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Original Research Paper

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TO STUDY THE INCIDENCE AND RISK FACTORS OF RETINOPATHY OF PREMATURITY IN A TERTIARY CARE HOSPITAL IN NORTHERN INDIA

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ABSTRACT

BACKGROUND: Retinopathy of prematurity (ROP) is a multifactorial retinal vaso-proliferative disorder which remains a leading cause of childhood blindness worldwide despite improvements in neonatal care and management guidelines. This study was conducted to determine the incidence of ROP among preterm neonates and to determine the risk factors.

METHODS: All preterm infants with birth weight <1750 gm and gestation <34 weeks were screened for ROP at 4 weeks of birth for first screening. Prenatal and postnatal risk factors, neonatal problems, treatment given, procedures and interventions done during stay in neonatal intensive care unit were recorded as per the proforma. The data from the study was systematically collected, compiled and statistically analyzed with SPSS Statistics-26 version to draw relevant conclusions.

RESULTS: The incidence of ROP in 89 infants who were screened was 44%. The mean gestational age of babies with ROP was 32 weeks. In our study, pneumonia, apnea, sepsis, thrombocytopenia, NEC, shock, acidosis, IVH, BPD, the use of Bubble CPAP, Venti-CPAP and mechanical ventilator, the vasopressor use and blood transfusion were significant risk factors.

CONCLUSIONS: The incidence of ROP was significantly higher in babies <34 weeks. It was observed in our that lower the birth weight and lower the gestational age, higher is the risk for the development of ROP. Careful and timed retinal examination of all at risk infants will minimize the development of ROP and later on blindness.

KEYWORDS : Risk Factors, Retinopathy Of Prematurity, Sepsis, Apnea, Transfusion

INTRODUCTION

Retinopathy of prematurity (ROP) is a multifactorial retinal vaso-proliferative disorder that increases in incidence with decreasing gestational age.[1] The outcome associated with ROP ranges from no effect on vision in milder cases to bilateral, irreversible and total blindness in advanced cases. Despite improvements in neonatal care and management guidelines ROP remains a leading cause of childhood blindness worldwide. Current screening guidelines are primarily based on: birth weight, gestational age, and oxygen exposure however other risk factors, including maternal factors, prenatal and perinatal factors, demographics, medical interventions, comorbidities of prematurity, nutrition, and genetic factors have their role in development of ROP.[2]

Increased vascular endothelial growth factor (VEGF) induced by hypoxia delays physiologic retinal vascular development by interfering with ordered vascular development; decreased VEGF in high oxygen also delays physiologic retinal vascular development by reducing developmental angiogenesis.[3]

The World Health Organisation (WHO) programme of Vision 2020 targeted against ROP mentioned that the incidence of ROP can be reduced by early screening and referral for treatment.[4] American Academy of Pediatrics (AAP) recommends screening of infants born at ≤30 weeks gestational age (GA) and/or ≤1500 g birth weight (regardless of supplemental oxygen), 1500 to 2000 g birth weight if supplemental oxygen was administered and the infants had an unstable clinical course.[5]

As per the Rashtriya Bal Swasthya Karyakram screening guidelines for ROP, birth weight less than 2000 gm, gestational age less than 34 weeks , gestational age between 34 to 36 weeks but with risk factors such as: a) Cardio-respiratory support, b) Prolonged oxygen therapy, c) Respiratory distress syndrome, d) Chronic lung disease, e) Fetal hemorrhage, f) Blood transfusion, g) Neonatal sepsis, h) Exchange transfusion, i) Intraventricular haemorrhage, j) Apnea, k) Poor postnatal weight gain and infants with an unstable clinical course who are at high risk (as determined by the neonatologist or paediatrician) were considered for screening for ROP.[6]

METHODS

All premature infants <34 weeks gestational age (GA) or birth weight (BW) <1750 grams admitted in neonatal intensive care unit (NICU) of pediatrics department were enrolled in the present study after taking informed consent from the parents. Baseline variables of all the enrolled neonates were recorded as per proforma. Further prenatal and postnatal risk factors, neonatal problems, treatment given, procedures and interventions done during stay in neonatal intensive care unit were recorded as per the proforma. All these neonates were screened for ROP at 4 weeks of gestation age. Cross-sectional study was conducted by Department of Pediatrics, SGRDIMSR, Amritsar in collaboration with Department of Ophthalmology, SGRDIMSR, Amritsar from December 2018 to May 2020. The study was conducted after taking permission from thesis and ethical committee of the institution.

Inclusion Criteria:

1. Premature infants <34 weeks gestational age (GA) or birth weight (BW) <1750 grams.

Exclusion Criteria:

A case with any of the following conditions will not be included in the study.

1. Babies dying before completion of ROP screening.
2. Babies >34 weeks of gestation.
3. Infants with major congenital malformations.
4. Infants with suspected chromosomal anomalies.

