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ASSOCIATED RISK FACTORS OF RETINOPATHY OF PREMATURITY AND ITS INCIDENCE IN A TERTIARY CARE TEACHING HOSPITAL OF EASTERN UTTAR PRADESH.

Ophthalmology

Dr. Alka Gupta* Assistant Professor, Department of Ophthalmology, Hind Institute of Medical Sciences, Safedabad Barabanki, Uttar Pradesh *Corresponding Author

Dr. Ashutosh Rastogi Consultant Ophthalmologist , Sun Eye Hospital Lucknow

Dr. Astha Trivedi Senior Resident, Department of Ophthalmology, Hind Institute of Medical Sciences, Safedabad, Barabanki, Uttar Pradesh

ABSTRACT

Purpose: To find out incidence of ROP in high risk babies admitted to neonatal units and in whom who attended eye OPD, and to study common risk factors for its development. **Methods:** Detailed ophthalmic examination including history regarding risk factors was documented of all Infants of < 35 weeks or <1500 gram admitted to neonatal units of HIMS Safedabad , Barabanki or attended eye OPD during July 2021 to june2022 and they were followed till full maturation of retina. **Results:** Twenty four out of eighty nine {26.9%) children were diagnosed with ROP. Low gestational age and low birth weight were common risk factors among cases that developed ROP: association of ROP with oxygen therapy, blood transfusion, multiple pregnancy, phototherapy, hyperbilirubinemia, and preterm labour found insignificant. **Conclusion:** As survival of preterm infants increases because of better neonatal care and well equipped setup, ROP will become increasingly important potential cause of blindness. This emphasizes the critical need for ophthalmologic examination in premature infants, with immediate initiation of treatment when ROP is diagnosed.

KEYWORDS

Retinopathy of prematurity (ROP), high risk babies, ROP blindness

INTRODUCTION

ROP, a vasoproliferative disorder of the retina in premature and very low birth weight infants, is a potentially blinding but preventable disease. The condition was first described by Terry in 1942 as retrolental fibroplasia.[1,2]

Recently, a multicentre trial on cryotherapy for ROP has demonstrated that cryotherapy of the peripheral retina reduces by half the incidence of an unfavourable outcome [1, 3,4,5,6] and this has renewed the interest in screening for ROP.

Among high risk populations in India, the incidence of ROP is between 20 and 47.27% [1, 7,8,9,10]. Currently recommended guidelines are based on birth weight of <1501 g or a gestational age of 30 weeks or less[11].

The international classification of retinopathy of prematurity revisited"[12, 13] should be used to classify, diagram, and record these retinal findings at the time of examination.

We conducted this prospective study to screen the high-risk premature neonates, with the main purpose to investigate the incidence of ROP and to determine the possible risk factors associated with the development of ROP.

Good screening can work miracles as it targets all "at-risk"babies and can easily be performed in the field.

MATERIALS AND METHODS

Location of the study:
Hind institute of medical sciences level 3 Hospital and research Center Safedabad, Barabanki

Study period: 12 months from July 2021 to June 2022

Study design: it was a hospital based prospective study

Method of data collection

Eye examination schedule:
As per the guideline given by American academy of paediatrics [12, 14] in 2006 following protocol is suggested for screening of infants for ROP. Infants with a birth weight of less than 1500 g or gestational age of 32 weeks or less.

The initial examination was carried out between 2nd and 4th week after birth using +20D lens by ophthalmologist at HIMS, Safedabad, Barabanki.

Eye examination method:
Pupillary dilatation was done with a mixture of 2.5%phenylephrine and 0.4%tropicamide instilled twice at intervals of 15 minutes, dilution done with methylcellulose eye drops.

Firstly a quick flashlight evaluation of adnexa and anterior segment (to rule out any congenital ocular anomaly) was done before instilling the dilating drops. While awaiting dilatation over the next 10-15 minutes, all the data about the baby was obtained

A condensing lens of +20 D was used for this purpose. The anterior segment is first examined with the +20 D condensing lens focused on the cornea, iris, pupil and lens to look for any media opacity, tunica vasculosa lentis or dilated tortuous iris new vessels. Any evidence of plus disease, vascular loops or retinal avascularity is ruled out. First the nasal periphery should be examined till the oraserrata. Complete vascularisation of the nasal periphery with the avascular area in the temporal periphery would qualify the disease for zoneIII.

Identification of risk factors:
Prospective collection of the data was done for each patient, and the following risk factors were examined. The perinatal variables documented included presence of foetal distress, antepartum haemorrhage, preeclampsia (PE), prolonged rupture of membranes (PROM), maternal pyrexia and maternal betamethasone and beta agonist use.

