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RESEARCH ARTICLE

RISK FACTOR ASSOCIATED WITH RETINOPATHY OF PREMATURITY: A HOSPITAL BASED STUDY

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ABSTRACT

Background: Retinopathy of prematurity (ROP), which was previously called as Retrolental Fibroplasia (RFL), is a vaso-proliferative disorder of the retina. Preterm low birth weight infants are more prone for this disease those are exposed to large amount of Oxygen. **Objectives**: Identify the risk factor which could influence the development of ROP. To study the incidence of ROP in preterm infants with a gestational age of ≤ 32 weeks or a birth weight of less than 1500 grams admitted to NICU for a period of 1 year. To **Methods:** This was a prospective observational study, conducted at NICU, Gauhati Medical College, Guwahati, from 1st July 2017 to 30thJune 2018. **Result**: Out of 347 admission to NICU, 122 satisfied inclusion criteria. 20 babies developed any stage of ROP and 102 babies who did not develop ROP were termed as NON ROP. The mean birth weight among ROP was calculated 1178.70 ±309.513gm and NON ROP was1288.69±148.447gm .Overall incidence of ROP in this study was 16.39%. Statistical analysis showed Birth weight (p<0.001), Gestational age(p<0.016).Oxygen supplementation(p=0.000),Apnea(p<0.001),Sepsis(p=0.009),Anemia needing blood transfusion(p=0.0329), CPAP(P=0.000) were found risk factor for developing ROP. However Surfactant therapy, Mechanical Ventilation and Phototherapy were found insignificant. **Conclusion:** The timely retinal screening in high-risk preterm infants is important to prevent the development of ROP and its complications.

INTRODUCTION

Retinopathy of prematurity (ROP) is a vasoproliferative disorder of the retina among premature babies. ROP begins to develop between 32 and 34 weeks after conception, regardless of gestational age at delivery and has two distinct phases. During the acute first phase, the normal vasculogenesis of the retina is disturbed by the relative hyperoxia of the extrauterine environment. This causes vaso-obliteration and non-vascularization of some areas of the anterior retina. The subsequent hypoxia causes a second chronic phase, characterized by the proliferation of vascular and glial cells, arteriovenous shunt formation, occasionally leading to involution or permanent cicatricial changes and visual impairment. It is the major cause of preventable blindness in infants.Spectrum of ROP is broad and ranges from a spontaneously recovering stage to a vision threatening sequelae. In infants with birth weight less than 1000 grams, the risk of ROP is 82%, and 9.3% of them are potentially under the risk of blindness.[1]

The pathogenic process involved in causation of ROP is multifactorial. It is attributed to many possible risk factors like prematurity, hyperoxia, sepsis, necrotizing enterocolitis, intraventricular hemorrhage (IVH), low birth weight (LBW), prolonged exposure to Oxygen, severity of neonatal illnesses, severe respiratory distress requiring mechanical ventilation, shock, hypoxia, prolonged ventilatory support, need for blood transfusion, acidosis, anemia, high ambient light and vitamin E deficiency.The present study was conducted in Gauhati Medical College, Neonatal Intensive Care Unit (NICU) with the following aims and objectives: To identify the risk factor which could influence the development of ROP. To study the incidence of ROP in preterm infants with a gestational age of ≤ 32 weeks or a birth weight of less than 1500 grams admitted to the Neonatal Intensive Care Unit (NICU), for a period of 1 year.

MATERIAL AND METHODS

Study Design: A prospective observational study.

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***Place of Study**:* The study was conducted at Neonatal Intensive Care Unit (NICU) under the Department of Paediatrics Gauhati Medical College and Hospital.

Duration of Study: Study was carried out for a period of one year from 1st of july 2017 to 30th june 2018.

***Study Population**:* All babies admitted in NICU, Gauhati Medical College and Hospital who were ≤ 32 weeks gestation or with birth weight <1500 grams during study period were screened.

Consent and Ethical Clearance: Informed consent of parents was taken after explaining in detail about procedure involved in the present study. Ethical clearance was obtained.

Inclusion Criteria

- Babies with birth weight <1500 gm
- Babies born at ≤32 weeks of gestation
- Selected preterm infants with a birth weight between 1500 and 2000g or gestational age of more than 32 weeks with sickness like-
- need of cardiorespiratory support
- prolonged oxygen therapy
- apnea of prematurity
- anemia needing blood transfusion and neonatal sepsis or believed by their attending pediatrician or neonatologist to be at high risk.