Examination:

Each selected case was subjected to a comprehensive eye examination after explaining the nature of the study and obtaining the informed written consent from parents in their own vernacular language. Pupils were dilated with a mixture of phenylephrine 2.5% and tropicamide 0.5% instilled 3 times at 10 minutes interval about 1 hour before the procedure.

Procedure:

It was done under topical anesthesia by instilling paracaine eye drops 0.5% to avoid systemic side effects of general

anesthesia or sedation.

A sterile pediatric lid speculum was introduced carefully into the conjunctival sac. Assistant held the head while the surgeon will stabilize the chin with the ring finger and the little finger, simultaneously holding the lens with the other three fingers.

Screening was done according to following table.

	NO PLUS DISEASE			PLUS DISEASE
	ZONE 1	ZONE 2	ZONE 3	
IMMATURE				
STAGE 1				
STAGE 2				
STAGE 3				
STAGE 4				
STAGE 5				

In this study we considered pre and postnatal risk factors for ROP to identify association of risk factors with the development of various forms of disease.

Prenatal variables were the presence of meconium stained liquor, pregnancy induced hypertension (PIH), maternal diabetes mellitus, maternal anemia, PPROM, antenatal steroid use.

Postnatal variables were perinatal asphyxia (PNA-considered history of delayed cry at birth or need for bag and mask ventilation or mechanical ventilation at birth), hyaline membrane disease (HMD), pneumonia, apnea, polycythemia, hyperbilirubinemia, sepsis (positive blood culture), thrombocytopenia, NEC, seizure, shock, acidosis, IVH, BPD, oxygen therapy (through nasal prongs, hood, continuous positive airway pressure i.e. CPAP or mechanical ventilation), phototherapy for hyperbilirubinemia, blood transfusion, hypotension requiring vasopressor use and days of stay in hospital.

The neonates with unstable clinical course were considered having presence of one or more of various risk factors enumerated above and the neonates with uneventful post natal period were considered having none of the above enumerated risk factors.

Statistical Analysis

The data from the present study was systematically collected, compiled and statistically analysed with SPSS Statistics-26 version to draw relevant conclusions. The observations were tabulated in the form of number, percentage and Mean ± Standard Deviation (SD). Categorical variables were correlated using chi square test. The level of significance was determined as its 'p' value with $p<0.05$ as significant and $p<0.001$ as highly significant.

RESULTS

In present study 89 neonates screened over a period of one year who fulfilled the screening criteria for ROP. Out of total 89 cases, 41 cases were positive for Retinopathy of prematurity (ROP). Hence incidence of ROP was 44% in present study. The mean gestation age in our study was 32.01 weeks. (Table 1)

Table 1: Incidence Of ROP In Neonates < 34 Weeks

GESTATION AGE	<34 Weeks	
	n	%
ROP Present	39	44%
ROP Absent	50	56%
Mean Gestation Age	32.01±1.49	

Birth weight usually correlates with maturity of the newborn. Incidence of ROP with various birth weight groups shown in Table 2. Incidence of ROP decreased as birth weight increases. Maximum incidence was in ≤1000 grams group. Neonates with BW less than 1000 grams with ROP were 3, (75%) among the 4 neonates under 1000 grams. In the range of between 1,000 and1499 grams, 18 neonates (43%) were with ROP. And in the range of 1500 to 1750 grams, 38% of the 34 neonates suffered from ROP. (Table 2).

Table 2: Birth Weight Wise Distribution Of ROP

Birth Weight	ROP Present		ROP Absent		Total	
	n	%	n	%	n	%
<1000	3	75%	1	25%	4	100%
1000-1499	18	43%	23	57%	41	100%
1500-1750	13	38%	21	62%	34	100%

Among the maternal factors, no significant factor was found in our study. Among the neonatal factors, in Group A, pneumonia, apnea, sepsis, thrombocytopenia, NEC, shock, acidosis, IVH, BPD were significant risk factors (p value < 0.05). Among the methods of use of oxygenation, the use of Bubble CPAP, Venti-CPAP and mechanical ventilator was found to be significantly contributing to the development of ROP. According to the treatment given to neonates, the vasopressor use and blood transfusion were significant factors.

