Original Research Article **Allied Science**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

INCIDENCE AND RISK FACTORS OF RETINOPATHY OF PREMATURITY

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ABSTRACT

The objective of the study was to find out the incidence of Retinopathy of Prematurity (ROP) in preterm babies < 35 weeks and or low birth weight babies <1750 gm and to identify risk factors which could influence the development of ROP. All babies born in our hospital who were <35 weeks gestation or with birth weight <1750 grams admitted to our NICU during the study period were screened for ROP. Relevant patient data including maternal and neonatal risk factors, problems during NICU stay were recorded. Ophthalmoscopic examination was performed at 3-4 weeks of chronological age or 32 weeks post conceptional age and later based on stage of ROP. Out of the 138 preterm babies (eligible for screening) 100 babies could be registered and completed follow-up. The incidence of ROP in study group was 13%. Out of 13 babies who developed ROP, 6 were in stage – 1, 3 were in stage – 2 and 2 were in stage – 3 and 2 in stage 3 with plus disease. On univariate analysis of risk factors lower gestational age, lower birth weight, exposure to oxygen, RDS, hyperoxia>100mmHg, hypoxia <40mmHg, apnea, sepsis, PDA, shock anemia, IVH, ventilation were statistically significant. The incidence of ROP among babies with gestational age <35 weeks or birth weight <1750 gms was 13%. The main risk factors associated with ROP are lower gestational age, lower birth weight, exposure to oxygen, RDS, hyperoxia (>100 mmHg), hypoxia(<40mmHg), apnea, sepsis, PDA, shock, anemia, IVH, ventilation as noted on univariate analysis of risk factors from this study.

KEY WORDS: PREMATURITY, HYEROXIA, RISK FACTORS

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INTRODUCTION

Retinopathy of Prematurity (ROP) is a vasoproliferative disorder of retina among premature low birth weight infant[1] Out of the approximate 26 million annual live births in India, approximately 87% of newborn in India are <2000g in weight[2]. The incidence of ROP in India is reported to vary between 38 – 51.9% in low birth weight infants[3,4]. Research has identified several factors which have been shown to have some casual association with ROP. However, three factors that have consistent association are low gestational age, LBW, prolonged exposure to oxygen. Other putative risk factors include mechanical ventilation, anemia needing blood transfusion, sepsis, apnea, IVH, hyperbilirubinemia, phototherapy, male gender, poor postnatal weight gain, surfactant therapy, PDA, hyperglycemia, maternal risk factors etc[5], which need further study. The utility of identification of risk factors has implication in prevention, prediction of severity and management. Thus the purpose of this study was to know the incidence and the risk factors for ROP in our level III neonatal unit.

Objectives of the study

To find out the incidence of ROP in preterm babies < 35 weeks and or low birth weight babies < 1750 gm. To identify risk factors which could influence the development of ROP

MATERIALS AND METHODS

Study Design

A prospective observational study.

Place of Study

The study was conducted at NICU and neonatal follow up clinic of tertiary teaching hospital.

Duration of Study

Study was carried out during April 2012 to April 2013

Study Population

All babies born in our hospital who were less than 35 weeks gestation or with birth weight <1750 gram admitted to our NICU during study period were screened.

Inclusion criteria

Babies born < 35 weeks gestation Babies with birth weight < 1750 grams

Exclusion Criteria

Babies who died before they could be examined or before full vascularization of retina

Babies who did not complete follow-up for other reasons

Babies with other ocular defects, congenital retinal abnormalities

Consent and Ethical Clearance

Informed consent of parents was taken after explaining in detail about the procedure involved in this study. Ethical clearance was obtained.

METHODS

Relevant patient data including maternal and neonatal risk factors, problems during NICU stay were recorded and entered into prepared proforma. Eligible candidates were subjected for ROP screening.

Screening

Preparation for Examination

Pupils were dilated using 2.5% phenylephrine and 0.5% tropicamide eye drops, instilled three times in each eye at intervals of 15 minutes about 1 hour before the scheduled examination.

Instruments used

Indirect ophthalmoscope with 20 D 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 an ophthalmologist. If no ROP was detected at initial examination the infants were reevaluated every 2 weeks until complete vascularization of retina. If ROP was detected follow up examination was based on stage of ROP[6,7] .

Procedure

All aseptic precautions were taken. First the posterior pole was visualized for plus disease, then peripheral retina was examined to look for the extent of the changes. Details of ROP were recorded in the proforma as per International Classification of ROP (ICROP).

