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INCIDENCE AND RISK FACTORS PREDISPOSING TO RETINOPATHY OF PREMATURITY AND TREATMENT OUTCOME: A RETROSPECTIVE COHORT STUDY

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ABSTRACT

Purpose: Retinopathy of prematurity is a disorder of the 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 was to assess the incidence of ROP and its risk factors and outcome for those who needed treatment. **Methods:** A retrospective cohort study of the preterm infants born in a tertiary intensive care unit was conducted from January 2017 to October 2020. A total of two hundred three newborns included for this study based on the following criteria, Gestational age (GA) at the time of 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 disease resolution or until treatment criteria were achieved. **Results:** A total of two hundred three babies enrolled in this study. There were 126 (62.1%) males and 77 (37.9%) females. ROP seen in 41 babies and 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 the incidence of 3.4% and received treatment. A significant association 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 the incidence of any stage of ROP was 20.2%, and the incidence of type-1 disease was 3.4%. A significant association 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 the developing retina. It ranges from the mild disease without any visual loss to advanced disease leading to irreversible blindness.[1] ROP depends on multiple risk factors like Oxygen supplementation, low gestational age (GA), low birth weight(BW), small for gestational age(SGA), intraventricular hemorrhage(IVH), neonatal sepsis, blood transfusion, patent ductus arteriosus(PDA), respiratory distress syndrome(RDS), mechanical ventilation.[2] Out of those oxygen supplementation is most common factor but it is seen that ROP can develop without supplementation of oxygen.[2,3]

The incidences of ROP vary between different countries. In developed countries, ROP associated blindness incidence has reported to be <10% of extremely preterm born children, but in middle-income countries, the incidence is greater than 40%.[4] Incidence of ROP among low birth weight babies In India is between 38% and 51.9%.[5] Previous studies showed the incidence of any stage of ROP was 68% among infants weighing <1251 gm. Although most of the 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.[2]

The aim of our study to estimate incidence of ROP and to find out the association between ROP and its potential risk factors in newborns who admitted in our neonatal intensive care unit (NICU). Here we follow strict saturation protocol.

MATERIALS AND METHODS

Setting

This study conducted in MAX Super Specialty Hospital Delhi as a retrospective observational study involving babies at ROP risk.

Duration and type of study

This 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 included:

a. Gestational age (GA) at the time of 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 expire before retinal examinations

b. Incomplete follow-up

Procedure

All relevant information, including that related to NICU care and risk factors for ROP, duly recorded in an excel sheet. Risk factors assessed were as follows: duration of oxygen therapy, respiratory distress syndrome (RDS), sepsis, history of blood transfusion, multiple gestations, and intraventricular hemorrhage. From the patient's chart, maternal and neonatal co-morbid conditions, if any, were noted and recorded.

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

A senior retina specialist with ROP experience examined the babies using an indirect ophthalmoscope with a 28D lens and Schoket`s depressor. The findings recorded in a chart. The international classification of ROP used to document all retinal examination findings.[8] As per the standard schedule for screening, babies were called for further examinations. The highest ROP stage in either eye recorded. In the absence of ROP, screening continued till vascularisation reached zone 3 or completion of 45 weeks post-menstrual age, whichever was earlier. Treatment offered to babies who fulfilled the criteria for treatment.

Data analysis

Statistical analysis performed; the results presented in frequencies, percentages and mean±SD. The Chi-square test applied to compare the categorical variables. The Unpaired t-test used to compare continuous variables. If the p-value came <0.05 then it's considered significant. Analysis carried out on the SPSS 16.0 version (Chicago, Inc., USA).

RESULTS

Two hundred three babies enrolled for the study on the basis of 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 the majority of cases (88.7%), Singleton birth was in more than half of cases (64%), LSCS mode of delivery was among the majority of cases (83.3%). ROP present 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 fell into type 1 disease and received treatment. So the 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 a significant association of the incidence of ROP with gestational age (Table: 2). the incidence of ROP was inversely related to gestational age.