Exclusion Criteria

- Infants who died before sufficient number of eye examinations could be done to diagnose ROP
- Infants who were lost to follow up before sufficient number of eye examinations could be done to either rule out ROP or see the progression/regression of established ROP
- Congenital cataract, hazy cornea, abnormal anterior chamber.
- Consent not given

Preparation and Precautions

During examination, all the precautions were taken as per the AAP 2013 guidelines.[2] Babies were fed at least one hour before examination to avoid vomiting and aspiration. Hand washing was done and asepsis maintained before examination. Trained person in neonatology was available throughout the procedure in anticipation of any complications.

Dilatation of the pupil: Pupils were dilated with Phenylephrine 2.5% and Tropicamide 0.5%. One drop of Tropicamide was instilled every 10-15 minutes for 4 times starting 1 hour before the scheduled time for examination. This was followed by Phenylephrine, one drop just before examination.

Instruments used: Indirect ophthalmoscope with 20D lens, pediatric wire speculum, scleral indenter.

First Examination and follow up

The first indirect ophthalmoscopic examination was performed in NICU at 3-4 weeks of chronological age or 32 weeks post conceptional age whichever was later by ophthalmologist. If no ROP was detected at initial examination the infants were re-evaluated every 2 weeks until complete vascularization of retina.

Procedure

The Screening of ROP involves indirect ophthalmoscopy using 20D or 28/30D lens by an experienced ophthalmologist. 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 sclera depressor is often used to indent the eye externally to examine areas of interest, rotate and stabilize the eye. Ophthalmological notes should be made after each ROP examination, detailing zone, stage and extent in terms of clock hours of any ROP and the presence of any pre-plus or plus disease. These notes should include a recommendation for the timing of the next examination (if needed) and be kept with the baby's record .Details of ROP were recorded in the proforma as per International Classification of ROP (ICROP) as shown in figure below-

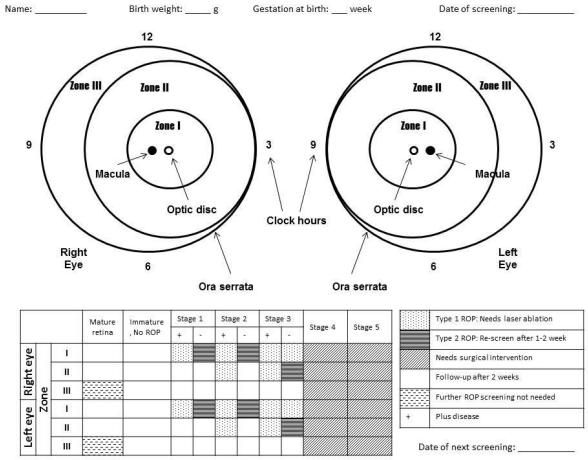

Figure 1 Retinopathy of Prematurity Screening record

Statistical Methods: A prospective analysis was done on the data available to identified risk factors associated with ROP and Non ROP infants. The Excel , INSTAT.EXE, SSPS software (Version 21.0) were used for data entry and analysis. P value <0.05 is statistically significant.

RESULTS AND OBSERVATIONS

Of the total 347 admission to NICU, 122 babies (35.15%) satisfied the inclusion criteria and were enrolled in present study. Neonates who developed any stage of ROP were considered as ROP and the neonates without ROP were considered as NON ROP.

Table 1 Incidence of Rop Among Study Subjects (N = 122)

In the present study, the overall incidence of ROP was 16.36% (20 babies). Among these 15 babies(75.00%) had stage 1 ROP, 1 baby(5.00%) had stage 2, 1 baby(5.00%) had stage 3, 1 baby(5.00%) had stage 1+, 1 baby(5.00%) had stage 2+, 1 baby(5.00%) had stage 3+ respectively.

	Number	Percentage
Non ROP	102	83.60%
ROP	20	16.39%

Stage 1	15	75.00%
Stage 2	1	5.00%
Stage 3	1	5.00%
Stage 1+	1	5.00%
Stage 2+	1	5.00%
Stage3+	1	5.00%

Table 2 Analysis of Neonatal Risk Factors And Rop

Parameter	Response	ROP	NON ROP	P Value
Birth weight in grams	Mean	1178.70	1288.69	<0.001(Significant)
	Standard Deviation	309.513	148.447	
Gestational age (in weeks)	Mean	29.25	30.73	<0.016(Significant)
	Standard Deviation	1.618	1.260	
Oxygen supplementation in days	Yes	19	45	0.000(Significant)
	No	1	57	
Apnea	Yes	13	19	<0.001(Significant)
	No	7	83	
Sepsis	Yes	7	12	0.009(Significant)
	No	13	90	
Anemia needing blood transfusion	Yes	5	6	0.0329 (Significant)
	No	15	96	
Cpap	Yes	13	21	0.000(Significant)
	No	7	81	
Mechanical ventilation	Yes	2	3	0.145(Not Significant)
	No	18	99	
Surfactant therapy	Yes	5	19	0.512 (Not Significant)
	No	15	83	
Phototherapy	Yes	4	22	0.876 (Not Significant)