Among the neonates, who developed ROP the maximum number of neonates had Stage 3 Zone 2 ROP (n= 20,52%) followed by APROP with 11 neonates (2 in Zone 1, n=2,5%, 9 in Zone 2, n=9, 23%). Plus disease was seen along with different stages in 12 neonates with maximum incidence of plus disease seen with stage 3 zone (n=5, 42%) followed by with stage 2 zone 2 (n=4, 34%). (Table 3)

Table 3: Distribution Of ROP In Stage And Zones

		(<34 weeks)			
		ROP Present		Plus Disease	
		n	%	n	%
Stage 1	Zone 1	1	2.5	1	8
	Zone 2	-	-	-	-
	Zone 3	-	-	-	-
Stage 2	Zone 1	-	-	-	-
	Zone 2	4	10	4	34
	Zone 3	-	-	-	-
Stage 3	Zone 1	1	2.5	-	-
	Zone 2	20	52	5	42
	Zone 3	2	5	2	16
APROP	Zone 1	2	5	-	-
	Zone 2	9	23	-	-
Total		39	100	12	100

DISCUSSION

ROP being clinically silent in the neonatal period, screening aims at reducing the incidence of ROP with prompt case detection and optimal treatment for ROP, thus reducing the severity and overall burden of childhood blindness. Due to lack of gold standard tests for ROP, the screening process may also be referred as "case detection initiative".[7]

The overall incidence of ROP in the present study was 44%. This was comparable to study conducted by Sengodi E et al.[8] in 2020 in which the incidence of ROP at a medical college hospital in rural Tamil Nadu was 33%. The neonates screened by Sengodi E et al were with gestational age (GA) less than or equal to 36 weeks or birth weight less than 2000 grams or with GA more than 36 weeks and birth weight more than 2000 gram with significant risk factors. Another study by Ahuja AA et al.[9] included babies with gestational age at birth of ≤36 weeks and a birth weight (BW) of ≤1900 g and had incidence of 32.6%. In 2010, the Vermont Oxford Network Database (VON) estimated that the incidence of any form of ROP in all very low birthweight (VLBW) infants i.e., BW <1500gms was 33.2%.[10] A

retrospective cohort study of preterm infants born in a tertiary neonatal intensive care unit which was conducted by Freitas et al,[11] had ROP incidence of 33.9% and their selection criteria included infants with BW >1500 gm or GA >32 weeks with determined risk factors. These variations in the ROP incidence reflected the differences in study populations, mortality rates, and neonatal care in different centres, thus providing evidence for the need to further investigate the risk factors for the development of ROP.

In our study incidence of ROP in neonates with weight <1750 grams was 43%. On further birthweight wise distribution in our study, the neonates with BW less than 1000 grams with ROP were 3, (75%) among the 4 neonates under 1000 grams. In the range of between 1,000 and 1499 grams, 18 neonates (43%) had ROP. And in the range of 1500 to 1749 grams, 38% of the 34 neonates suffered from ROP. Similarly, in a study by conducted by Saeidi R et al[12] newborns with BW less than 1000 grams (ELBW) with ROP were 7, (50%) of the whole group under 1000 grams). In the range of between 1,000 and 1250 grams, 40% of the 8 infants suffered from ROP. In the range of 1250 to 1500 grams, 34.5% were present, with 10 neonates with ROP, and in the range of 1500 to 1750 grams, 11.2% of the 3 infants suffered from ROP. Finally, in newborns over 1750 g, 4.3%, 3 infants with ROP. In another study conducted by Le C et al[13] all infants with ROP weighed <1750 g at birth, with 33% weighing between 1500 and 1750 g, 32% between 1000 and 1499 g, and 17% between 750 and 999 g. Thus, as the BW increases, the incidence of ROP decreases.

In present study the risk factors for ROP were pneumonia, apnea, sepsis, thrombocytopenia, NEC, shock, acidosis, IVH, BPD, the use of Bubble CPAP, Venti-CPAP and mechanical ventilator, the vasopressor use and blood transfusion. In a study done by Chen YI et al the risk factors identified were low birth weight, apnea >20 sec, anemia, placental abruption.[14] Risk factors identified by Hungi BI et al in their study were respiratory distress syndrome, oxygen therapy, neonatal jaundice and sepsis were higher in the ROP group but was not statistically significant.[15] Mahuya Pal Chattopadhyay et al in their study found that in univariate analysis, spontaneous vaginal delivery, non- administration of antenatal steroids to mothers and apnea were associated with the development of ROP and on multivariate analysis using a stepwise method, after controlling for various potential confounders, showed that apnea was the only significant risk factor for the development of retinopathy of prematurity.[16] Risk factors like VLBW, multiple gestation, resuscitation at birth, blood transfusion more than 45 mL/kg, oxygen therapy for more than five days, and age more than 10 days to regain birth weight were associated with retinopathy in the study by Sabzehei MK et al.[17]Risk factors for threshold or worse disease were, outborn babies, respiratory distress syndrome, and exchange transfusion as per observations made by Vinekar A et al in their study.[18]

CONCLUSION

We concluded in our study that lower the birth weight and lower the gestational age, higher is the risk for the development of ROP. Though the incidence of ROP is more in low birth weight and low gestational age individuals, it should also be taken into consideration that ROP can even occur in mature babies and normal birth weight neonates. Early screening for retinopathy of prematurity is of great importance. Careful and timed retinal examination of all at risk infants will minimize the development of ROP and later on blindness. Screening should be escalated in the presence of factors like oxygen administration, pneumonia, sepsis, apnea, thrombocytopenia, NEC, shock, acidosis, IVH, BPD, vasopressor use, blood transfusion and prolonged stay in hospital. By controlling and minimizing the risk factors, and diligent management of sick babies, it may be possible to reduce the incidence of ROP and blindness which will lower the social and economic burden on the society and the nation.

