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RETINOPATHY OF PREMATURITY- A STUDY OF INCIDENCE & RISK FACTORS AT A TERTIARY CARE CENTER IN NORTH-WEST INDIA

Ophthalmology

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ABSTRACT

PURPOSE-to determine incidence of Retinopathy of prematurity (ROP) in a tertiary centre in North-west India and associated risk factors promoting development of ROP

METHODS-Newborns fulfilling the screening criteria of National Neonatology Forum of India, underwent fundus examination using indirect ophthalmoscope. Risk factors including gestational age, birth weight, sex, and mode of delivery, respiratory distress syndrome, oxygen therapy, sepsis, intraventricular hemorrhage & blood transfusion were noted

RESULT-out of the studied 200 consecutive infants over 12 months study period, 59 developed ROP. 43 infants required treatment in form of LASER photocoagulation or AntiVEGF. There was a significant relationship between occurrence of ROP & gestational age (p=0.0001), birth weight (p=0.0001), oxygen therapy (p=0.0337), sepsis (p=0.0094) & blood transfusions (p=0.0085).

CONCLUSION-Our study outlines the prevalence of risk factors for the development of ROP & thus highlights the need to strategize the screening guidelines to better assess the Indian population

KEYWORDS

India, Risk Factors, Retinopathy Of Prematurity

INTRODUCTION

Retinopathy of prematurity (ROP) is a significant cause of preventable childhood blindness across the world. The continuous rise in the incidence of ROP is mainly because of the recent advancements in neonatal health care and so, an increase in survival rate of low birth weight infants[1]. Globally, 50,000 infants are affected by ROP every year. In India, annual blindness from ROP is around 500 children[2]. A well planned and effective screening strategy is the most important diagnostic and prognostic factor for ROP management program and also decreases the incidence of the blinding advance stage of ROP [3].

The retina of premature infants have poorly developed vascularization, this sometimes leads to the abnormal neovascular development. These abnormal new blood vessels are fragile and are prone to leak or bleed, can cause fibrovascular proliferation and finally retinal detachment in late stages, which is the main cause of visual impairment in ROP [4]. According to the literature, there is significant and consistent association of three factors with ROP: low gestational age, low birth weight and prolonged exposure of oxygen following delivery [5].

This study aimed to determine the prevalence of ROP in a tertiary center in North-West India and associated risk factors promoting development and progression of ROP. Our research also aimed to contribute to the existing knowledge of ROP in the Indian population and hence, will help in the development of unified screening guidelines in the country.

METHODS

After getting approval from institute ethical committee for conducting this prospective interventional trial, in accordance with the Declaration of Helsinki. Written informed consent was taken from each patient for the undergoing procedure. Study was conducted in the Department of Ophthalmology, in a tertiary center of North-west India in the year 2017. As per the screening guidelines, 200 consecutive newborns who were referred from the Pediatrics Department and those who attended Ophthalmology Outdoor were included in this study. All the relevant perinatal data including gestational age, post conceptional age and risk factors like exposure to oxygen, sepsis, anemia and blood transfusion, acidosis, total parenteral nutrition, intraventricular hemorrhage, were documented.

Prenatal variables were gestational age, birth weight, sex, mode of delivery. Postnatal variables were respiratory distress syndrome, oxygen therapy, sepsis, intraventricular hemorrhage (cranial ultrasound) and blood transfusion.

SCREENING

Screening guidelines were according to national neonatology forum (NNF) of India. Screening for ROP was performed in all preterm neonates who were born < 34 weeks gestation and/or < 1750 grams birth weight; as well as in newborns 34-36 weeks gestation or 1750-2000 grams birth weight if they had risk factors for ROP. The first retinal examination was performed not later than 4 weeks of age or 30 days of life in infants born ≥ 28 weeks of gestational age. Infants born < 28 weeks or < 1200 grams birth weight should be screened early, by 2-3 weeks of age, to enable early identification of Aggressive Posterior Retinopathy of Prematurity (AP-ROP).