Infants in whom ROP was detected were followed every week. Before moving we explain the disease status to neonatologist and parents. Treatment followed the protocol used in the ETROP study[15].Treatment generally accomplished, when possible, within 72 hours of determination of treatable disease to minimize the risk of retinal detachment, or on follow-up.

Cryotherapy or laser treatment for threshold ROP was done. Babies were then seen weekly until the regression of the disease.

Statistical analysis:
Statistical analysis was performed using the statistical package for social sciences (SPSS) V-18 programme. Univariate comparison of risk factors between the groups with or without ROP was done using the Chi-square test and student 't'test with appropriate significance of $p<0.05$.

RESULTS AND OBSERVATIONS:

Three hundred and sixty-five babies with birth weight of ≤1500gm and

gestational age of ≤32 weeks admitted to neonatal units of the Hind institute of medical sciences, level 3 hospital and research center, Safedabad, Barabanki from July 2021 to June 2022 were enrolled into the study .Two hundred seventy six babies were excluded from the study because one of them died and other lost follow up before full vascularisation of the retina.

Sex distribution in the study

Table1 Incidence of ROP by patient gender

Sex	No of babies	No of ROP babies	% of babies with ROP
Male	64	17	26.5%
Female	25	7	28.0%
Total	89	24	26.9%

The difference of ROP incidence between the male and female babies was not statistically significant. (p= 0.891)

Incidence of ROP by gestational age

The incidence of ROP in babies with gestational age of less than 28 weeks was 70%, 27.4% in babies between 28 to 32 weeks and 10.7% in babies with gestational age more than 32 weeks.

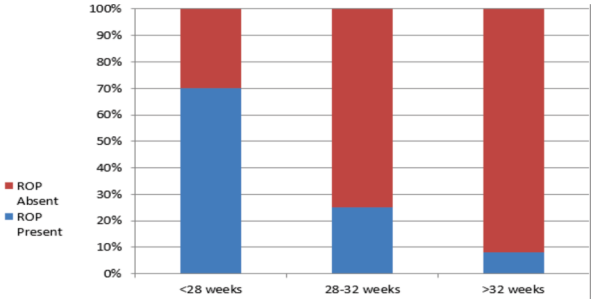

Fig 1 gestational age vs incidence of ROP

The Pearson chi square significant (p) value was .001 i.e. <.05.Thus the association is not due to chance i.e. it is statistically significant.

Incidence of ROP by Birth weight

The incidence of ROP in babies with birth weight of <1200 gram was 42.4%, 21.9% in babies between 1200.1500 grams and 6.6% in babies with gestational weight more than 1500 grams. (fig 2)

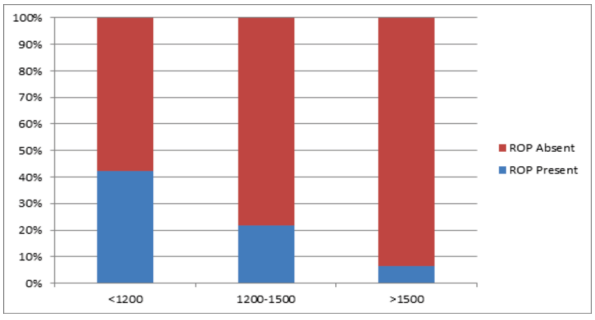

Fig: 2 Birth weight vs incidence of ROP

The Pearson chi square significant (p) value was 0.022 i.e. <0.05. Thus the association is not due to chance or in other word it is statistically significant.

Supplemental oxygen and ROP

Out of 89 babies in the study, 68 had received oxygen (76.4%).of 65 babies in whom ROP was absent, 53 had received oxygen. Among 24 babies who had ROP only 15 had received oxygen during their NICU stay.

Supplemental oxygen administration was an insignificant risk factor in the development of ROP (p>0.05)

Phototherapy and ROP

Eighty-one out of 89 babies had received phototherapy in present study. Of 24 babies with ROP, 20 babies (83.3%) had received phototherapy. Of 65 babies who had no ROP, 61 (93.8%) had received phototherapy.

Present study did not show any significant association between phototherapy and ROP (p >0.05)

Exchange transfusion and ROP:

Thirteen out of 89 babies had exchange transfusion in present study. Of 24 babies with ROP, 6 babies (25%) had received exchange transfusion. Of 65 babies with no ROP, 7 babies (10.7%) had exchange transfusion.