DISCUSSION

Incidence Rop: The overall incidence of ROP in the present study was 16.39%. The overall incidence of ROP found in various Indian studies and from various international studies were 17.5% to 51.9% and 10.0% to 45.4% respectively.[3, 4 , 5,6]

Table 3 Incidence of Rop In Various Indian Studies

Author / Year	Gestational Age(In Weeks)	Birth Weight(In Grams)	Incidence of ROP
Maheshwari R/1996[3]	<35	<1500	20%
Patil J / 1997[7]	<32	<1250	21.7%
Gupta VP/2004[8]	≤32	≤1700	21.7%
Chaudhari S/2009[9]	≤32	<1500	22.3%
Balakrishnan U/ 2016[10]	≤34	≤1750	18.45
Kumar N /2017[11]	<35	<1500	16.00%
Present study	≤32	<1500	16.39%

Table 4 Showing Incidence of Rop In Various International Studies

International Studies	Gestational Age(In Weeks)	Birth weight(In Grams)	Incidence
Nair P /2003[12]	≤32	≤1500	25.4%
Fortes Filho JB/2009 [13]	<32	<1500	24.2%
Lomuto CC/2010[14]	<32	<1500	26.2%
Mitsiakos G/2016[15]	<32	<1500	15.06%
Yau GS/2016[16]	<32	<1500	18.5%

Significant Risk Factors of Various Studies

Following risk factors were discussed with other studies as follows-

Birth weight and gestation

Table 5

Author/year	Parameter		N0N ROP n	N0N ROP %	ROP n	ROP %	P value
Rao KA/2013[17]	Birth weight(in grams	≤999	14		14		<0.001
		1000-1249	49		23		0.001
		1000-1500	85		17		0.12
		>1500	73		7		-
	Gestational age (weeks)	≤30	38		21		<0.001
		31-32	78		29		0.001
		>32	105		11		-
Shivaprasad B /2014[18]	Birth weight(in grams)	<1000	5	5.7%	5	38.5%	0.001
		1001-1500	42	48.3%	6	46.2%	
		1501-1750	40	46.0%	2	15.4%	
	Gestational age(weeks)	24-28	1	1.1%	4	30.8%	0.000
		28-33	47	54.0%	8	61.5%	
		33-35	39	44.8%	1	7.7%	
Vijayalaxmi Gagandeep/2016[19]	Birth weight(in grams	<1000(3)	1		2		0.002
		1000-1500(149)	119		30		
		>1500(42)	41		1		
	Gestational age(weeks)	≤32	100		28		0.01
		>32	61		5		
Present Study	Birth weight(in grams)	<1000	2	1.96%	6	30%	<0.001
		1000-1499	89	87.25%	12	60%	
		1500-2000	11	10.78%	2	10%	
	Gestational age(weeks)	27	0		2		0.030
		28	4		6		0.0041
		29	15		4		0.7422
		30	20		4		1.000
		31	32		2		0.165
		32	25		1		0.125
		33	6		1		1.000

Other risk Factors Are Discussed With Various Studies As Follows

Oxygen Therapy

Table 6 a

Author/year	Oxygen therapy ROP N	ROP %	NON ROP N	NON ROP %	P value
Rekha S/1996[4]	46		54		0.005
Chaudhuri S/2009[9]		64.5%		39.7%	0.031
Shivaprasad. B/2014[18]	10	76.9%	35	40.2%	0.013
Kumar N/2017[11]	8		25		0.027
Vasavada D/2017[20]	45	83%	140	63%	0.004
Ahuja AA/ 2018[21]	40		12		0.01
Present Study	19		45		0.000

Duration of oxygen therapy

Table 6 b

Author/year	Mean duration of Oxygen(in days) ROP	Mean duration of Oxygen(in days) NON ROP	P value
Shah VA /2005[22]	55.8±75.6	10.4±22.1	0.0001
Freitas AM /2018[23]	27	6	<0.001
Bas AY/2018[24]	65±53	10±23	<0.001
Present study	7.74±2.725	1.50±2.062	<0.001

