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Incidence and Risk Factors Predisposing to Retinopathy of Prematurity and Treatment Outcome: A Retrospective Cohort Study

Mayank Jain*, Deepak Mittal, Poonam Sidana, Aparna Gupta and AP Mehta

Department of Neonatology, Max Healthcare, Shalimar Bagh, Delhi, India

***Corresponding author:** Mayank Jain, Department of Neonatology, Max Healthcare, Salimar Bagh, Delhi, India, E-mail: dr.mjain.10@gmail.com

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Abstract

Purpose: Retinopathy of prematurity is a disorder of developing retina. The survival rate of preterm infants increased due to advance neonatal care, with a consequent increase in retinopathy of prematurity cases. The aim of our study was to access the incidence of ROP and its risk factors and outcome those who needed treatment.

Methods: A retrospective cohort study of preterm infant born in tertiary intensive care unit was conducted from January 2017 to October 2020. 203 newborns were included based on the following criteria, Gestational Age (GA) at birth of ≤ 35 weeks, birth weight of ≤ 2000 gm and babies with GA>35 weeks and BW>2000 if the treating Paediatrician recommended ROP screening due to stormy course in NICU. Data were review to determine the incidence and risk factors of ROP. Neonates were followed up until diseases resolution or until treatment criteria were achieved.

Results: Two hundred three babies were enrolled for the study. There were 125 (62.1%) males and 77 (37.9%) females. ROP was seen in 41 babies giving an incidence of 20.2%. About half of cases had stage 1 ROP (51.2%) followed by stage 2 (24.4%), APROP (22%) and stage 3 (2.4%). No case of stage 4 and stage 5 ROP were detected. 7 out of 41 ROP cases were type 1 disease with incidence of 3.4%, and received treatment. A significant association was noted between ROP and PDA, sepsis, PVL, BPD, RDS, Postnatal steroids, oxygen therapy blood transfusion, TPN ($P<0.05$). No significant association was found for PIH, Preeclampsia, GDM, receiving antenatal steroids, IVH, multiple gestations, SGA, NEC, invasive and non-invasive respiratory support need.

Conclusion: This study found incidence of any stage of ROP was 20.2% and incidence of type 1 disease was 3.4%. A significant association was noted between ROP and PDA, sepsis, PVL, BPD, RDS, Postnatal steroids, oxygen therapy blood transfusion, TPN.

Keywords: Retinopathy of prematurity; Risk factors; Type 1 ROP disease; Incidence

Introduction

Retinopathy of Prematurity (ROP) is a vaso proliferative disease of developing retina. It ranges from mild disease without any visual loss to advanced disease leading to irreversible blindness [1]. Oxygen supplementation is identified to be an important risk factor for development of ROP [2]. ROP is a multi-factorial disease and can develop without supplementation of oxygen so other risk factors are low Gestational Age (GA), low birth weight(BW), Small for Gestational Age (SGA), Intra Ventricular Haemorrhage (IVH), neonatal sepsis, blood transfusion, Patent Ductus Arteriosus (PDA), Respiratory Distress Syndrome (RDS),

mechanical ventilation [3].

The incidence of ROP is varied between different countries. In developed countries, ROP associated blindness incident has been reported to be <10% of extremely preterm born children but in middle income countries, the incidence is greater than 40% [4]. In India, the incidence of ROP is between 38% and 51.9% in low birth weight babies [5]. Recent studies have shown that the incidence of any stage of ROP among infants weighing <1251 gm was 68%. Although majority of infants who develop ROP have spontaneously regressed, approximately 6% of low birth weight infants (1251 gm) develop severe ROP that requires treatment to prevent visual loss [3].

The aim of this retrospective study to estimate incidence of ROP and to assess the association between ROP and potential risk factors for this condition in neonates in our Neonatal Intensive Care Unit (NICU) where a strict protocol of saturation limits has been implemented.

Materials and Methods

Settings

This study was conducted in MAX Super speciality Hospital Delhi as a retrospective observational study involving babies at risk of ROP. MAX SHBG is NNF accredited and equipped with advanced facilities for neonatal care and resuscitation.

Duration and type of study

This was a retrospective study conducted to assess the incidence of ROP in premature infants and to determine risk factors for its development. Data reviewed from January 2017 to 31st October 2020.

Inclusion criteria

All babies fulfilling the following criteria were included:

a. Gestational Age (GA) at birth of ≤ 35 weeks

b. Birth Weight of ≤ 2000 gm

c. Babies with GA>35 weeks and BW>2000 if the treating paediatrician recommended ROP screening due to stormy course in NICU

Exclusion criteria

a. Those expires before retinal examinations

b. Incomplete follow-up

Procedure

All relevant information including that related to NICU care and risk factors for ROP were duly recorded in a excel sheet. Risk factors that were assessed were as follows: Duration of oxygen therapy, Respiratory Distress Syndrome (RDS), sepsis, history of blood transfusion, multiple gestations, and intra ventricular haemorrhage. From the patient's chart, maternal and neonatal co morbid conditions, if any, were noted and recorded.