Table 1: Distribution of the incidence of ROP.

Incidence of ROP	No. (n=203)	%
With ROP	41	20.2
Without ROP	162	79.8

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

Gestational age in weeks	No. of patients (n=203)		With ROP		Without ROP		p-value[1]
	No.	%	No.	%	No.	%	
<28	10	4.9	8	80.0	2	20.0	0.0001*
28-29	22	10.8	8	36.4	14	63.6	
30-31	65	32.0	17	26.2	48	73.8	
32-34	92	45.3	8	8.7	84	91.3	
≥35	14	6.9	0	0.0	14	100.0	

[1]Chi-square test, *Significant

Table-3: Distribution of the birth weight of the baby and its association with the 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	40.0	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	

[1]Chi-square test, *Significant

Table-3 shows the distribution of the birth weight of the baby and its association with the incidence of ROP. The incidence of ROP was highest among babies 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 noted between ROP and PDA, sepsis, PVL, BPD, RDS, Postnatal steroids, oxygen therapy blood transfusion and TPN. No significant association was noted between 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.

Table 4: Distribution of Maternal and neonatal parameters and its association with the 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	0.60
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	0.0	4	100.0	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	0.0	0.0001*

[1]Chi-square test, *Significant, #Multiple responses

DISCUSSION

ROP is a preventable cause of blindness that affects the retina. Prematurity is a root cause of developing ROP. So screening of ROP is important to prevent vision loss. Multiple risk factors are responsible for the development of ROP. But gestational age and birth weight are considered the important risk factor for the disease.

Various studies showed the incidence of any stage ROP is between 20% to 52%.[6–11] In our study, the incidence of any stage ROP was 20.2 %, and the incidence of the same was 80 % and 50.7% in the babies born <28 weeks and < 32 weeks, 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 the literature and also showed a known association of low gestational age and low birth weight.[12–18] Similarly, birth weight is indirectly proportional to the incidence of ROP, and our results follow this relation except in the less than 1 kg age group, possibly due to a small number of babies in that group.

In this study, stage-1 ROP is most commonly (51.2 %) found among all ROP cases, and all regressed spontaneously. No case of stage-4 and stage-5 ROP seen. All babies screened in a timely manner and we also followed a strict optimal saturation policy in our NICU. In our study, 22% of 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 the rest two APROP cases spontaneously resolved without treatment.

The presence of pulmonary disease in the form of RDS, BPD was an important risk factors for the development of ROP.[19,20] The need for oxygen, invasive ventilation, non-invasive ventilation was a marker of severity of the pulmonary disease. Our study showed RDS, BPD, and oxygen therapy as potential risk factors for the development of ROP. However our study did not find significance in terms of a mechanical ventilator and noninvasive respiratory support. Previous studies showed the association of ROP with RDS and oxygen therapy.[21–28]

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

Maheshwari et al.[31] and Hakeem et al.[32] suggest that the sepsis in the newborn is an important risk factor for developing ROP. A similar association found in our study. Similarly, literature suggest that NEC is also described as a risk factor for ROP, but our study did not found an association for NEC.[12,32,33]

Maternal growth factors such as preeclampsia GDM, PIH found to be responsible for the development of ROP.[22,27,29,30,32,33] In our study, no such association found. We found that the incidence of ROP among multiple gestations was not statistically significant. Cryotherapy for ROP study showed the likelihood of developing threshold ROP disease to be 36% greater in multiple gestation births.[34] Larger sample size is 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 the severity of ROP and the incidence of ROP.[35] But our study did not found such an association.

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

CONCLUSION

The present study reflects the incidence of any stage ROP was 20.2 %. Risk factors like prematurity, Birth Weight, PDA, sepsis, PVL, BPD, RDS, Postnatal steroids, oxygen therapy, blood transfusion, TPN were responsible for the development of ROP in neonates. Because of advancements in neonatal intensive care in developing countries and the 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 ROP treatment are essential.