Exchange transfusion was found to be a significant factor in development of ROP on univariate analysis (p value<0.05%)

Hyperbilirubinemia and ROP

Sixty –two out of 89 babies had hyperbilirubinemia in present study. Of 24 babies with ROP, 14 babies (58.33%) had hyperbilirubinemia. of 65 babies who had no ROP, 48(73.84%) had hyperbilirubinemia.

Present study did not show any statistically significant association between hyperbilirubinemia and ROP (p > 0.05)

Respiratory distress syndrome and ROP

Three babies presented with respiratory distress all three babies had ROP. RDS was found to be significant risk factor for development of ROP (P< 0.05)

Multiple pregnancy and ROP

Present study had 12 cases of multiple pregnancy; five of them had ROP There was no reliable difference in ROP between multiple pregnancy and singletons (p>0.05)

Preterm Labor and ROP

Preterm labor was found in 43 mothers in the study. Among 24 babies who had ROP, 11 (45.8%) mothers had preterm labor.Preterm labor was not a statistically significant factor in the development of ROP (p>0.05)

Mode of delivery and ROP

Present study group had 12 mothers who had delivery by LSCS. Five babies born to this group of mothers had ROP. Of 77 mothers who had normal vaginal delivery, 19 babies had ROP.

Pregnancy induced hypertension and ROP

Our study group had 12 mothers who had pregnancy induced hypertension. None of the babies born to this group of mothers had ROP. Of 24 babies with ROP, none of the mothers had hypertension. Of 65 babies who had no ROP, 12 mothers (18.4%) had hypertension.

Prolonged rupture of membrane and ROP

There were 44 mothers who had prolonged rupture of membranes (PROM) in this study group. Of 24 babies with ROP, PROM was found in mothers of 8 babies (33.3%).of 65 babies with no ROP, PROM was seen in 36 babies (55.3%)

Present study found no association between development of ROP and any of the maternal risk factors like PROM, PIH, PTL and multiple pregnancy.

Number of babies and different stages of ROP

The incidence of ROP in the present study was 26.9 %(24 out of 89 babies had ROP.).All the babies except 1 had a bilateral disease. Stage 1 was seen in 6 babies, stage II was seen in 9 babies,stageIII in 7 babies, one baby had stage 1Va and one baby had 1Vb disease.1 baby had zone 1 disease, zone 2 disease was seen in 18 patients, and 5 had zone 3 disease.(Table 2)

Stages of ROP	Number of Babies	% of Babies
Stage 1	6	25.0
Stage II	9	37.5
Stage III	7	29.2
Stage IV	2	8.3
Stage V	0	0

Out of 24 babies, plus disease was found in 18(75.0%) babies. In this study all infants with plus disease had a birth weight less than 1500 gram except one baby of birth weight of 1700 who is having birth weight of 1700 who is having stage 2 with plus disease. Stage 2 disease in 8 babies and stage 3 disease in 6 babies were associated with plus disease. Two of the babies with stage 1 ROP had plus disease.

Mean gestational age of ROP and Non ROP babies

The mean gestational age of ROP babies varied from 24 to 36 weeks.

The mean gestational age of the ROP babies was 29.0±2.87 weeks, whereas the mean gestational age of the non ROP babies was 30.8± 2.59 weeks. ROP babies were almost 2 weeks younger than non ROP babies (table3)

ROP Present or absent	Mean	N	Std Deviation	Median	Minimum	Maximum
No	30.8	65	2.59	30	27	34
Yes	29	24	2.87	28.5	24	36
Total	30.35	89	2.78	30	24	36

Mean Birth weight of ROP and non ROP babies

The birth weight of ROP babies varied from 650 to 1700 grams. The mean birth weight of the ROP babies was 1174.1± 286.6 gram, whereas the mean birth weight of the non ROP babies was1423.7 ± 418.0 grams. Non ROP babies were almost 300 grams heavier than ROP babies (table 4)

ROP Present or absent	Mean	N	Std deviation	Median	Minimum	Maximum
No	1423.7	65	418	1500	600	2300
Yes	1174.1	24	286.6	1124	650	1700
Total	1356.4	89	401.2	1500	600	2300

Student "t" test

Cross tabulation procedures revealed significant association between gestational age vs ROP and birth weight vs ROP. Student t was performed to compare the mean gestational age and mean birth weight for the two groups one with ROP and other without ROP (table 5)

Table 5. Independent sample't' Test for comparison of means with ROP and without ROP