Initial screening of all premature infants was done at 3 or 4 weeks after delivery. Diluted 0.8% tropicamide and 5% phenylephrine eye drops were used to dilate the pupils. Eyes were kept open with the help of eye speculum.

A senior retina specialist with experience in ROP examined the babies using indirect ophthalmoscope with 28D lens and schoket`s depressor. The findings were recorded in a chart. The international classification of ROP was used to document all retinal examination findings. As per standard schedule for screening, babies were called for further examinations. The highest ROP stage in either eye was recorded. In the absence of ROP, screening was continued till vascularisation reached zone 3 or completion of 45 weeks post menstrual age, whichever was earlier. Treatment was offered to babies who fulfilled criteria for treatment.

Data analysis

Statistical analysis was performed; the results are presented in frequencies, percentages and mean ± SD. The Chi-square test was used to compare the categorical variables. The Unpaired t-test was used to compare continuous variables. The p-value <0.05 was considered significant. All the analysis was carried out on SPSS 16.0 version (Chicago, Inc., USA).

Results

Two hundred three babies were enrolled for the study, on the basis the inclusion criteria detailed above. There were 126 (62.1%) males and 77 (37.9%) females. In other characteristics multi parity was among more than half of cases (52.7%), AGA was among majority of cases (88.7%), Singleton birth was in more than half of cases (64%), LSCS mode of delivery was among majority of cases (83.3%). ROP was seen in 41 babies giving an incidence of 20.2%. About half of cases had stage 1 ROP (51.2%) followed by stage 2 (24.4%), APROP (22%) and stage 3 (2.4%). No case of stage 4 and stage 5 ROP were detected. Out of 41 ROP cases only 7 cases were fall in to type 1 disease and received treatment. So incidence of severe ROP was 3.4%.

More than one third of cases had gestational age 32-34 weeks (45.3%) followed by 30-31 (32%), 28-29 (10.8%), ≥ 35 (6.9%) and <28 (4.9%) weeks. ROP was highest in gestational age <28 weeks (80%) and was nil in ≥ 35 weeks. There was significant association of incidence of ROP with gestational age (**Tables 1 and 2**) the incidence of ROP was inversely related to gestational age.

Table 3 shows the distribution of birth weight of baby and its association with incidence of ROP. The incidence of ROP was highest among baby with birth weight 1.01-1.25 kgs (47.1%) was lowest with birth weight >2kgs (2.9%).

Table 4 shows the association between ROP and other risk factors. A significant association was noted between ROP and PDA, sepsis, PVL, BPD, RDS, Postnatal steroids, oxygen therapy blood transfusion as well as TPN. No significant association was noted between occurrence of ROP and maternal risk factors including PIH, Preeclampsia, GDM, receiving antenatal steroids and neonatal risk factors like IVH, multiple gestations, SGA, NEC invasive and non-invasive respiratory support need.

Incidence of ROP	No. (N=23)	%
With ROP	41	20.2
Without ROP	162	79.8

Table 1: Distribution of incidence of ROP.

birth weight of baby in kgs	162		162		162		p-value[1]
	No.	%	No.	%	No.	%	
<1	10	4.9	4	40.0	6	60.0	0.0001*
1.01-1.25	34	16.7	16	47.1	18	52.9	
1.26-1.50	37	18.2	6	16.2	31	83.8	
1.51-1.75	46	22.7	8	17.4	38	82.6	
1.76-2.0	41	20.2	6	14.6	35	85.4	
>2	35	17.2	1	2.9	34	97.1	

Table 2: Distribution of gestational age and its association with incidence of ROP.

birth weight of baby in kgs	No. of patients (N=203)		With ROP		Without ROP		p-value[1]
	No.	%	No.	%	No.	%	
<1	10	4.9	4	40	6	60	0.0001*
1.01-1.25	34	16.7	16	47.1	18	52.9	
1.26-1.50	37	18.2	6	16.2	31	83.8	
1.51-1.75	46	22.7	8	17.4	38	82.6	
1.76-2.0	41	20.2	6	14.6	35	85.4	
>2	35	17.2	1	2.9	34	97.1	

Table 3: Distribution of birth weight of baby and its association with incidence of ROP.