International classification of ROP (ICROP) was taken as the standard for classification of ROP in 3 zones and 5 stages [6]. Schedule for follow up was according to the recommendation of American Academy of Ophthalmology (AAO), American Academy of Pediatrics (AAP), and American Academy of Pediatric Ophthalmology (AAPO) [7].

Screening was performed by a single retina specialist using an indirect binocular ophthalmoscope with a + 20 diopter lens using all aseptic precautions.

The stage of ROP at the time of diagnosis, treatment intervention, and treatment outcomes, gestational age, birth weight, the current age of the patient and the risk factors were documented. The success of treatment was measured by regression of neovascularization and absence of recurrence.

STATISTICAL ANALYSIS

Data was analyzed by software IBM SPSS 19.0. The prevalence rate of ROP was described in simple proportion. Group comparisons were done by the Chi-squared test or Fisher's exact test for categorical variables. A probability of less than 0.05 was considered significant.

RESULTS

200 consecutive newborns who fulfilled the inclusion (screening) criteria were considered in our study. There were 112 (56%) males and 88 (44%) females. Out of the 200 newborns, 59 (29.5%) developed ROP.

The birth weight of ROP newborns ranged from 700-1800 grams with a mean weight of 1220±270 gm, while that of non-ROP newborns ranged from 820-1900 gm, with a mean weight of 1430± 340 grams. And, the gestational age of ROP newborns ranged from 22-34 weeks with a mean gestational age of 28.83±1.96 weeks; while that of non-

ROP newborns ranged from 24-38 weeks with a mean age of 31.50±2.88 weeks. The difference of mean weights between two groups was statistically significant with a p-value of 0.0001 ($p< 0.05$). Also, the difference of mean gestational age between the two groups was significant with a p-value of 0.0001 ($p< 0.05$).

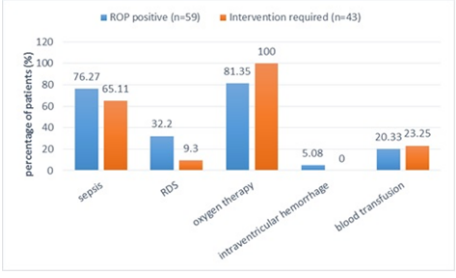
Various risk factors were evaluated in our study including sex, mode of delivery [vaginal (55%) or cesarean (45%)}, respiratory distress syndrome (RDS) (32.5%), sepsis (62.5%), oxygen therapy (71%), intraventricular hemorrhage (5.5%) and blood transfusion (34%). Table 1 shows the relationship between ROP and risk factors. Statistically, significant relationship had been shown between the occurrence of ROP and oxygen therapy (p=0.0337), sepsis (p=0.0094) and blood transfusions (p=0.0085). No significant relationship was found with sex (p=0.5249), mode of delivery (p=0.4462), RDS (p=0.9549) and intraventricular hemorrhage (p=0.8684). Mean duration of oxygen therapy required was 6 days (range 2-46 days).

Table 1 patient demographics and risk factors

RISK FACTOR	n	ROP positive	*p* value
Sex	Male 112 Female 88	31 28	0.5249
Mode of delivery	Vaginal 110 Cesarean 90	30 29	0.4462
Respiratory distress syndrome	65	19	0.9549
Sepsis	125	45	0.0094
Oxygen therapy	142	48	0.0337
Intraventricular hemorrhage	11	3	0.8684
Blood transfusion	68	12	0.0085

Out of 59 ROP positive newborns, 6 had stage 4 or 5 disease for which they were referred to AIIMS, New Delhi and 43 newborns underwent interventions in form of LASER photocoagulation or AntiVEGF. Mean birth weight for intervention required group was 28.90±2.09 weeks and mean gestation age was 1200±299 grams. Other 10 cases regressed spontaneously without any intervention. All the 43 newborns, who required intervention, had history of oxygen therapy for an average of 10 days. Out of these 43 newborns, 28 had sepsis, 4 had respiratory distress syndrome, and 10 had requirement of blood transfusion

Figure 1- Percentage of risk factors among Retinopathy of prematurity



DISCUSSION

Due to the betterment of healthcare facilities in Paediatric Neonatal ICUs, there is better survival of high-risk newborns and hence increasing ROP incidence. It is one of the major and serious blinding issue in this age group. Severe ROP, if left untreated, leads to permanent visual loss and thus hampers the quality of life of an individual [8]. In India, the incidence of ROP is reported between 24% and 47% [9]. In our study, the incidence of ROP among preterm infants in a tertiary care hospital is 29.5%. In 2004, Gupta et al. (Indian study), reported the incidence of 21.7% [10].