REFERNCES

1. Raj R, Latha NV, Asha AV, George TA, Jacob S, Praveena KK. A comparative study of the incidence of retinopathy of prematurity between small-for-gestational-age and appropriate-forgestational-age preterm babies in North Kerala. Kerala J Ophthalmol, 2017; 29: 197-202.
2. Mitsiakos G and A Papageorgiou. "Incidence and factors predisposing to retinopathy of prematurity in inborn infants less than 32 weeks of gestation". Hippokratia, 2016; 20.2: 121-126.
3. Alajbegovic‐Halimic J, Zvizdic D, Alimanovic‐Halilovic E, Dodik I, Duvnjak S. Risk factors for retinopathy of prematurity in premature born children. Med Arch, 2015; 69: 409‐13.
4. Selim Cevher and Emine Alyamac Sukgen. "The Prevalence of Retinopathy of Prematurity and Relationship with Gestational Age and Birth-Weight; Contributing to Screening Programmes". EC Ophthalmology, 2019; 10.2: 94-99.
5. Anudeep K, Srikanth K, Sindal MD, Jha KN. Study of incidence, risk factors, and treatment outcomes in retinopathy of prematurity in a tertiary care center. TNOA J Ophthalmic Sci Res., 2019; 57: 24-6.
6. Clark DI, O'brien, Co, Weindling AM, Saeed M. Initial experience of screening for retinopathy of prematurity. Arch Dis Child, 1992; 67: 1233–1239.
7. Paranjpe, D. G., Sarwate, D. R., & Shetty, D. N. Risk factor and Outcome of Retinopathy of Prematurity among Premature Babies admitted to Tertiary Care Hospital: A Retrospective Observational Study. Journal of Current Medical

