48.3%
4	2	3.3%
5	2	3.3%

In this study maximum number of eyes, 48.3% (n=29), were found to have stage 3 on initial examination. 33.3% eyes (n=20) had stage 2. 11.6% eyes (n=7) had stage 1. 3.3% (n=2) had stage 3 and stage 4. (Table 5)

**Table – 6 :Correlation of various risk factors with ROP**

Risk Factor	ROP+	%	ROP-	%	P value
<b>Gestational age</b>					
<32 weeks	53	38.97%	83	61.02%	0.00752
>32 weeks	7	16.66%	35	83.33%	
<b>Birth weight</b>					
<1500 gm	46	46.93%	52	53.06%	0.00036
>1500 gm	14	17.5%	66	82.5%	
<b>Sex</b>					
Male	32	53.3%	66	55.93%	0.741
Female	28	46.6%	52	44.06%	
<b>Pregnancy</b>					
Single	54	90%	110	93.2%	0.4505
Multiple	6	10%	8	6.7%	
<b>Oxygen supplementation</b>					
Present	37	61.66%	43	36.44%	0.0013

Absent	23	38.33%	75	63.55%	
<b>Septicaemia</b>					
Present	24	40%	28	23.72%	0.024
Absent	36	60%	90	76.27%	
<b>Ventilator support</b>					
Present	24	40%	22	18.64%	0.00209
Absent	36	60%	96	81.35%	
<b>Respiratory distress syndrome</b>					
Present	26	43.33%	30	25.42%	0.014
Absent	34	56.66%	88	74.57%	
<b>Hyperbilirubinemia</b>					
Present	22	36.66%	56	47.45%	0.170
Absent	38	63.33%	62	52.54%	
<b>Apnea</b>					
Present	12	20%	6	5.08%	0.0081
Absent	48	80%	112	94.91%	
<b>Blood transfusion</b>					
Present	19	31.66%	29	24.57%	0.313
Absent	41	68.33%	89	75.42%	
<b>Asphyxia</b>					
Present	16	26.66%	16	13.56%	0.031
Absent	44	73.33%	102	86.44%	

Low gestation age (0.00752) and low birth weight (0.000036) were significant risk factor ROP development. However, no difference in ROP was seen in male and female infant in this study. On analysing various risk factors for development of ROP oxygen supplementation (0.0013), ventilator support (0.0029), septicaemia (.024), respiratory distress syndrome (0.014), apnoea (0.0018), asphyxia (0.031) were found to be significant risk factor for ROP development. However there was no significant difference of ROP in single and multiple pregnancies (0.45). Blood transfusion (0.313) and hyperbilirubinaemia (0.170) were also not significant risk factor for ROP development in this study. (Table 6)

#### IV. Discussion

Various studies show ROP incidence to vary from 20% to 46%.<sup>8,10,11</sup> ROP incidence in this study was 33.70%, which was higher than the study done by Gebeşçe A et al (20.1%)<sup>12</sup> Gopal L et al (38%)<sup>13</sup> and Mostafa Feghhi et al (32%)<sup>14</sup> in their study found incidence similar to this study.

There was a significant difference in mean gestation age and mean birth weight of ROP infant in this study ( $p < .05$ ). No difference was found by Shohat M et al<sup>6</sup> in his study. Low birth weight in our study was a significant risk factor for ROP development ( $p < .05$ ). Chaudhari S et al<sup>15</sup> and Sneha R<sup>5</sup> found similar relationship in studies done on Indian population. However Murthy et al<sup>16</sup> and Hakeem K H et al<sup>17</sup> found that L.B.W had no influence ROP. Inverse relationship of incidence of ROP and BW was seen in our study, which was in similar to a study by Qing Liu et al.<sup>18</sup>

In this current study type of pregnancy (single/multiple) was not found to be risk factor ( $p > .05$ ). However Yau GS et al<sup>19</sup> in his study found that infants born from twin pregnancy was at risk for ROP development. Gender of infant was not a significant risk factor for ROP in this study, in contrast to Chaudhary et al<sup>12</sup> who in their study found ROP was more common in male infant.

Use of oxygen and mechanical ventilation in post natal period were significant risk factor for ROP in the current study. Shah et al<sup>7</sup> and Chaudhari et al<sup>15</sup> also reported similar result. Hakeem K H et al<sup>17</sup> in their study found insignificant relationship between ROP and RDS. However in the present study a significant correlation was revealed between them, which was in line with results of Yau GS et al.<sup>19</sup>

Septicaemia was found to be a statistically significant ( $p < .05$ ) risk factor for ROP development in the present study and this agreed with studies of Shah et al.<sup>7</sup> In our study, we found blood transfusion ( $p > .05$ ) to be a non significant risk factor for ROP development, which was in agreement with, Cut Badriah et al.<sup>20</sup> In present study apnoea and Asphyxia were found to be a statistically significant ( $p < .05$ ) risk factor for ROP development. Chaudhari S et al<sup>15</sup> found that apnoea was a significant risk factor for ROP. Shah et al<sup>7</sup> in his study concluded asphyxia as a significant risk factor.