All infants who developed ROP in our study weighed <1,800 gram at birth. The majority of the infants had a birth weight between 1000 & 1499 gram (69%). The second most common range was <1000 gram (18.64%). This low rate of cases less than 1000 gram in the current study could be explained by the inadequate and poor nursery and health care systems for premature infants resulting in greater mortality of infants less than 1000 gram. And also due to the lack of proper education on the necessity of visual examination, parents skip follow up. And lastly, there is a low presentation rate because of our poor referral system.

ROP being a multifactorial disease, poses a necessity to study various risk factors. The most significant risk factors for the development of ROP in our study are low birth weight and low gestational age as also shown in many studies [11, 12]. Shah et al [13] and Fortes at al [14] also had similar results. It is because of the increase susceptibility to oxidative damage due to poorly developed vascularization. In our study, the other significant risk factors were oxygen therapy, sepsis, and blood transfusion [15].

Sepsis causes secretion of endotoxins that effects retinal blood vessels and this may lead to ROP. This significant effect of sepsis on ROP occurrence was also proved by Shah et al. [13], and Vinekar et al [16]. On the other hand, Chaudhari et al. [17] disagree with this significance.

Shah et al [13] and Weinberger et al [18] proved the significant relationship between ROP and oxygen therapy. According to some studies, duration of oxygen therapy > 7 days was a significant risk factor for the development of ROP [13]. But, like Dutta et al. [19], it was insignificant in our study.

Deepak et al. [20] found that the frequency of blood transfusions was an independent risk factor for the development of ROP. This can be explained as, transfused adult RBCs are rich in 2, 3 DPG and adult hemoglobin, which have less affinity for oxygen, thus release excess oxygen to the retinal tissue. While Hirano et al. [21], stated that iron overload is a major culprit in the development of ROP.

Other risk factors including respiratory distress syndrome and intraventricular hemorrhage, showed an insignificant relationship with the occurrence of ROP. Taqui et al., [22] reported the insignificant relation between ROP and intraventricular hemorrhage, but according to them systemic hypoxia results in retinal hypoxia and more need for oxygen therapy and thus there is a significant relationship between the development of ROP and respiratory distress syndrome.

Laser photocoagulation was found to be very effective in regressing ROP. In agreement with Coats et al [1], there was a regression of neovascularization of the retina with regular follow up, following laser photocoagulation, supporting the need for rapid treatment intervention to preserve vision. Laser is now considered more effective and precise than cryotherapy to treat severe forms of ROP [23,24].

Our study outlines the prevalence of pre- and postnatal risk factors for the development of ROP and thus highlights the need to strategize the screening guidelines to better assess the Indian population. Genetic, social, economic, nutritional factors should be the focus of future studies in view of developing incidence of ROP.

What is already known
Prematurity with oxygen administration, sepsis and blood transfusion are risk factors for ROP, no epidemiological data available for North West India
What this study adds
Tertiary centers provide facility for ROP screening but awareness programs and referral service are need to be get stronger to meet the increasing need. Anti- VEGF and laser photocoagulations are effective measures in advanced cases