Statistical Methods

A prospective analysis was done on the data available from the cohorts to identified risk factors associated with ROP and Non ROP infants. The associations between potential related risk factors with ROP were studied initially through a Univariate analysis. The categorical variables were assessed using Pearson chisquare. The variables were included if their respective Univariate analysis yielded P value <0.10. Statistical tests were carried out at 5% level of significance. The Excel and SPSS (SPSS Inc, Chicago) software packages were used for data entry and analysis.

RESULTS

During the study period total of 398 admissions were made in NICU. Among them 138 were preterm with gestational age of 35 weeks and birth weight less than 1750 grams. Out of the 138 babies 100 babies could be registered and completed follow-up. 30 infants met criteria but lost to follow up. 8 babies expired. The incidence of ROP in study group was 13%. Among the 13 cases of ROP, stage 1 was comprising highest number of cases and stage 3 plus disease found in 2 cases who underwent laser therapy(Table-1). Risk of ROP was highest in lower birth weight and lesser gestational age and it was statistically significant as noted in table 2. Maternal factors were not statistically significant in relation to risk of ROP in babies as shown

in table 3.Many neonatal risk factors were statistically significant in causing ROP like hypoxia, hyperoxia, RDS, apnea, sepsis, PDA, shock, anemia, IVH, oxygen, ventilation as shown in table 4.

Table 1: Incidence of ROP according to ICROP stages and zones

Stages and zones	ROP (n = 13)	
	n	%
Stage 1	6	46.2%
Stage 2	3	23.1%
Stage 3	2	15.4%
Stage 3+	2	15.4%
Stage 4	-	-
Stage 5	-	-
Zone 2	8	38.5%
Zone 3	5	61.5%

Table 2: Analysis of basic risk factors

Parameters	Response	ROP				X^2 value	P value
		Non ROP		ROP			
		n	%	n	%		
Gender	Male	43	49.4%	7	53.8%	0.088	0.766
	Female	44	50.6%	6	46.2%		
Birth weight (gms)	< 1000	5	5.7%	5	38.5%	14.635	0.001
	1001-1500	42	48.3%	6	46.2%		
	1501-1750	40	46.0%	2	15.4%		
Gestational age	24 – 28 wks	1	1.1%	4	30.8%	23.861	.000
	28 – 33 wks	47	54.0%	8	61.5%		
	33 – 35 wks	39	44.8%	1	7.7%		

Table 3: Analysis of Maternal obstetric factors and ROP

Parameters	Response	ROP				X^2Value	p' value
		Non ROP		ROP			
		n	%	n	%		
DM	No	83	95.4%	13	100.0%	0.623	0.430
	Yes	4	4.6%	0	0%		
PIH	No	42	48.3%	4	30.6%	1.395	0.237
	Yes	45	51.7%	9	69.2%		
PROM	No	80	92.0%	12	92.3%	0.002	0.965
	Yes	7	8.0%	1	7.7%		
AN.STEROID	No	42	48.3%	8	61.5%	0.796	0.372
	Yes	45	51.7%	5	38.5%		
Mode of delivery	No	36	41.4%	3	23.1%	1.593	0.207
	yes	51	58.6%	10	76.9%		

Table 4: Analysis of neonatal risk factors and ROP

Parameter	Response	ROP				X^2 value	P value
		Non ROP		ROP			
		n	%	n	%		
Hypoxia	No	86	98.9%	8	61.5%	27.918	<0.001
	Yes	1	1.1%	5	36.5%		
Hyperoxia	No	83	95.4%	3	23.1%	49.138	<0.001
	Yes	4	4.6%	10	76.9%		
RDS	No	82	94.3%	5	38.5%	31.127	<0.001
	Yes	5	5.7%	8	61.5%		
Apnea	No	80	92.0%	7	53.8%	14.522	<0.001
	Yes	7	8.0%	6	46.2%		
Sepsis	No	79	90.8%	7	53.8%	12.831	<0.001
	Yes	8	9.2%	6	46.2%		
PDA	No	87	100.0%	9	69.2%	27.885	<0.001
	Yes	0	.0%	4	30.8%		
Shock	No	86	98.9%	11	84.6%	7.876	0.005
	Yes	1	1.1%	2	15.4%		
HB	No	17	19.5%	1	7.7%	1.076	0.300
	Yes	70	80.5%	12	92.3%		
PT	No	18	20.7%	1	7.7%	1.241	0.265
	Yes	69	79.3%	12	92.3%		
Anemia	No	86	98.9%	5	38.5%	50.361	<0.001
	Yes	1	1.1%	8	61.5%		
IVH	No	86	98.9%	11	84.6%	7.876	0.005
	Yes	1	1.1%	2	15.4%		
O2	No	52	59.8%	3	23.1%	6.153	0.013
	Yes	35	40.2%	10	76.9%		
Ventilation	C	15	17.2%	3	23.1%	45.139	<0.001
	M	5	5.7%	1	7.7%		
	C+M	0	0.0%	6	46.2%		
	No	67	77.0%	3	23.1%		
APGAR 1min	<6	8	9.2%	1	7.7%	0.031	0.860
	>=6	79	90.8%	12	92.3%		
APGAR 5min	<6	0	0.0%	0	0.0%	-	-
	>=6	87	100.0%	13	100.0%		

DISCUSSION

ROP continues to be an important cause of potentially preventable blindness worldwide. During the study period 398 babies were managed in our NICU out of which 138 were premature <35weeks or weight<1750gms.