Research and Opinion, 2019; 2(11): 334-338. https://doi.org/10.15520/jcmro.v2i11.226.
8. International committee for the classification of retinopathy of prematurity. The international classification of retinopathy of prematurity revisited. Arch Ophthalmol, 2005; 123: 991–1000.
9. Katz X, Kychenthal A, Dorta P. Zone I retinopathy of prematurity. J AAPOS, 2000; 4(6): 373–379.
10. Palmer EA. Results of US randomized clinical trial of cryotherapy for ROP (CRYO-ROP). Doc Ophthalmol, 1990; 74(3): 245–51.
11. Varughese S, Jain S, Gupta N, Singh S, Tyagi V, Puliyel JM. Magnitude of the problem of retinopathy of prematurity. Experience in a large maternity unit with a medium size level-3 nursery. Indian J Ophthalmol, 2001; 49: 187–187.
12. Hwang JH, Lee EH, Kim EA. Retinopathy of Prematurity among Very-Low-Birth-Weight Infants in Korea: Incidence, Treatment, and Risk Factors. J Korean Med Sci., 2015; 30(1): S88- S94. 3.
13. Gunn DJ, Cartwright DW, Gole GA. Incidence of retinopathy of prematurity in extremely premature infants over an 18-year period. Clin Exp Ophthalmol, 2012; 40: 93-99.
14. Cerman E, Balci SY, Yenice OS, Kazokoglu H, Celiker H, Eraslan M. Screening for retinopathy of prematurity in a tertiary ophthalmology department in Turkey: incidence, outcomes, and risk factors. Ophthalmic Surg Lasers Imaging Retina, 2014; 45: 550-555.
15. Stoll BJ, Hansen NI, Bell EF, Shankaran S, Laptook AR, Walsh MC, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Neonatal outcomes of extremely preterm infants from the NICHD Neonatal Research Network. Pediatrics, 2010; 126: 443-456.
16. Xu Y, Zhou X, Zhang Q, Ji X, Zhang Q, Zhu J, et al. Screening for retinopathy of prematurity in China: a neonatal units-based prospective study. Invest Ophthalmol Vis Sci., 2013; 54: 8229-8236.
17. Austeng D, Källen K, Hellström A, Jakobsson P, Lundgren P, Tornqvist K, et al. Regional differences in screening for retinopathy of prematurity in infants born before 27 weeks of gestation in Sweden--the EXPRESS study. Acta Ophthalmol, 2014; 92: 311-315.
18. Isaza G, Arora S. Incidence and severity of retinopathy of prematurity in extremely premature infants. Can J Opthalmol, 2012; 47: 296-300.
19. Freitas, André Moraes et al. "Incidence and risk factors for retinopathy of prematurity: a retrospective cohort study." International journal of retina and vitreous, May. 2018; 4 20. 31. doi:10.1186/s40942-018-0125-z.
20. Saugstad OD, Aune D. Optimal oxygenation of extremely low birth weight infants: a meta-analysis and systematic review of the oxygen saturation target studies. Neonatology, 2014; 105: 55–63.
21. Shah VA, Yeo CL, Ling YL, Ho LY. Incidence, risk factors of retinopathy of prematurity among very low birth weight infants in Singapore. Ann Acad Med Singapore, 2005; 34: 169-78.
22. Maini B, Chellani H, Arya S, Guliani BP. Retinopathy of prematurity: Risk factors and role of antenatal betamethasone in Indian preterm newborn babies. J Clin Neonatol, 2014; 3: 20-4.
23. Lucey JF, Dangman B. A reexamination of the role of oxygen in retrolental fibroplasia. Pediatrics, 1984; 73: 82-96.
24. Madan A, Penn JS. Animal models of oxygen-induced retinopathy. Front Biosci, 2003; 8: d1030-43.
25. Penn JS, Tolman BL, Lowery LA. Variable oxygen exposure causes preretinal neovascularization in the newborn rat. Invest Ophthalmol Vis Sci., 1993; 34: 576-85.
26. Procianoy RS, Garcia-Prats JA, Adams JM, Silvers A, Rudolph AJ. Hyaline membrane disease and intraventricular haemorrhage in small for gestational age infants. Arch Dis Child., 1980; 55: 502-5.
27. Chaudhari S, Patwardhan V, Vaidya U, Kadam S, Kamat A. Retinopathy of prematurity in a tertiary care center – Incidence, risk factors and outcome. Indian Pediatr, 2009; 46: 219-24.
28. Chan-Ling T, Gock B, Stone J. The effect of oxygen on vasoformative cell division. Evidence that "physiological hypoxia" is the stimulus for normal retinal vasculogenesis. Invest Ophthalmol Vis Sci., 1995; 36: 1201-14.
29. Shohat M, Reisner SH, Krikler R, Nissenkorn I, Yassur Y, Ben-Sira I, et al. Retinopathy of prematurity: Incidence and risk factors. Pediatrics, 1983; 72: 159-63.
30. Seiberth V, Linderkamp O. Risk factors in retinopathy of prematurity. A multivariate statistical analysis. Ophthalmologica, 2000; 214: 131-5.
31. Maheshwari R, Kumar H, Paul VK, Singh M, Deorari AK, Tiwari HK, et al. Incidence and risk factors of retinopathy of prematurity in a tertiary care newborn unit in New Delhi. Natl Med J India, 1996; 9: 211-4.
32. Hakeem AH, Mohamed GB, Othman MF. Retinopathy of prematurity: A study of prevalence and risk factors. Middle East Afr J Ophthalmol, 2012; 19: 289-94.
33. Kim TI, Sohn J, Pi SY, Yoon YH. Postnatal risk factors of retinopathy of prematurity. Paediatr Perinat Epidemiol, 2004; 18: 130-4.
34. Palmer EA, Flynn JT, HardyRJ, Phelps DL, Phillips CL, Schaffer DB, et al. Incidence and early course of retinopathy of prematurity. The Cryotherapy for Retinopathy of Prematurity Cooperative Group. Ophthalmology, 1991; 98: 1628-40.
35. Higgins RD, Mendelsohn AL, DeFeo MJ, Ucsel R, Hendricks‐Munoz KD. Antenatal dexamethasone and decreased severity of retinopathy of prematurity. Arch Ophthalmol, 1998; 116: 601-5. 8. Watts P, Adams GG.