	T	Df	Significance (2-tailed)	Mean Difference	Std Error Difference	95%cofidance interval of the difference Lower	upper
Ges.age in weeks	2.90	87	0.00	1.85	.64	.58	3.11
Birth weight in grams	2.70	87	0.01	249.61	92.59	65.59	433.63

This revealed that difference in gestational age in weeks between the subjects with and without ROP which found to be statistically significant (p=0.00).similarly the difference of birth weight between two groups with or without ROP was found to be significant (0.01)

Table 6. Individual risk factors and their univariate analysis

Risk Factor	Total babies	Babies with ROP	p-value Significance
GES.AGE <28 wks 28-32wks >32 wks	 10 51 28	 7 14 3	S
BIRTH WT <1200g 1200g-1500g >1500g	 33 41 15	 14 9 1	S
PIH	12	0	Ns
PROM	44	8	Ns
PRETERM LABOR	43	11	Ns
MULTIPLE BIRTHS	12	5	Ns
OXYGEN THERAPY	68	15	Ns
EXCHANGE TRANSFUSION	13	6	Ns
HYPERBILIRUBINEMIA	62	14	Ns
PHOTOTHERAPY	81	20	Ns
RDS	3	3	S

DISCUSSION:

The impact of ROP on vision in the premature infant has been well appreciated since the early report by terry (1942)[2]

The frequency of ROP varies from 16 to 60% around the world. Table7 compares the incidence of ROP in the present study with other studies.

Table 7.comparison of different studies regarding incidence of ROP

Study name	Criteria	Number	Percentage
Ng et al(uk) 16	<1701	505	60.1%
Bassiouny et al 17	<1501	73	34%
Hussain et al 18	<1800	950	21.3%
Shah et al 19	≤1500	564	29.2%
Charan et al 1	≤1700	165	47.2%
Gopal lingam et al 20	≤2000	50	38%
Rekha s et al 8	<1500	100	46%
Maheswari et al 7	<1501	66	20%
Murthy et al 21	≤1750	50	24%
Present study	≤1500	89	26.9%

The incidence of ROP in the present study is 26.9%, nearly similar to the 20% incidence Maheshwari et al [7], Murthy et al [21] 24%, 29.2% in Singapore study [19] and Hussain et al [18] 21.3% The possible causes may be [22]

1. Very high infant mortality rate in up 43/1000 in comparison to national figure of 27 /1000(2022)
2. High fall outs from the study(average follow up period is only 2.6 weeks)
3. Poor health awareness, low education and high number of non-institutional deliveries.so, either the baby dies or lost to follow up before full vascularisation of retina.

Risk factors

In babies of ≤1500 g in present study the incidence was 26.9%.There was a high rate of blindness in spite of widening our inclusion criteria for screening.

This can be explained by the poor compliance for follow up by the parents who could not recognize blindness in their babies. This can be avoided by more frequent eye examination and by not discharging any suspicious cases from the hospital during the early stages of ROP.

Birth weight

Retinopathy of prematurity was reported in India over a decade ago.[1,20] While the babies who developed ROP in the present study population had significant lower birth weight (p=0.02) comparable to other studies, [1,7,19,20] we still were not able to predict which of these babies would eventually develop severe ROP. The Cryo-ROP study [23] also did not report a significant difference in the mean birth weight for the various stages of ROP. These facts highlight the importance of surveillance programme for all babies in present study population.

Gestational age

Age of onset of ROP The importance of the clinical screening of high risk premature infants has been confirmed because of the improved clinical outcome in infants with acute active ROP after cryotherapy or transpupillary laser therapy.[3,4]

The American academy of paediatrics, the American association of paediatric ophthalmologist and strabismus and American academy of ophthalmology released a joint statement recommending that the initial screening examination be performed between 4 and 6 weeks of chronological age or 31 to 33 weeks postconception.

In present study, maximum yield of diagnosis of ROP was at a median of 28.5 weeks corrected age (range, 24 to 36) the timing of retinal vascular events of ROP correlated with more closely with the post conceptional age than the chronological age.

Oxygen therapy

Present study did not specify the concentration and duration of oxygen therapy used in the babies. However, oxygen therapy is no longer the only and most important factor for the development of ROP. The cause of ROP is multifactorial, of which oxygen therapy is only one of the factors.

Respiratory distress syndrome

Similar to other studies, [21,24] present study shows significant association (p=0.003) between RDS and ROP, but finding is unreliable because of small sample size.

Preterm labour

No significant association found with preterm labour and ROP in our

study (p=0.77) Among the significant risk factors (Table 6) stronger association seen with gestational age.

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