REFERENCES

1) Vanderveen DK, Zupancic JAF. Retinopathy of Prematurity. In: Cloherty JP, Eichenwald EC, Stark AR, editors. Manual of neonatal care. 8th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2017. p.986-92
2) Kim SJ, Port AD, Swan R, Campbell JP, Chan RVP, Chiang MF. Retinopathy of prematurity: a review of risk factors and their clinical significance. Surv Ophthalmol. 2018;63(5):618-37
3) Hartnett ME, Penn JS. Mechanisms and management of retinopathy of prematurity. N Engl J Med. 2012;367(26):2515-26.
4) Gilbert C, Foster A. Childhood blindness in the context of VISION 2020--the right to sight. Bull World Health Organ. 2001;79(3):227-32.
5) Screening examination of premature infants for retinopathy of prematurity. Section on Ophthalmology, American Academy of Pediatrics. American Academy of Ophthalmology. Pediatrics. 2006;117(2):572-6
6) Rashtriya bal swasthya karyakram. Guidelines for Universal Eye Screening in Newborns Including Retinopathy of Prematurity [Internet]. Rashtriya bal swasthya karyakram; 2017 [cited 2020 Jul 1]. Available from: https://www.nhm.gov.in/images/pdf/programmes/RBSK/Resource_Documents/Revised_ROP_Guidelines-Web_Optimized.pdf
7) Shah PK, Prabhu V, Karandikar SS, Ranjan R, Narendran V, Kalpana N. Retinopathy of prematurity: Past, present and future. World J Clin Pediatr 2016; 5(1): 35-46
8) Sengodi E, Rajasekaran K, Venkatesh G. Incidence and risk factors for retinopathy of prematurity at a medical college hospital in rural Tamil Nadu, India. Int J Contemp Pediatr 2020;7(11):2119-24.
9) Ahuja AA, V Reddy YC, Adenuga OO, Kewlani D, Ravindran M, Ramakrishnan R. Risk factors for retinopathy of prematurity in a district in South India: A prospective cohort study. Oman J Ophthalmol. 2018;11(1):33-7.
10) Cavallaro G, Filippi L, Bagnoli P, et al. The pathophysiology of retinopathy of prematurity: an update of previous and recent knowledge. Acta Ophthalmol. 2014;92(1):2-20.
11) Freitas AM, Mörschbächer R, Thorell MR, Rhoden EL. Incidence and risk factors for retinopathy of prematurity: a retrospective cohort study. Int J Retina Vitreous. 2018;4:20.
12) Saeidi, R., Taraghi, B., saeidi, M. Incidence of Retinopathy of Prematurity (ROP) in Low Birth Weight Newborns. IJN, 2017; 8(4): 102-6.
13) Le C, Basani LB, Zurakowski D, Ayyala RS, Agraharam SG. Retinopathy of prematurity: Incidence, prevalence, risk factors, and outcomes at a tertiary care center in Telangana. J Clin Ophthalmol Res 2016;4(3):119-22.
14) Chen Y1, Li XX, Yin H, Gilbert C, Liang JH, Jiang YR, Zhao MW, Beijing ROP Survey Group. Risk factors for retinopathy of prematurity in six neonatal intensive care units in Beijing, China. Br J Ophthalmol. 2008 Mar;92(3):326-30.
15) Hungi B, Vinekar A, Datti N, Kariyappa P, Braganza S, Chinnaiah S et al. Retinopathy of Prematurity in a rural Neonatal Intensive Care Unit in South India--a prospective study. Indian J Pediatr. 2012 Jul;79(7):911-5.
16) Chattopadhyay MP, Pradhan A, Singh R, Datta S. Incidence and Risk Factors for Retinopathy of Prematurity in Neonates, Indian Pediatr. 2015;52:157-8.
17) Sabzehei MK, Afjeh SA, Dastjani Farahani A, Shamshiri AR, Esmaili F. Retinopathy of prematurity: incidence, risk factors, and outcome. Arch Iran Med. 2013 Sep;16(9):507-12
18. Vinekar A, Dogra MR, Sangtam T, Narang A, Gupta A. Retinopathy of prematurity in Asian Indian babies weighing greater than 1250 grams at birth: Ten year data from a tertiary care center in a developing country. Indian J Ophthalmol. 2007;55:331-6.