	No. of patients (N=203)		With ROP		Without ROP		p-value[1]
	No.	%	No.	%	No.	%	
Maternal parameters							
Antenatal steroids	165	81.3	34	20.6	131	79.4	0.76
PIH	46	22.7	11	23.9	35	76.1	0.47
Preeclampsia	11	5.4	2	18.2	9	81.8	0.86
GDM	30	14.8	5	16.7	25	83.3	0.6
LSCS	169	83.3	31	18.3	138	81.7	0.14
Primigravida	96	47.3	22	22.9	74	77.1	0.36
Neonatal parameters							
Male	126	62.1	32	25.4	94	74.6	0.01
Twins	67	33	9	13.4	58	86.6	0.08
Triplets	6	3	0	0	6	100	
SGA	23	11.3	5	21.7	18	78.3	0.84
IVH	9	4.4	37	44.4	157	55.6	0.06
PDA	26	12.8	11	42.3	15	57.7	0.003*
Sepsis	64	31.5	20	31.2	44	68.8	0.008*
PVL	14	6.9	6	42.9	8	57.1	0.03*
BPD	13	6.4	11	84.6	2	15.4	0.0001*
NEC	4	2	0	0	4	100	0.31
Postnatal steroids	8	3.9	7	87.5	1	12.5	0.0001*
RDS	155	76.4	37	23.9	118	76.1	0.01*
Ventilator required	52	25.6	15	28.8	37	71.2	0.07
CPAP required	168	82.8	36	21.4	132	78.6	0.33
Required oxygen	78	38.4	27	34.6	51	65.4	0.0001*
Blood treatment	19	9.4	11	57.9	8	42.1	0.0001*
TPN required	68	33.5	26	38.2	42	61.8	0.0001*
TT required	8	3.9	8	100	0	0	0.0001*

Table 4: Distribution of Maternal and neonatal parameters and its association with incidence of ROP.

Discussion

ROP is preventable cause of blindness which affects retina. Prematurity is root cause of developing ROP. So screening of ROP is very important to prevent poor vision. There are several risk factors for the development of ROP. But gestational age and birth weight are considered the most important risk factor for the disease.

Various studies showed incidence of any stage ROP is between 20% to 52% [6-11]. In our study the overall incidence of any stage ROP was 20.2% and incidence of same was 80% and 50.7% in the babies born <28 week and <32 week respectively. So this is highlighting the fact that prematurity is directly related to the occurrence of ROP. Similar kind of findings found with all published data in literature and also showed known association of low gestational age and low birth weight [12-18]. Similarly birth weight is indirectly proportional to incidence of ROP and our results follow this relation except in less than 1 kg age group possibly due to small number of babies in that group.

In our study stage 1 ROP is most commonly (51.2%) found among all ROP cases and all were regressed spontaneously. No case of stage 4 and stage 5 ROP was seen. As all cases were screened in timely manner and we also followed strict optimal saturation policy in our NICU. In our study 22% cases were diagnosed as APROP out of all ROP cases. Out of that seven patients fall in to type 1 ROP disease category and all were received laser treatment and rest two APROP cases spontaneously resolved without treatment.

Presence of pulmonary disease in form of RDS, BPD were important risk factor for the development of ROP [19,20]. Need of oxygen, invasive ventilation, non-invasive ventilation were marker of severity of pulmonary disease. Our study showed RDS, BPD and oxygen therapy as a potential risk factor for development of ROP. Although our study did not find significance in terms of mechanical ventilator and non-invasive respiratory support, previous studies were showed association of ROP with RDS and oxygen therapy [21-28].

Shohat et al. [29] Seiberth and Linderkamp [30] and Maheshwari et al. [31] showed association of ROP with blood transfusion. Our study showed 58% babies develop ROP those who received blood transfusion which was clinically significant. PDA and TPN were not the direct cause of ROP but they express the severity of condition of baby. Our study showed significant association with above 2 parameters.

Maheshwari et al. [31] and Hakeen et al. [32] studies were suggestive of that sepsis in the postnatal period is an important risk factor for developing ROP. Similar association was found in our study. Similarly literature was suggestive of that NEC is also described as a risk factor for ROP but our study did not found association for NEC [12,32,].

Maternal growth factors such as preeclampsia GDM, PIH were also found to be responsible for development of ROP [22,27,29,30,32,33]. In our study no such association was found. We found that incidence of ROP among multiple gestation was not statistically significant. Cryotherapy for ROP study showed the likelihood of developing threshold ROP disease to be 36% greater in multiple gestation birth [34]. A larger sample size needed to confirm this hypothesis.

There is no direct relationship between antenatal steroids and ROP but antenatal steroid prevents respiratory distress syndrome and IVH. These are two important risk factors for ROP. Many studies also suggest that antenatal steroid decreases severity of ROP and decrease incidence of ROP also [35]. But our study did not found such association.

The limitation of present study includes its retrospective nature limiting the control over quality of measurement. Another limitation is small sample size including only three year data. Advantage of our study is that the data belongs to both high income subset of population as well as lower social class of population because as a private hospital we serve both class of community.

Conclusion

The present study reflects the incidence of any stage ROP was 20.2%. Prematurity, Birth Weight, PDA, sepsis, PVL, BPD, RDS, Postnatal steroids, oxygen therapy, blood transfusion, TPN were found to be independent risk factors in the development of ROP in neonates. Because of advancements in neonatal intensive care in developing countries and higher survival rate of premature infants, the incidence of ROP has increased. Unrecognized and untreated ROP will cause potential blindness in children. Hence, to prevent the adverse visual outcome and possible blindness; timely screening, recognition, and treatment of ROP is essential.

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