REFERENCES

1. Coats DK, Aaron MM, Mohamed AH. Involution of retinopathy of prematurity after laser treatment: Factors associated with development of retinal detachment. Am J Ophthalmol 2005; 140:214-22
2. Gilbert C. Retinopathy of prematurity: A global perspective of the epidemics, population of newborns at risk and implications for control. Early Hum Dev 2008;84(2):77-82.
3. Jefferies A. Retinopathy of prematurity: Recommendations for screening. Paediatr Child Health. 2010;15(10):667-74.
4. Hartnett ME, Penn JS. Mechanisms and management of retinopathy of prematurity. N Engl J Med. 2013;368(12):1162–1163.
5. Kim T, Sohn J, Yoon YH. Postnatal risk factors of retinopathy of prematurity. Paediatr Perinat Epidemiol 2004; 18(2);130-4
6. International committee for classification of retinopathy of prematurity. The International classification of retinopathy of prematurity revisited. Arch Ophthalmol 2005; 123(7);991-9
7. Fierson WM; American Academy of Pediatrics Section on Ophthalmology; American Academy of Ophthalmology; American Association for Pediatric Ophthalmology and Strabismus; American Association of Certified Orthoptists. Screening examination of premature infants for retinopathy of prematurity. Pediatrics 2013;131(1):189-95.
8. Shah PK, Prabhu V, Karandikar SS, Ranjan R, Narendran V, Kalpana N. Retinopathy of prematurity: Past, present and future. World J Clin Pediatr. 2016 Feb 8;5(1):35–46.
9. Murthy KR, Murthy PR, Shah DA, Nandan MR, S NH, Benakappa N. Comparison of profile of retinopathy of prematurity in semi urban/rural and urban NICUs in Karnataka, India. Br J Ophthalmol 2013;97(6):687-9.
10. Gupta VP, Dhaliwal U, Sharma R, Gupta P, Rohatgi J. Retinopathy of prematurity risk factors. Indian J Pediatr. 2004;71(10):887-92.

11. Dammann O, Brinkhaus MJ, Bartels DB. Immaturity, perinatal inflammation and retinopathy of prematurity: A multihit hypothesis. Early Hum Dev 2009 May;85(5):325-9.
12. Chattopadhyay MP, Pradhan A, Singh R, Datta S. Incidence and risk factors for retinopathy of prematurity in neonates. Indian Pediatr. 2015 Feb;52(2):157–8.
13. 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(2):169–78.
14. Fortes Filho JB, Eckert GU, Procianoy L, Barros CK, Procianoy RS. Incidence and risk factors for retinopathy of prematurity in very low and in extremely low birth weight infants in a unit-based approach in southern Brazil. Eye (Lond) 2009;23(1):25–30.
15. Rao KA, Purkayastha J, Hazarika M, Chaitra R, Adith KM. Analysis of prenatal and postnatal risk factors of retinopathy of prematurityin a tertiary care hospital in South India. Indian J Ophthalmol 2013;61(11):640-4.
16. Vinekar A, Dogra M, Sangtam T. Retinopathy of prematurity in Asian Indian newborns weighting greater than 1250 gram at birth; ten years data from tertiary care center in a developing country. Indian J Ophthalmol. 2007;55(5):331–6.
17. Chaudhari S, Patwardhan V, Vaidya U. Retinopathy of prematurity in a tertiary care center, incidence, risk factors and outcomes. Indian Pediatr. 2009;46(3):219–24.
18. Weinberger B, Laskin DL, Heck DE. Oxygen toxicity in premature infants. Toxicol Appl Pharmacol. 2002;181(1):60–7.
19. Dutta S, Alaraop S, Narang A. Risk factors of threshold retinopathy of prematurity. Indian Pediatr. 2004;41(7):665–71.
20. Deepak C, Ramesh A, Ashok KD. Retinopathy of prematurity. Indian J Pediatr. 2008;75(1):73–6.
21. Hirano K, Morinobu T, Kirn H. Blood transfusion increases radical promoting non-transferrin bound iron in preterm infants. Arch Dis Child Fetal Neonatal Ed. 2001;84(3):188–93.
22. Taqui AM, Syed R, Chadry TA. Retinopathy of prematurity: Frequency and risk factors in a tertiary care hospital in Karachi, Pakistan. J Pak Med Assoc. 2008;58(4):186–90.
23. Tawse KL, Jeng-Miller KW, Baumal CR. Current practice patterns for treatment of retinopathy of prematurity. Ophthalmic Surg Lasers Imaging Retina 2016;47(5):491–495.
24. Gupta MP, Chan RV, Anzures R, Ostmo S, Jonas K,Chiang MF. Practice patterns in retinopathy of prematurity treatment for disease milder than recommended by guidelines. Am J Ophthalmol 2016;163:1–10.