Mean of Maximum SPO_2

Table 6c

Author/year	ROP		NON ROP		P value
	Mean of Maximum SPO_2(%)	Standard Deviation	Mean of Maximum SPO_2(%)	Standard Deviation	
Shetty SP/2015[25]	97.429	3.780	99.212	1.152	0.01
Present Study	95.26%	1.195	93.56%	2.062	0.001

Apnea

Table 7

Author/year	Apnea				
	ROP		NON ROP		P value
	n	%	n	%	
Rekha S/1996[4]					0.001
Chaudhuri S/2009[9]		38.4%		10.7%	0.0001
Rao KA/2013[17]	10		16		0.03
Shivaprasad B/2014[18]	6	46.2%	7	8.0%	<0.001
Sneha R/2014[26]	7	19.4%	4	7.4%	0.108
Kumar N/2017[11]	1		4		0.797
Present Study	13			19	<0.001

Sepsis

Table 8

Author /year	Sepsis				
	ROP		NON ROP		P value
	n	%	n	%	
Rekha S/1996[4]					0.04
VAShah/2005[22]	42	25.5%	32	8%	0.0001
Chaudhuri S/2009[9]		22.0%		11.4%	0.001
Rao KA/2013[17]	7		19		0.03
Kapoor R/2014[27]	13	35.1%	24	64.9%	0.0001
Sneha R/2014[26]	17	31.4%	18	50%	0.122
Shivaprasad B/2014[18]	6	46.2%	8	9.2%	<0.001
Kumar N/2017[11]	6		26		0.68
Freitas AM/2018[23]	165	83.5%	285	71.6%	0.001
Present Study	7	35%	12	11.76%	0.009

Anemia Needing Blood Transfusion

Table 9

Author/year	Blood transfusion				
	ROP		NON ROP		
	n	%	n	%	P value
Al-Essa M/1999[28]	55	93%	56	79%	0.025
Chaudhuri S/2009[9]		23.6%		14.2%	0.125
Rao KA/2013[17]	13		17		0.002
Present Study	5	25%	6	5.88%	0.0329

CPAP

Table 10

Author/year	CPAP				
	ROP		NON ROP		P value
	n	%	n	%	
Chaudhuri S/2009[9]		68.9%		67.4%	0.578
Shivaprasad B/2014[18]	3	23.1%	15	17.2%	0.000
Present Study	13	65%	21	20.59%	<0.001

Mechanical Ventilation(MV)

Table 11

Author/year	Mechanical Ventilation				
	ROP		NON ROP		P value
	n	%	n	%	
ChaudhuriS/2009[9]		41.7%		24.8%	0.031
Chen M/2011[29]	48		20		0.0106
Vijayalaxmi Gagandeep/2016[19]		5	16		0.365
Present Study	2	10.0%	3	2.94	0.145

Surfactant Administration

Table 12

Author/year	Surfactant therapy				
	ROP		NON ROP		P value
	n	%	n	%	
VA Shah/2005[22]	41	24.9%	59	14.8%	0.037
Vander Merwe SK/2013[30]	7	50%	110	33.5%	0.2035
Kumar N/2017[11]	1		7		0.768
Dhillon SP /2017[31]	1		2		0.447
Present Study	5		19		0.512

Phototherapy

Table 13

Author/year	Phototherapy				
	ROP		NON ROP		
	n	%	n	%	P value
Al-Essa M/1999[27]	56	95%	60	84.5 %	0.08
Sneha R/2014[26]	22	61.1%	24	44.4	0.137
Vijayalaxmi Gagandeep/2016[19]	12		59		0.876
Dhillon SP/2017[31]	3		19		0.598
Present Study	4		22		

The present study was discussed with various other studies as mentioned in above tables.The present study correlates well with other studies. Mechanical Ventilation, Surfactant therapy and phototherapy were not found statistically significant risk factors of ROP in present study.

CONCLUSION

The incidence of ROP in present study was 16.39%. A treatment was performed in 20% of ROP cases. ROP remains a major complication in pre-mature newborns despite all the advances that have been made in recent years. The excellence in neonatal care, screening and early treatment of ROP are keys to prevent vision loss induced by this disease. It is mandatory to do ophthalmological check up of those newborns who have satisfied the criteria.

In present study the most significant risk factors to development of ROP were low birth weight, low gestational age, need for oxygen therapy, neonatal sepsis, apnea of prematurity, need of cardiopulmonary support (CPAP), and anemia needing blood transfusion. However, phototherapy, use of surfactant, MV were not seen significantly associated with ROP in present study.

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