Incidence of ROP

The incidence of ROP in the present study is 13%.Various studies have shown that about 9.4 – 38% of babies with gestational age 32 or less develops some degree of ROP. Studies in literature usually use a cutoff point of birth weight of 1250 or 1500 or 1750 grams a gestational age of 28 or 32 or both. Using a birth weight of 1750 or less and gestational age of <35 weeks or both as inclusion criteria explains the lower incidence of ROP (13%). Similar results were shown by a study done by Conrath[8] et al (9.4%). The other Indian studies demonstrated slightly higher incidence Chaudhuri[13] *et al*. (22.3%) and Agarwal[10] et *al*. (32%) . In our Study Stage-I ROP was found in 46.2%, Stage 2 ROP was found in 23.1% and Stage 3 in 15.4% and stage3 with plus disease in 15.4%. Most cases had similar ROP in both eyes. Incidence of severe ROP in our study was 2% of the babies screened. The incidence of severe ROP varies from 4.8% to 23% in other Indian Studies and 4 – 16% in international studies. The incidence of severity was less compared to other studies. The decreased incidence in the present study could be attributed to the use of surfactant, continuous pulse oximetry, improved neonatal nutritional support, judicious use of oxygen and rigid blood transfusion policies. The difference seen in the study could also be due to low survival of extreme preterm babies, limited sample size and loss of follow up. In our study 2 infants had severe disease and received laser therapy with success rates of 100%.

Neonatal risk factors

Though accumulating evidence indicates that ROP is a multi factorial disease, immaturity of retina and a period of hyperoxia are the main contributing etiological factors in pathophysiology of ROP. In our study the incidence

of ROP was significantly inversely proportional to both birth weight and gestational age (p<0.001).Flynn[9] *et al*. reported that during acute care of sick preterm neonate, ROP is more likely to develop if partial pressure of oxygen is more than 80 mm Hg. In our study hyperoxia more than 100mm Hg was shown to be associated risk factor among ROP infants (p<0.001). Mean Fio2 among ROP infants was noted to be 45%. In our study lower gestational age, lower birth weight, exposure to oxygen RDS, hyperoxia>100mmHg, hypoxia <40mmHg, apnea, sepsis, PDA, shock anemia, IVH, ventilation were found to be statistically significant on univariate analysis. Agarwal[10] *et al*. study had showed that birth weight < 1500, GA< 35, RDS < 0.05, Apnea(p<0.001), Sepsis (p<0.01), Oxygen (p<0.01), Ventilation (p<0.05) blood transfusion (p<0.01) were significant risk factors for development of ROP. Bassiouny[15] *et al*. reported lower birth weight, lower gestational age, apnea, blood transfusion / mechanical ventilation, metabolic acidosis, total parental nutrition, intra ventricular hemorrhage, sepsis were associated with development of ROP.

Maternal obstetric factors

Holmstrom[11] G *et al*. in a population based study had suggested maternal risk factors associated with ROP. In our study maternal obstetric factors such as preeclampsia, diabetes mellitus, prolonged rupture of membranes, mode of delivery were studied, none of these factors showed statistically significant correlation. Antenatal steroids have been reported to reduce the incidence of ROP as reported by Blair[14] *et al*. and Smith[12] *et al*. In our study out of 13 infants who developed ROP 5 mothers (38.5%) had received steroids and 8 mothers (61.5%) had not received steroids, however it was not statistically significant.

CONCLUSION

The incidence of ROP among babies with gestational age <35 weeks or birth weight <1750 gms was 13% .The main risk factors associated with ROP are lower gestational age, lower birth weight, exposure to oxygen, RDS, hyperoxia (>100 mmHg), hypoxia (<40mmHg), apnea, sepsis, PDA, shock, anemia, IVH, ventilation as noted on univariate analysis of risk factors from this study. Maternal risk factors like Pre-eclampsia, diabetes, prolonged rupture of membranes, antenatal steroids were not statistically significant risk factors for ROP.

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