#### V. Conclusion

ROP is a multifactorial disease and is a preventable cause of childhood blindness. In this study Small for gestation, Low birth weight, septicaemia, Oxygen therapy, Ventilator support, Respiratory Distress syndrome, Apnoea and asphyxia were significant factors for ROP development. Since ROP is essentially asymptomatic in the early stages, standards of practice now demand carefully timed retinal examination of at-

risk infants by an ophthalmologist experienced in the examination of the retina, to prevent the development of advanced ROP and serious sequelae leading to complete blindness.

### References

- [1]. Terry TL. Extreme prematurity and fibroplastic overgrowth of persistent vascular sheath behind each crystalline lens. *Am J Ophthalmol* 1942;25:203-4.
- [2]. Gilbert C, Foster A. Childhood blindness in the context of VISION 2020: the right to sight. *Bulletin of the World Health Organization*. 2001 Jan;79(3):227-32.
- [3]. Shah PK, Prabhu V, Karandikar SS, Ranjan R, Narendran V, Kalpana N. Retinopathy of prematurity: Past, present and future. *World J Clin Pediatr* 2016; 5(1): 35-46
- [4]. Ober R.R., Palmer E.A., Drack A.V., Wright K.W.; Retinopathy of Prematurity. In: *Pediatric ophthalmology and strabismus*. Springer, New York, NY; Wright K.W., Spiegel P.H. (eds); 2nd edition, 2003, pp 600-628
- [5]. Sneha R, Poornima Shankar. "A Clinical Study on Incidence of Retinopathy of Prematurity Changes in Preterm Infants and Associated Risk Factors in Tertiary Centre". *Journal of Evolution of Medical and Dental Sciences* 2014; Vol. 3, Issue 10, March 10; Page: 2603-2607,
- [6]. Shohat M, Reischer SH, Krikler R, Nissenkorn I, Yassar Y, Ben-Sira I. Retinopathy of prematurity: incidence and risk factors. *Pediatrics*. 1983 Aug;72(2):159-63.
- [7]. Shah VA, Yeo CL, Ling YL. Incidence, risk factors of retinopathy of prematurity among very low birth weight infants in Singapore. *Ann Acad Med Singapore* 2005;34:169-78.
- [8]. Rekha S, Battu RR. Retinopathy of prematurity: incidence and risk factors. *Indian Pediatr* 1996; 33: 999-1003.
- [9]. Dutta S, Narang A, Dogra MR, Gupta A. Risk factors of threshold retinopathy of prematurity. *Indian Pediatr* 2004; 41: 665-671.
- [10]. Charan R, Dogra MR, Gupta A, Narang A. The incidence of retinopathy of prematurity in a neonatal care unit. *Indian J Ophthalmol* 1995;43(3):123-126.
- [11]. Maheshwari R, Kumar H, Paul VK, Singh M, Tiwari HK. Incidence and risk factors of retinopathy of prematurity in a tertiary care newborn unit in New Delhi. *National Medical Journal of India* 1996;9(5):211-214.
- [12]. Gebeşçe A, Uslu H, Keleş E, Yildirim A, Gürler B, Yazgan H et al. Retinopathy of prematurity: incidence, risk factors, and evaluation of screening criteria. *Turk J Med Sci*. 2016 Feb 17;46(2):315-20.
- [13]. Lingam Gopal, T Sharma, Sudha Ramachandran, R Shanmugasundaram, V Asha. Retinopathy of prematurity. *Indian J ophthalmic A study*. 1995;43(2):59-61.
- [14]. Mostafa Feghhi, Seyed Mohammad Hassan Altayeb, FoadHaghi, Ali Kasiri, et al. Incidence of Retinopathy of Prematurity and Risk Factors in the South-Western Region of Iran. *Middle East Afr J Ophthalmol*. 2012;19(1):101-106.
- [15]. Chaudhari S, Patwardhan V, Vaidya U, Kadam S, Kamat A. Indian Pediatr. Retinopathy of prematurity in a tertiary care centre-incidence, risk factors and outcome. *Indian Pediatr*. 2009 Mar;46(3):219-24.
- [16]. Murthy KR, Nagendra BK et al. Analysis of risk factors for the development of ROP in preterm infants at a tertiary referral hospital in South India. *Acta MedicalLituonica*. 2006;13(3):147-51.
- [17]. Hakeem AH, Mohamed GB, Othman MF. Retinopathy of prematurity: A study of prevalence and risk factors. *Middle East Afr J Ophthalmol*. 2012;19(3):289-294.
- [18]. Qing Liu, Ning Ke, Xin-Ke Chen, Lin Chen, Jing Fang et al. Incidence of Retinopathy of Prematurity in South-western China and Analysis of Risk Factors. *Med Sci Monit*. 2014;20:1442-1451.
- [19]. Yau GS, Lee JW, Tam VT, Liu CC, Chu BC, Yuen CY. Incidence and risk factors for retinopathy of prematurity in extreme low birth weight Chinese infants. *Int Ophthalmol*. 2015;35(3):365-373.
- [20]. Cut Badriah, Idham Amir, Elvioza, Evita KB Ifran. Prevalence and risk factors of retinopathy of prematurity. *Paediatric Indones*. 2012;52(3):138-144.

Dr. Sanandan Patel. "An Analysis of Incidence and Risk Factors for Retinopathy of Prematurity in a Tertiary Care Center of Central India." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, vol. 18, no. 12, 2019, pp 37-41.